

***2012 Medical Student Anesthesia
Research Fellowship Symposium***

**Tuesday, October 16, 2012
2:30 – 5:30 PM
West Salon H, Walter E. Washington Convention Center
Washington, DC**

Objective

The Medical Student Anesthesia Research Fellowship (MSARF) program provides support to both medical students and host departments for eight weeks of anesthesia-related research experience and is an element of FAER's commitment to attract scientific talent to academic anesthesiology. The symposium provides an opportunity for MSARF participants to present research findings from their MSARF experience.

Moderator: Paloma Toledo, MD, MPH

Dr. Toledo is a FAER Director and an obstetric anesthesiologist at Northwestern University in Chicago, IL. Following her obstetric anesthesia fellowship, she completed her Master's in Public Health and a postdoctoral fellowship in health services research. Her research interest centers around racial and ethnic disparities in the use of labor analgesia. She is a past-president of the ASA Resident Component and is currently a Director in the Society for Obstetric Anesthesia and Perinatology.

2012 MSARF Symposium Participants

Hasan Ahmad

Host Department: Texas Children's Hospital
Medical School: Edward Via College of Osteopathic Medicine - Virginia Campus
Title of Research Project: The association between perioperative anesthetic agent exposure and brain injury in infants with congenital heart disease – a preliminary analysis

Brenton Alexander

Host Department: University of California Irvine
Medical School: University of California, Irvine
Title of Research Project: Determining the Efficacy of a Novel Anesthesiology Focused Ultrasound Curriculum

Stephen Arndt

Host Department: Ochsner Health System
Medical School: Tulane School Of Medicine
Title of Research Project: A Prospective Study on Inadvertent Perioperative Hypothermia and Development of a Novel Predictive Tool.

Amlan Bhattacharjee

Host Department: Vanderbilt University
Medical School: SUNY Downstate College of Medicine
Title of Research Project: Identification of Non-Routine Events During Pediatric Cardiac Surgery

Keith Carver

Host Department: Medical University of South Carolina
Medical School: Medical University of South Carolina
Title of Research Project: Transcranial Direct Current Stimulation (tDCS) in the Management of Acute Post-Spine Surgery Pain: A Prospective Randomized Controlled Trial

Vida Chen

Host Department: University of Maryland School of Medicine
Medical School: University of Maryland School of Medicine
Title of Research Project: Inhibition by Propofol of Respiration by Mature and Immature Cultured Rat Cortical Neurons

Matthew Chia

Host Department: Northwestern University's Feinberg School of Medicine
Medical School: University of Illinois College of Medicine
Title of Research Project: The Effect of Race/Ethnicity on the Quality of Patient-Physician Communication during Obstetric Analgesic Counseling

Angela Chiang

Host Department: The Johns Hopkins University School of Medicine
Medical School: University of Maryland School of Medicine
Title of Research Project: Choking Child with Goldenhar Syndrome: MedicAlert Foundation National Difficult Airway Registry role in disseminating critical information to first responders and medical institutions

Junghoon Choi

Host Department: SUNY Downstate Medical Center
Medical School: SUNY Downstate Medical Center
Title of Research Project: The effect of a peri-articular injection mixture of ropivacaine, epinephrine, ketorolac, and morphine, in addition to an established multimodal perioperative analgesic regimen for total knee arthroplasty, on postoperative pain and rehabilitation

Benjamin Cobb

Host Department: University of Pittsburgh
Medical School: University of Pittsburgh
Title of Research Project: Efficacy of the Bilateral Ilioinguinal-Iliohypogastric Block with Intrathecal Morphine for Postoperative Cesarean Delivery Analgesia

Daniel Condie

Host Department: UT Southwestern Medical Center at Dallas
Medical School: UT Southwestern Medical Center
Title of Research Project: Estimates of Minimally Important Differences (MIDs) for Four Patient-Reported Outcome Measurement Information System Computer-Adaptive-Tests in Chronic Pain Outpatients

Patricia de Luna

Host Department: BRIGHAM AND WOMEN'S HOSPITAL
Medical School: Dartmouth Medical School
Title of Research Project: Fluid restriction in neurosurgical patients: Does it make a difference?

Mark DeWood

Host Department: Northwestern University's Feinberg School of Medicine
Medical School: University of Cincinnati College of Medicine
Title of Research Project: The use of adenosine-induced flow arrest to facilitate intracranial aneurysm clip ligation does not worsen neurologic outcome

Rachel Douglas

Host Department: The University of Texas MD Anderson Cancer Center
Medical School: Touro College of Osteopathic Medicine - Harlem
Title of Research Project: Increased Activation of STAT3 Signaling Proteins and Astroglia in the Sensorineural Area of the Dorsal Horn After Paclitaxol Exposure

Michael Ernst

Host Department: State University of NY (SUNY) Stony Brook
Medical School: Stony Brook University School of Medicine
Title of Research Project: Effect of Preoperative Mental Health Status on Outcomes Following Minimally Invasive Lumbar Decompression

Charles Fraser

Host Department: Texas Children's Hospital
Medical School: University of Texas Medical School At Houston
Title of Research Project: Inducible blood pressure changes to delineate the frequency limit of the cerebral vascular autoregulatory response

Kevin Friede

Host Department: Duke University Medical Center
Medical School: Duke University School of Medicine
Title of Research Project: MicroRNA-146b attenuates myocardial NF-kB signaling following ischemia-reperfusion: early translation to perioperative cardioprotection

Amanda Gelineau

Host Department: Mount Sinai School of Medicine
Medical School: Tulane University School of Medicine
Title of Research Project: Pain in Laparoscopic vs Open Surgery

Antasia Giebler

Host Department: University of Colorado Denver
Medical School: Midwestern University Arizona College of Osteopathic Medicine
Title of Research Project: Equilibrative nucleoside transporter (ENT)-1-dependent elevation of extracellular adenosine protects the liver during ischemia and reperfusion

Aneesh Goel

Host Department: Vanderbilt University
Medical School: University of Virginia School of Medicine
Title of Research Project: Identification of Postoperative Acute Kidney Injury Following Inpatient Nonrenal Surgery

Sheena Hembrador

Host Department: UCSF Department of Anesthesia
Medical School: University of Michigan Medical School

Title of Research Project: The Effect of Fetal Descent on Pain during the First Stage of Labor

Jason Hsieh

Host Department: Cleveland Clinic

Medical School: Cleveland Clinic Lerner College of Medicine at Case Western Reserve University

Title of Research Project: The Association Between Intraoperative Hypotension and Stroke in General Surgery Patients

Zachary Hudson

Host Department: Emory University

Medical School: Medical College of Georgia, Georgia Health Sciences University

Title of Research Project: Isoflurane enhances the function of alpha9/10 nicotinic acetylcholine receptors

Markus Jackson

Host Department: Stanford University, Dept. of Anesthesia

Medical School: University of Rochester School of Medicine and Dentistry

Title of Research Project: Acupuncture for the Treatment of Cystic Fibrosis in Teenagers and Young Adults

Sonia Jackson

Host Department: University of Alabama at Birmingham

Medical School: Meharry Medical College

Title of Research Project: Inhaled Chlorine Inhibits Locomotion in Mice – Potential Beneficial Effects of Inhaled Local Anesthetics

Benjamin Kwittken

Host Department: Beth Israel Deaconess Medical Center, Boston, MA

Medical School: University of Arizona College of Medicine

Title of Research Project: Assessing lower extremity perfusion following percutaneous revascularization using tissue oxygen monitoring.

Tomas Lazo

Host Department: Stanford University, Dept. of Anesthesia

Medical School: SUNY Stony Brook School of Medicine

Title of Research Project: Hypothermia after Cesarean Delivery: Incidence, predictors, and associated adverse outcomes

Cheng-ting Lee

Host Department: Massachusetts General Hospital

Medical School: University of Texas Southwestern Medical Center

Title of Research Project: Drug Abuse Patterns in Pain Subjects on Opioid Therapy

Rosie Li

Host Department: Columbia University

Medical School: University of Colorado School of Medicine

Title of Research Project: Midazolam Induces Tau Hyperphosphorylation Under Normothermic Conditions In Vivo and In Vitro

Andrew Lohse

Host Department: Regents of the University of Michigan

Medical School: University of Michigan
Title of Research Project: The Impact of Centralized Pain on the Analgesic Response to First Diagnostic Medial Branch Block

Shu Lu

Host Department: University of Pittsburgh
Medical School: University of Pittsburgh Medical School
Title of Research Project: Rocking Stored Blood during Acute Normovolemic Hemodilution Impairs Clotting Dynamic and Platelet function

Michelle Mahanian

Host Department: Mount Sinai School of Medicine
Medical School: UCLA David Geffen School of Medicine
Title of Research Project: Predictors of postoperative delirium in non-cardiac surgery patients

Alex McGaughy

Host Department: Medical University of South Carolina
Medical School: Medical University of South Carolina
Title of Research Project: Isoflurane Reduces Lifespan and Impairs Development in *C. elegans*

Joanna Miller

Host Department: SUNY Downstate Medical Center
Medical School: New York University School of Medicine
Title of Research Project: Incidence of perioperative dysglycemia in patients with chronic kidney disease undergoing ambulatory surgery

Leela Mirafzali

Host Department: Regents of the University of Michigan
Medical School: University of Michigan Medical School
Title of Research Project: High Risk of Obstructive Sleep Apnea is Associated With Increased Perioperative Pain

Rochelle Molitor

Host Department: Mayo Clinic Rochester
Medical School: Mayo Medical School
Title of Research Project: The Association of Preoperative Heat-Pain Threshold and Tolerance as Determined by Quantitative Sensory Testing on Pain Scores and Postoperative Analgesic Consumption in Patients Undergoing Primary Total Knee Arthroplasty

Niti Patel

Host Department: Massachusetts General Hospital
Medical School: Rush University
Title of Research Project: Identification of subjects with endothelial dysfunction for a human volunteer study of stored blood autotransfusion with inhaled nitric oxide administration

Cameron Rice

Host Department: UCLA
Medical School: Saint Louis University School of Medicine
Title of Research Project: Sympathetic Innervation of the Ventricular Walls by the Right and Left Stellate Ganglia

Giulia Rosanova

Host Department: University of Pennsylvania School of Medicine

Medical School: University of Maryland

Title of Research Project: A pharmacokinetic approach to rapid titration of propofol in a drug induced sleep endoscopy for anatomic diagnosis of sleep apnea

David Rotstein

Host Department: Montefiore Medical Center The University Hospital for the Albert Einstein College of Medicine

Medical School: UMDNJ- Robert Wood Johnson Medical School

Title of Research Project: A randomized controlled trial evaluating the effectiveness of regional vs local anesthetic technique in creating AV fistulae for dialysis

Courtney Schilling-Mechling

Host Department: The Children's Hospital of Philadelphia

Medical School: Drexel University College of Medicine

Title of Research Project: Obesity and Pediatric Heart Disease in the Kids Inpatient Database: Does obesity affect length of stay and cost of care for children with heart disease undergoing non-cardiac surgery?

Kiely Schultz

Host Department: University of Colorado Denver

Medical School: University of New England College of Osteopathic Medicine

Title of Research Project: Protective Characteristics of Critically Ill Patients against the Development of Delirium

Kinza Sentissi

Host Department: Beth Israel Deaconess Medical Center, Boston, MA

Medical School: Tufts Medical School, Boston MA

Title of Research Project: The use of endoscopic ultrasound to measure cardiac function and parameters.

Janki Shah

Host Department: UMDNJ/New Jersey Medical School

Medical School: UMDNJ/New Jersey Medical School

Title of Research Project: The Effect of Gabapentin on Postoperative Orthopedic Pain and Sleep: A Randomized, Double-Blind, Placebo-Controlled Trial

Andrew Smith

Host Department: Columbia University

Medical School: SUNY Stony Brook School of Medicine

Title of Research Project: Isoflurane induces interleukin-11 via ERK MAPK in human endothelial cells

Kathryn Steckelberg

Host Department: Mayo Clinic Rochester

Medical School: Mayo Medical School

Title of Research Project: Characterization of Use Patterns and Complications associated with Brachial Arterial Catheterization

Steven Vanhoy

Host Department: University of Utah

Medical School: The University of Arizona - Phoenix

Title of Research Project: Rescue Echocardiography Findings are Different Based on Patient Setting.

Alisa Vitkus

Host Department: University of Rochester

Medical School: University at Buffalo Medical School

Title of Research Project: The Effects of Tau on Nrf2 Activity

Deva Wells

Host Department: University of Washington

Medical School: University of Washington School of Medicine

Title of Research Project: Patterns of injury and liability in neurosurgical anesthesia: A closed claims analysis

John Williams

Host Department: Oregon Health & Science University

Medical School: Oregon Health & Science University

Title of Research Project: Patient and Family Centered Care in Pediatric Sedation

Britanny Winckler

Host Department: University of California Irvine

Medical School: University of California, Irvine

Title of Research Project: Behavioral Recovery after Tonsillectomy and Adenoidectomy: The Proximal-Distal Model

Valerie Wong

Host Department: State University of NY (SUNY) Stony Brook

Medical School: Stony Brook University School of Medicine

Title of Research Project: Penile Tumescence as a Measure of Caudal Block Efficacy

Tian Xia

Host Department: UMDNJ/NEW JERSEY MEDICAL SCHOOL

Medical School: NEW JERSEY MEDICAL SCHOOL -UMDNJ

Title of Research Project: A Prospective Study to Establish a Correlation between Infusion Rate of Propofol and Bispectral Index in Patients Receiving Total Intravenous Anesthesia

Katie Yang

Host Department: Duke University Medical Center

Medical School: Duke University School of Medicine

Title of Research Project: Memantine for Postoperative Analgesia Following Radical Retropubic Prostatectomy

David Zacharias

Host Department: BRIGHAM AND WOMEN'S HOSPITAL

Medical School: Mayo Medical School

Title of Research Project: Clinical assessment and utility of near-infrared cerebral oximetry in cardiac surgery

MSARF Symposium Poster Presentations

Student Name: Hasan Ahmad

Host Department: Texas Children's Hospital

Primary Mentor Name: R. Blaine Easley, MD

Additional Mentor(s): Dean Andropoulos, MD, MHCM

Title of Research Project: *The association between perioperative anesthetic agent exposure and brain injury in infants with congenital heart disease – a preliminary analysis*

Background: Anesthetic neurotoxicity is a growing concern for infants who require general anesthetic. Children undergoing congenital heart surgery require recurrent, prolonged anesthetic exposure, possibly influencing their multifactorial neurodevelopmental delay. We hypothesized an association between anesthetic exposure and neurodevelopmental score.

Methods: In this pilot study, we did a retrospective analysis of prospectively collected data containing MRI results and Bayley III neurodevelopmental scores of children who had corrective heart surgery as infants. Fifty-nine children had perioperative MRI results, and their exposures to intravenous (IAA) and volatile (VAA) anesthetic agents were quantified from operating room and ICU records. Patients were categorized as injured or uninjured from MRI results. Age-adjusted minimum alveolar concentration (MAC)-hours were calculated using end-tidal concentrations. We performed univariate analyses to examine relationships between VAA, MRI injury, ICU and hospital length of stay (LOS), and 12-month neurodevelopmental scores.

Results: MRI injury was present in 66% of patients. MAC-hour and IAA exposure were similar between injured and uninjured patients. ICU LOS was associated with increased IAA for both groups. ICU LOS was associated with poor cognitive ($p=0.04$) and language ($p=0.03$) scores in uninjured patients. VAA was associated with poor cognitive ($p=0.0006$) and motor ($p=0.01$) scores in injured patients.

Conclusion: Patients without MRI-detectable brain lesions had a greater association between ICU LOS and developmental delay than IAA and developmental delay. Patients with MRI-detectable lesions showed an association between VAA exposure and developmental delay. To study VAA effects in this population, sufficient sample size must account for MRI-detectable brain injury and ICU LOS.

Student Name: Brenton Alexander

Host Department: University of California Irvine

Primary Mentor Name: Dr. Davinder Ramsingh

Additional Mentor(s): Dr. Joseph Rinehart; Dr. Maxime Cannesson

Title of Research Project: *Determining the Efficacy of a Novel Anesthesiology Focused Ultrasound Curriculum*

Introduction: In the past decade, ultrasound has emerged as a strong diagnosis and point of care assessment tool in a wide variety of medical specialties and sub-specialties. Anesthesiology is no exception. From pre-op clearances through intraoperative interventions and, ultimately, post op evaluations, ultrasonography has shown its utility and is staged to be incorporated in much more significant way into the anesthesiologists' tool belt throughout the next few years. Our novel educational approach and verification of such an approach, using model-based and written examinations, is described here.

Materials and Methods: Six attending anesthesiologists at the University of California, Irvine Medical Center were educated and evaluated. A 53 question written examination and a 26 question model examination

were performed before and after one hour of an interactive, one-on-one, model based education session. The curriculum simultaneously combined a clinically directed model based session with a more traditional PowerPoint presentation and summative handouts. The specific focus of this curriculum was cardiopulmonary function, volume status, and evaluation of severe thoracic/abdominal pathologies. Post-examinations were administered between 7 and 21 days after the education session. Non parametric Mann Whitney tests were performed and p values of less than 0.05 were considered significant.

Results: Average scores on the pre-education written tests (Mean \pm SD) and pre-education model examinations (Mean \pm SD) were significantly lower than post-education written tests (Mean \pm SD) and post-education model examinations (Mean \pm SD) ($p=$ ____). Due to the small sample size (secondary to scheduling difficulties), data was determined to be non parametric and therefore the Mann Whitney U test was used for statistical purposes.

Discussion: In order for point of care ultrasonography to become increasingly incorporated into the skill set of anesthesiologists, an effective approach for the education of current physicians must be designed and tested. We have shown that one acceptable approach is utilizing an interactive, model based education session. As ultrasound education progresses we hope this approach will be utilized in order to allow for cost effective training of the time restricted anesthesiologist.

Student Name: Stephen Arndt

Host Department: Ochsner Health System

Primary Mentor Name: Bobby D Nossaman, MD

Additional Mentor(s): David M Broussard, MD, MBA; Armin Schubert, MD, MBA

Title of Research Project: *A Prospective Study on Inadvertent Perioperative Hypothermia and Development of a Novel Predictive Tool.*

Introduction: In spite of active intervention, inadvertent perioperative hypothermia (iPH) continues to occur. We report the development of a new statistical tool, the Predictive PACU Temperature Tool ([PT]2) to assist anesthesiologists in providing proactive thermal therapy. We also investigated the role of iPH in adverse events in the PACU.

Methods: After receiving IRB approval, perioperative data and adverse events were collected on 780 patients undergoing elective or emergency surgery excluding obstetric and minor same day surgical procedures in a four-month period. Statistical analysis for predictors of PH, adverse PACU events, and mathematical construction of a patient profiler, [PT]2, were executed with the computer program, JMP® (SAS Inc., Gary, IN).

Results: Multivariate analysis associated Age (F-ratio = 11.7, $P = 0.0007$), Type of Anesthesia (F-ratio = 8.1, $P = 0.0003$), Magnitude of Surgery (F-ratio = 3.9, $P = 0.021$), and Total IV Fluids (F-ratio = 7.9, $P = 0.005$) with iPH. iPH was not statistically associated with adverse events in the PACU. These data allowed construction of a dynamic tool [PT]2 to provide anesthesiologists a means to predict PACU admission temperature to within 0.4oF and institute proactive thermal therapy.

Conclusions: As iPH continues to occur and is difficult to predict, the [PT]2 can allow the anesthesiologist to proactively institute corrective action. Finally, associations were found between perioperative variables and iPH, although iPH was not statistically associated with the measured adverse events in the PACU.

Student Name: Amlan Bhattacharjee

Host Department: Vanderbilt University

Primary Mentor Name: Shilo Anders, PhD

Additional Mentor(s): Scott Watkins, MD; Matthew Weinger, MD; Jesse Ehrenfeld, MD, MPH

Title of Research Project: *Identification of Non-Routine Events During Pediatric Cardiac Surgery*

The operating room (OR) is a complex, dynamic work environment that requires seamless integration of a large array of expert clinicians and complicated high-tech instrumentation. We used the construct of non-routine events (NREs) —“any event that is perceived by care providers or skilled observers to be unusual, out-of-the-ordinary, or atypical” —to identify potential areas for improvement. NREs encompass adverse events, medical errors, and near-misses, and can more generally paint a fuller picture of flaws in process and not just outcome (Weinger 2002).

Previous studies on adult patients at Vanderbilt have revealed NREs in over 30% of OR cases. In this preliminary study, we examined pediatric cardiac procedures because they are particularly complex, and high rates of NREs were expected. After obtaining consent, three video views and audio recordings were captured of selected pediatric cardiac procedures at Vanderbilt Children’s Hospital, and a preliminary NRE list was catalogued during each surgery. Systematic identification and confirmation of NREs by expert clinician video review is ongoing.

Preliminary data analysis revealed that every case had at least one NRE, confirming that pediatric cardiac cases are more NRE-prone than general adult cases. A total of 8 cases were recorded, with a mean patient age of 761 days and a mean procedure time of 7:28 h. Number of NREs ranged from 1 to 11, with a mean of 4. Future directions include more rigorous operationalization of NREs to a pediatric context and using more quantitative methods to predict patient outcomes.

Student Name: Keith Carver

Host Department: Medical University of South Carolina

Primary Mentor Name: Scott Reeves, MD

Additional Mentor(s): Jeffrey J. Borckardt, PhD; John Glaser, MD; Mark S. George, MD

Title of Research Project: *Transcranial Direct Current Stimulation (tDCS) in the Management of Acute Post-Spine Surgery Pain: A Prospective Randomized Controlled Trial*

Background: Transcranial direct current stimulation (tDCS) has shown promise in decreasing post-operative pain. The purpose of this study is to assess the effectiveness of tDCS on subjective pain-ratings and PCA opioid usage among patients receiving spinal fusion surgery.

Methods: Sixteen patients who underwent lumbar spinal fusion surgery completed the study. Pain inventories were collected at the time of admission and discharge from the hospital. After surgery, participants were randomly assigned to receive 4 20-minute sessions of real or sham tDCS. PCA hydromorphone usage was tracked and pain ratings were collected via visual analogue scales twice per day.

Results: Participants who received real tDCS used an average of 9.04 mg of hydromorphone and subjects receiving sham tDCS used an average of 11.13 mg (ns). However, using estimated marginal means to correct for a pre-operative pain difference detected between groups (higher pre-op pain in the real tDCS group), sham tDCS was associated with significantly increased PCA hydromorphone usage (mean 13.63 mg) compared to real tDCS (mean 6.53 mg, $p=0.037$). VAS scores from admission to discharge indicated a greater percent increase in pain at its worst for the sham group ($\pm 9.68\%$) compared to the real group ($\pm 1.51\%$), and a greater percent decrease in pain at its least for the real group ($\pm 33.23\%$) compared to the sham group ($\pm 13.33\%$).

Conclusions: These preliminary findings indicate that tDCS may significantly decrease post-operative hydromorphone usage and improve pain ratings among lumbar spinal fusion patients.

Student Name: Vida Chen

Host Department: University of Maryland School of Medicine

Primary Mentor Name: Gary Fiskum, PhD

Title of Research Project: *Inhibition by Propofol of Respiration by Mature and Immature Cultured Rat Cortical Neurons*

Background: Propofol can exhibit neurotoxicity, possibly through inhibition of mitochondrial respiration. In adults, propofol sedates brain activity by stimulating receptors for the inhibitory neurotransmitter GABA. In contrast, GABA receptor activation in the immature brain results in neuronal excitation and possibly neurotoxicity.

Specific Objectives: We tested the hypothesis that propofol exhibits dose-dependent inhibition of respiration by primary cultures of rat cortical neurons at days in vitro associated with either inhibitory or excitatory GABA receptor activity.

Methods: Oxygen consumption by mature (DIV12) and immature (DIV4) cortical neurons in the presence of artificial CSF plus 5 mM glucose was measured using cell respirometry. Rates included basal oxygen consumption rate (OCR) and the maximal OCR following addition of respiratory uncoupler FCCP and then pyruvate. Maximal OCR were obtained at both 1.5 hours and 6.5 hours after exposure to propofol or drug vehicle.

Results: Exposure of either DIV4 or DIV12 neurons to propofol at concentrations from 10 to 1,000 μ M for 1.5 hours had no effect on either baseline or maximal OCR. In contrast, exposure to propofol for 6.5 hours resulted in partial inhibition at 250 μ M and complete inhibition at 500 to 1,000 μ M. However, this inhibition was the result of massive cell death.

Conclusions: Acute exposure of cultured cortical neurons to propofol at even suprapharmacologic levels does not impair cellular respiration. Prolonged exposure to propofol at extremely high concentrations inhibits oxygen consumption due to cell death. These results do not support the hypothesis that propofol directly inhibits mitochondrial respiration at clinically-relevant concentrations.

Student Name: Matthew Chia

Host Department: Northwestern University's Feinberg School of Medicine

Primary Mentor Name: Paloma Toledo, MD, MPH

Title of Research Project: *The Effect of Race/Ethnicity on the Quality of Patient-Physician Communication during Obstetric Analgesic Counseling*

Introduction: A racial/ethnic disparity exists in the use of neuraxial labor analgesia. Patient-physician communication may be one possible origin of this disparity. The objective of this study was to examine the quality of patient-physician communication during the pre-anesthetic assessment and analgesic counseling session.

Methods: English-speaking Hispanic and white nulliparous patients were recruited upon admission to the Labor and Delivery unit. Their analgesic counseling session was audio-recorded, after which patients completed a demographics questionnaire and the interpersonal processes of care survey (IPC-18), a validated tool for evaluating patient-physician communication. A summary score (0-100) for counseling thoroughness

was calculated. Results were analyzed using the chi-square statistic and Wilcoxon rank-sum test. $P < 0.05$ was significant.

Results: Thirty-seven patients were interviewed (8 Hispanic, 29 white). The total time spent with patients did not differ by race/ethnicity. However, anesthesiologists spoke fewer utterances (median of 42 vs. 68, $P < 0.05$), for longer durations per utterance (median of 10.1s vs. 6.6s, $P < 0.001$), and had higher counseling thoroughness scores ($P = 0.03$) when speaking with Hispanic patients. Hispanic patients were more likely to report that the communication lacked clarity ($P = 0.03$), and that the physician did not work with them towards a decision ($P < 0.001$).

Conclusion: These results suggest that anesthesiologists communicate differently with Hispanic versus white patients. Although anesthesiologists were more thorough in their discussions with Hispanic patients, the resulting communication lacked clarity. Interventions to improve clarity of communications, and to reduce resulting racial/ethnic disparities should be evaluated.

Student Name: Angela Chiang

Host Department: The Johns Hopkins University School of Medicine

Primary Mentor Name: Lynette Mark, MD

Additional Mentor(s): Sarah Wyhs, MD; Kim Cover, MD; Deborah Schwengel, MD; Stacey L. Ishman, MD, MPH; Renee Cover, RN, BSN

Title of Research Project: *Choking Child with Goldenhar Syndrome: MedicAlert Foundation National Difficult Airway Registry role in disseminating critical information to first responders and medical institutions*

Emergency Medical Services (EMS) responded to a call: "2-year-old female choking on a foreign object." Upon arrival, the child's guardian was performing CPR and identified that the child had Goldenhar syndrome, followed by a nearby academic medical center.

EMS oral inspection was negative for foreign bodies. Bag-valve-mask (BVM) ventilation was initiated. The child was orally intubated, with bilateral breath sounds and capnometry measurement of 24 mmHg. Upon arrival to our emergency department, the child remained in full arrest. She had characteristic features of Goldenhar including dysmorphic head, micrognathia, and severely limited neck extension. The end-tidal CO₂ was 6 mmHg. The endotracheal tube was removed. BVM ventilation resulted in chest rise and improved O₂ saturations. She had spontaneous return of circulation. Our Difficult Airway Response Team (DART) was activated. The responding pediatric otolaryngologist unsuccessfully attempted rigid laryngoscopy. The patient was transported to the operating room with BVM ventilation. A laryngeal mask airway (LMA) was placed. A nasotracheal intubation was performed by passing a fiberoptic bronchoscope around the LMA. The LMA was withdrawn and the identified foreign body removed from the glottic aperture. Unfortunately, the patient suffered hypoxia during resuscitation efforts with resultant brain death.

Events review identified areas for process improvement including: (1) Collaborating with the primary medical center for identification of pediatric difficult airway patients and education of their families; (2) Developing a "Fast Facts" pediatric difficult airway reference for EMS; (3) Selective triage into the MedicAlert Difficult Airway Registry for 24/7 emergency access to critical airway information.

Student Name: Junghoon Choi

Host Department: SUNY Downstate Medical Center

Primary Mentor Name: Dennis Dimaculangan, MD

Additional Mentor(s): Joshua Mollov, MD; Rebecca Twersky, MD; Ms. Noelle Best, N.P.

Title of Research Project: *The effect of a peri-articular injection mixture of ropivacaine, epinephrine, ketorolac, and morphine, in addition to an established multimodal perioperative analgesic regimen for total knee arthroplasty, on postoperative pain and rehabilitation*

Introduction: Total knee arthroplasty (TKA) is a very painful operation. At SUNY Downstate a multimodal strategy is used to minimize pain and opioid-associated side effects. Peri-articular (PA) injection of local anesthetics has been shown to decrease opioid consumption and post-operative pain after TKA. Thus, we have designed this study to assess the effectiveness of PA injection when used in addition to our multimodal approach.

Methods: This is a one center, prospective, placebo-controlled, double blind study. Participating patients were randomized to receive either a PA injection administered during wound closure of either saline or a mixture containing ropivacaine, epinephrine, ketorolac, and morphine sulfate. Postoperative consumption of morphine, visual analog scores (VAS) and knee flexion range of motion (ROM) were used as outcome measures.

Results: Currently, 36 patients completed the study (treatment group n = 19; control group n = 17). Mean morphine consumption at 4 hours after surgery was significantly less in the treatment group compared to the control group (p = 0.0021) as well as for the first 24 hours postop (p = 0.0615). The mean VAS at 4 hours was also lower. Finally, the treatment group appeared to have a better response to PT in the ROM test 2 days after the surgery (p = 0.0177).

Discussion: Our preliminary data indicate that the addition of a PA injection led to significant decreases in opioid consumption and pain scores for the first day after TKA. The treatment group also appeared to have a better response to physical therapy.

Student Name: Benjamin Cobb

Host Department: University of Pittsburgh

Primary Mentor Name: Manuel Vallejo, MD DMD

Title of Research Project: *Efficacy of the Bilateral Ilioinguinal-Iliohypogastric Block with Intrathecal Morphine for Postoperative Cesarean Delivery Analgesia*

The ilioinguinal and iliohypogastric (IIH) block can be used as part of a multimodal analgesic regimen for postoperative pain in patients undergoing lower abdominal and inguinal surgeries, including cesarean delivery (CD). Real-time ultrasound (US) guidance allows for direct visualization of the needle and deposition of local anesthetic in proximity to the nerves, which compared to the blind technique can increase block success rate, require less local anesthetic, and reduce complications. In patients undergoing elective CD with spinal anesthesia, intrathecal morphine (ITM) is administered to provide postoperative analgesia for up to 24 hours. We hypothesize that the bilateral IIH block will not reduce postoperative pain, nausea, or emesis for up to 48 hours in parturients undergoing a CD under spinal anesthesia with ITM. Participants were randomly assigned to 1 of 3 treatment groups: A) bilateral IIH Block, B) ipsilateral IIH block and contralateral IIH placebo block, and C) bilateral placebo block. US was used for all blocks. No differences were noted with respect to postoperative analgesic requirements and medications needed for treatment of nausea, emesis, or pruritus. No differences were noted between pain and nausea scores or patient satisfaction for 48 hours post CD. Median pain scores showed no differences between pain and nausea during the measured time periods from PACU to 48 hours post-CD (P > 0.05). We found that the IIH block with ITM does not improve

postoperative analgesia nor decrease opioid side effects such as nausea, vomiting, and pruritus for 48 hours post CD.

Student Name: Daniel Condie

Host Department: UT Southwestern Medical Center at Dallas

Primary Mentor Name: Carl Noe, MD

Additional Mentor(s): Eric Swanholm, PhD

Title of Research Project: *Estimates of Minimally Important Differences (MIDs) for Four Patient-Reported Outcome Measurement Information System Computer-Adaptive-Tests in Chronic Pain Outpatients*

Objective: We combined anchor- and distribution-based methods to evaluate responsiveness and establish minimally important differences (MIDs) for four Patient-Reported Outcomes Measurement Information System (PROMIS) measures in a chronic pain population.

Design: Participants undergoing a Behavioral Medicine Evaluation in an Interdisciplinary Pain Management clinic completed the computer adaptive test (CAT) version of four PROMIS and multiple clinical anchor measures. Participants completed three performance-based measures, which were collected by a physical therapist and incorporated as potential anchors. Three a priori criteria were used to select usable cross-sectional anchor-based MID estimates. For each PROMIS measure, the mean standard error of measurement was calculated and incorporated into MID analyses. The focus of this analysis was on the Item-Response Theory-based T-scores for the selected PROMIS CATs.

Results: Many cross-sectional T-score anchor-based MID estimates (56%) were excluded due to failure to meet a priori criteria. Based on analyses, the following T-score MID ranges are recommended: Pain Behavior CAT (2.0 – 3.5), Pain Interference (4.0 – 6.5), Physical Functioning (4.0 – 6.0), and Fatigue (3.0 – 5.0). The average effect sizes for MID estimates ranged from 0.37 – 0.71.

Conclusions: This study is among the first to address MIDs for PROMIS measures; it represents the first study to establish usable MIDs for outpatients with chronic or persistent pain. The inclusion of objectively-measured performance data adds another dimension of clinical reliability to the MID estimates. Results may be used to gauge minimally important clinical difference and/or treatment response for individuals within this patient population.

Student Name: Patricia de Luna

Host Department: Brigham and Women's Hospital

Primary Mentor Name: Linda Aglio, MD, MS

Additional Mentor(s): Sam Jiang, Jie Zhou, MD, MS, MBA, Raymond Huang, MD, PhD, Srinivasan Mukundan Jr., MD, PhD

Title of Research Project: *Fluid restriction in neurosurgical patients: Does it make a difference?*

Introduction: Hemodynamic stability and maintenance of cerebral perfusion pressure are crucial for managing patients with intracranial pathology. While decreased intravascular volume is easily corrected, excessive and even normal fluid replacement may result in brain swelling and longer hospital stays.

Methods: With IRB approval, we studied 22 neurosurgical patients undergoing tumor resection; 9 patients given <3ml/kg/hr of fluid; 13 patients given >3ml/kg/hr of crystalloid. Stroke volume variation (SVV) was acquired to assess fluid status/responsiveness. Arterial blood gases, a basic metabolic panel, serum lactic acid/osmolality and urine sodium/osmolality were obtained at the beginning, middle and end of each case.

Pre/post-operative white/gray apparent diffusion coefficient (ADC) and ventricular volume using T1, T2 and MRI pulse sequences MPRAGE/SPGR were calculated to assess cerebral edema.

Results: Average fluid load was 1.60ml/kg/hr for the <3ml/kg/hr cohort; 6.24 ml/kg/hr for the >3ml/kg/hr cohort ($p<0.0005$). No significant differences existed for lactic acid, serum/urine osmolality and urine Na values at all time points. Early Na was higher in the <3ml/kg/hr group (137.3 vs 133.6 $p=0.038$). Average case SVV was 14.89 in the <3ml/kg/hr group; 11.86 in the >3ml/kg/hr group ($p=0.28$). There were no significant pre/post-operative differences in gray/white ADC or ventricular volume on T1/T2/MPRAGE/SPGR images. Subset analysis of severe fluid restriction (<1ml/kg/hr vs >5ml/kg/hr) showed significant differences in saturation levels: mid-case O₂/PO₂, late-case urine BUN, creatinine, O₂/PO₂.

Conclusion: There appears to be no significant difference between intra-operative laboratory values and radiological outcomes of varying levels of fluid replacement. Subset analysis indicates tighter fluid restriction might have significant outcomes.

Student Name: Mark DeWood

Host Department: Northwestern University's Feinberg School of Medicine

Primary Mentor Name: Dhanesh K. Gupta, MD

Additional Mentor(s): Laura B. Hemmer, MD

Title of Research Project: *The use of adenosine-induced flow arrest to facilitate intracranial aneurysm clip ligation does not worsen neurologic outcome*

Background: Although the use of adenosine-induced flow arrest to facilitate intracranial aneurysm clip ligation has become more common, its effects on neurologic outcome have not been reported.

Objective: We hypothesized that adenosine-induced flow arrest would not worsen neurologic outcome after aneurysm clip ligation.

Methods: After IRB approval, univariate analysis ($P<0.15$) was used to identify perioperative variables to test in logistic regression models to predict poor neurologic outcome. Poor neurologic function 48 hours after surgery, as measured by a score >2 on the modified Rankin scale (mRs), was the primary outcome. Secondary outcomes were the neurologic outcome at hospital discharge and the occurrence of cardiac arrhythmias or myocardial ischemia in the initial 48 hours after surgery.

RESULTS: Between 05/2006-06/2012, adenosine-induced flow arrest was used in 72 of 413 patients who underwent intracranial aneurysm clip ligation. Adenosine did not predict poor neurological outcome at 48 hours after surgery ($P=0.524$), neurological outcome at discharge (0.741), or cardiac morbidity in the initial 48 hours after surgery (arrhythmia $P=0.155$, myocardial ischemia $P=0.898$). Sex (OR 1.9), age (OR 1.1), aneurysm size (OR 2.2), Hunt & Hess classification (OR 1.8), and the use of temporary arterial occlusion (OR 1.8) predicted poor neurological outcome at 48 hours after surgery.

Conclusion: When used to facilitate aneurysm clip ligation, adenosine-induced flow arrest was not associated with increased postoperative neurologic/cardiac morbidity. The use of adenosine for this indication is a safe option.

Student Name: Rachel Douglas

Host Department: The University of Texas MD Anderson Cancer Center

Primary Mentor Name: Dr. Patrick Dougherty

Additional Mentor(s): Dr. Haijun Zhang

Title of Research Project: *Increased Activation of STAT3 Signaling Proteins and Astroglia in the Sensorineural Area of the Dorsal Horn After Paclitaxol Exposure*

Paclitaxel is one of the most commonly utilized chemotherapeutic agents. However, taxol treatment can lead to sensory dysfunction beginning three days after administration and, after three or four treatments, the effects can last from months to years. Better understanding of the cellular signaling involved holds promise for preventive drug development. Research shows that after taxol exposure there is subsequent astrocyte activation. Astrocyte activation is known to lead to cytokine production that disrupts adherens junctions. This permits leukocyte entry into the CNS and resultant neuroinflammation. Research suggests that the Jak-STAT system plays a role in astrocyte activation in the dorsal horn post sciatic nerve lesion. However, the upstream signaling that leads to astrocyte activation post-taxol exposure is unknown. In this project, we used confocal microscopy to investigate the mean fluorescent intensity and colocalization of STAT3, and its downstream phosphorylated proteins, in relation to astrocytes within the dorsal horn of taxol treated rats. We found a statistically significant increase in mean intensity of GFAP, STAT3, STAT3p705, and STAT3p705 in the dorsal horn of rats on day 3 and day 14 of paclitaxol treated rats as compared to vehicle ($p < 0.001$). We are currently analyzing more taxol treated rats at a greater range of dates. We are also using a STAT3 inhibitor to assess for any changes in GFAP mean fluorescence. For comparison, the lab is currently replicating this experiment in rats with spinal nerve lesion.

Student Name: Michael Ernst

Host Department: State University of NY (SUNY) Stony Brook

Primary Mentor Name: Brian Durkin, DO

Additional Mentor(s): Jin Bae, MHS; Jamie Romeiser, MPH; Helene Benveniste, MD, PhD

Title of Research Project: *Effect of Preoperative Mental Health Status on Outcomes Following Minimally Invasive Lumbar Decompression*

Introduction: Preoperative mental health status has been shown to be predictive of pain and functional outcomes following spine surgery. We investigated the effect of patient's pre-operative depression and fatigue on pain and functional outcomes following minimally invasive lumbar decompression (MILD).

Methods: Data was collected from 50 patients under an IRB-approved QA Program and NIH-PROMIS questionnaires were given (to assess fatigue and depression) pre-operatively and at 1, 3, and 6 months post-MILD. The Numeric Rating Scale (NRS) and Oswestry Disability Index data were collected concurrently to assess pain and physical function, respectively. Success of MILD was defined as >2 -point reduction in NRS or $>20\%$ improvement in ODI.

Results: Pre-operative fatigue was significantly lower for MILD patients with improved NRS pain at 1-month ($p=0.0045$) and trended to be lower at 3-months ($p=0.087$) post-operatively than for those who did not. MILD patients who did not improve scored $59 \pm 8\%$ indicating worse than average fatigue compared to the general US population. Pre-operative depression was higher for patients who did not improve ($NRS < 2$) than for those who did ($p=0.047$) at 6-months post-MILD. Neither fatigue nor depression influenced functional outcomes.

Conclusion: PROMIS was used to assess the mental health of patients before and after MILD. Our results strongly suggest that higher levels of pre-operative fatigue may be associated with higher risk of no pain improvement after MILD. Similarly, pre-operative depression may impact pain outcomes. Fatigue and

depression have profound impact on social health, cognition and pain and need more investigation in MILD outcomes.

Student Name: Charles Fraser

Host Department: Texas Children's Hospital

Primary Mentor Name: Ken Brady, MD

Additional Mentor(s): R. Blaine Easley, MD

Title of Research Project: *Inducible blood pressure changes to delineate the frequency limit of the cerebral vascular autoregulatory response*

Background: We proposed a novel method to monitor cerebrovascular autoregulation that requires arterial blood pressure (ABP) oscillations induced by sinusoidal positive end-expiratory pressure (PEEP) modulation. Because the frequency-response of pressure autoregulation is undefined, the optimal frequency of PEEP modulation for measuring autoregulation is unknown. We hypothesized a frequency limit to autoregulation and delineated the highest frequency ABP oscillation that induces cerebrovascular reactivity.

Methods: Neonatal swine (n=8) were anesthetized using constant minute ventilation while PEEP was modulated between 6 and 0.75 cycles per minute (cpm). The animals were hemorrhaged until ABP was below the lower limit of autoregulation (LLA) and PEEP modulations were repeated. Vascular reactivity was quantified at each frequency as the phase angle difference between ABP and intracranial pressure (ICP) above and below LLA.

Results: ABP-ICP phase shift at frequencies > 2 cpm were small with no ability to differentiate cerebrovascular reactivity above from below LLA. At frequencies < 2 cpm, ABP and ICP showed phase shift when measured above LLA, and no phase shift when measured below LLA (above vs. below LLA at 1cpm: $156 \pm 17^\circ$ vs. $38 \pm 26^\circ$; $p < 0.001$ by two-way ANOVA for both frequency and state of autoregulation). Data taken above LLA fit a Butterworth high-pass filter model with a cutoff frequency at 1.8 cpm (95% C.I. 1.5-2.2).

Conclusion: Cerebrovascular reactivity occurs to sustained ABP changes lasting 30 seconds or longer. The ability to distinguish intact and impaired autoregulation was maximized by a 60-second wave (1 cpm), which was 100% sensitive and 100% specific in this model.

Student Name: Kevin Friede

Host Department: Duke University Medical Center

Primary Mentor Name: ihai Podgoreanu, MD

Additional Mentor(s): Michael P. Smith, MS; Zhiquan Zhang, PhD; Qing Ma, MD

Title of Research Project: *MicroRNA-146b attenuates myocardial NF- κ B signaling following ischemia-reperfusion: early translation to perioperative cardioprotection*

Introduction: MicroRNAs (miRs) are an abundant class of endogenous non-coding RNAs implicated in cardiac pathology but poorly understood in myocardial ischemia/reperfusion (I/R) injury. We prioritized miRs differentially regulated in I/R, conducted in vitro functional analysis of miR-146b in cardiomyocytes subjected to simulated I/R, and compared chemical- and nanoparticle-mediated transfection of miR modulators.

Methods: 1) Differentially regulated miR subtypes were identified in myocardial tissues from rat and pig models of cardioplegic arrest and deep hypothermic circulatory arrest. 2) Adult rat ventricular cardiomyocytes were chemically transfected with either miR-146b mimic or inhibitor oligonucleotides, subjected to oxygen-glucose deprivation and reoxygenated. 3) Rat H9c2 cells were transfected with miR-modulators complexed with nanoparticles. Transfection efficiency was monitored by Cy-labeled fluorescence, miR qPCR, and

Western blot of target proteins. Necrosis and apoptosis assays were used to assess biological effects of miR-modulator transfection.

Results: Robust myocardial miR-146b upregulation following I/R was conserved across experimental models and species. In vitro functional analyses suggest that miR-146b attenuates upregulation of IRAK 1, TRAF6 and NF-kB-p65 following simulated I/R, resulting in improved cardiomyocyte viability. Nanoparticles complexed with pre- and anti-miR 146b are stable and offer enhanced in vitro transfection efficiency.

Conclusion: We identified altered myocardial expression of miR-146b following surgical I/R and characterized its role in negative feedback inhibition of inflammatory signaling via targets IRAK1 and TRAF6. Therapeutic modulation of miR-146b may confer cardioprotective effects in the setting of I/R by attenuating acute perioperative myocardial inflammation. Nanoparticle delivery systems may be viable strategies to enhance transfection efficiency for therapeutic translation.

Student Name: Amanda Gelineau

Host Department: Mount Sinai School of Medicine

Primary Mentor Name: Ira Hofer, MD

Additional Mentor(s): Yury Khelemsky, MD, Hung-Mo Lin, ScD, David Reich, MD

Title of Research Project: *Pain in Laparoscopic vs. Open Surgery*

Introduction: Despite a trend toward laparoscopic surgery over the last two decades, the role of laparoscopic approaches in decreasing postoperative pain remains unclear. A retrospective study was conducted at our institution to review the post-operative pain outcomes following laparoscopic versus open surgery.

Methods: Records of adult patients undergoing non-emergent same day admission surgery between May 2011 and February 2012 were reviewed. Patients undergoing laparoscopic surgery were propensity score matched with those undergoing open surgery based on procedure type, ASA status, age, BMI, gender, attending anesthesiologist and pre-operative anti-anxiety, anti-depressant and opioid use. Exclusion criteria included use of pre-operative methadone, opioid agonist-antagonists, and the presence of a neuraxial analgesic technique. Outcome measures included surgical length, median pain score on post-operative days (POD) 1-3, and length of stay.

Results: Complete data were available for 1714 cases. After applying the exclusion criteria, 914 cases were included in the study. Median surgical time was found to be slightly shorter in the laparoscopic group (140 vs. 179 min) $p=0.056$. In addition POD 2 pain was slightly less in the laparoscopic group (2.29 vs 2.55, $p=0.01$), however the pain was equivalent during the other days. There was a trend toward decreased length of stay in the laparoscopic group (2.36 vs 3.15 days) however it did not reach statistical significance ($p=0.231$).

Conclusion: In this retrospective study of patients who underwent surgical procedures between 2011 and 2012, surgical length was found to be slightly shorter in the laparoscopic group and outcomes were equivalent between the two groups.

Student Name: Antasia Giebler

Host Department: University of Colorado Denver

Primary Mentor Name: Almut Grenz, MD, PhD

Additional Mentor(s): Holger Eltzhig, MD, PhD

Title of Research Project: *Equilibrative nucleoside transporter (ENT)-1-dependent elevation of extracellular adenosine protects the liver during ischemia and reperfusion*

Ischemia and reperfusion-elicited tissue injury contributes to the morbidity and mortality of hepatic surgery, including liver transplantation. Previous studies have implicated extracellular adenosine signaling in liver protection. Based on the notion that extracellular adenosine signaling is terminated by its uptake from the extracellular to the intracellular compartment via equilibrative nucleoside transporters (ENTs), we hypothesized a functional role of ENTs in liver protection from ischemia. During orthotopic liver transplantation in humans, we observed greater expression of ENT1 than ENT2, in conjunction with repression of ENT1 and ENT2 transcript and protein levels following warm ischemia and reperfusion. We confirmed these findings in a murine model of liver ischemia (45 min) and reperfusion (2 and 24 h) showing repression of ENT1 and ENT2 following liver ischemia and reperfusion. Treatment with the pharmacologic ENT inhibitor dipyridamole revealed elevations of hepatic adenosine levels and robust liver protection following liver ischemia and reperfusion with attenuated elevations of ALT and AST and less histologic injury. Subsequent studies in gene-targeted mice for Ent1 or Ent2 demonstrated selective protection from liver injury in Ent1^{-/-} mice. Ent1^{-/-} mice experienced less pronounced elevations of plasma ALT and AST levels and histologic liver injury. In contrast, Ent2^{-/-} mice showed similar levels of liver injury as corresponding littermate control mice. Hepatic adenosine levels following liver ischemia were significantly higher in Ent1^{-/-} compared to Ent2^{-/-}. Taken together, these findings implicate ENT1 in liver ischemia and reperfusion injury and suggest a role for ENT inhibitors in the prevention or treatment of ischemic liver injury.

Student Name: Aneesh Goel

Host Department: Vanderbilt University

Primary Mentor Name: Paul St. Jacques, MD

Additional Mentor(s): Jesse Ehrenfeld, MD, MPH

Title of Research Project: *Identification of Postoperative Acute Kidney Injury Following Inpatient Nonrenal Surgery*

Background: Acute Kidney Injury (AKI) is a significant, yet often undetected complication of inpatient surgery. Unrecognized AKI can have significant consequences for patients including longer lengths of stay, increased cost of care, and higher levels of morbidity and mortality (Khetarpal et al. 2007). We undertook a study to determine if a computerized query of an electronic health record could be used to identify cases of AKI for quality improvement purposes.

Methods: We evaluated 14,337 electronic anesthesia records from a large academic medical center for inpatient surgeries occurring from July 1, 2011 to June 30, 2012. Of the 14,337 patient records, 10,530 met our inclusion criteria of nonrenal surgeries and having pre- and postoperative creatinine determinations. We examined increases in creatinine levels up to 5 days postoperatively to determine if in fact AKI had occurred. We also reviewed a preexisting quality database for known, previously reported episodes of AKI.

Results: Of the 10,530 patient records meeting our inclusion criteria, 1,257 patients (11.94%) experienced AKI as defined by Mehta et al. (2007) as a creatinine increase of ≥ 0.30 mg/dL. Of these positive screen patients, only one had been previously entered into the quality improvement database.

Conclusions: AKI occurs more frequently in nonrenal inpatient surgeries than is currently being identified postoperatively. It is important to identify these previously undetected cases of AKI in order to determine if

any potentially avoidable causes of renal damage were present and to take steps to reduce the likelihood of future injury through improved perioperative management.

Student Name: Sheena Hembrador

Host Department: UCSF Department of Anesthesia

Primary Mentor Name: Pamela Flood, MD

Title of Research Project: *The Effect of Fetal Descent on Pain during the First Stage of Labor*

The goal of this study was to determine the impact of fetal descent on pain during the first stage of labor. We used nonlinear mixed effects modeling to analyze data containing pain-Numeric Rating Scale (NRS) scores, cervical dilation (CD), and station collected from 334 laboring women. NRS scores were modeled as a function of CD, station, or a combined function of CD and station in order to determine whether measurement of station helped predict pain. Variables were fit with a sigmoid equation, validated in previous literature.

Consideration of CD improved the prediction of reported pain ($p=4.7E-8$), as did descending station ($p=1.2E-11$). Since station and CD are linked such that station increases as CD increases, we determined the proportional contribution to pain from each source. Increasing CD is predictive of approximately 53% of the increase in labor pain, while descending station is responsible for 47% ($p=0.0001$). When considering pain throughout labor, we found that station plays a significant role in maximal pain ($p=0.009$), while CD affects both initial and maximal pain ($p=0.003, 0.002$).

It has been considered that CD is primarily responsible for increasing labor pain. Our results are novel in that they show that descent of the baby contributes almost equally. Thus, although fetal station is a difficult, potentially inaccurate measurement, it should be considered in labor pain management. One should not be surprised when a woman with advanced CD but high station reports limited pain or when a woman with small CD but low station reports substantial pain.

Student Name: Jason Hsieh

Host Department: Cleveland Clinic

Primary Mentor Name: Andrea M. Kurz, MD

Additional Mentor(s): Daniel I. Sessler, MD; Dr. Ehab S. Farag, MD; Jarrod Dalton, MA; Dongsheng Yang, MS

Title of Research Project: *The Association Between Intraoperative Hypotension and Stroke in General Surgery Patients*

Stroke is an uncommon but serious complication of surgery. Recent research, such as the POISE trial investigating the use of perioperative beta blockers in noncardiac surgery, has identified hypotension as a possible risk factor for postoperative stroke. We plan to test the hypothesis that intraoperative hypotension is associated with postoperative stroke in patients undergoing general surgery.

Data were obtained from the Cleveland Clinic Perioperative Health Documentation System (PHDS), a database containing perioperative records of over 200,000 patients, and the electronic medical record. We identified cases by the presence of stroke-related ICD9 codes. Patients who received general anesthesia with a hospital stay of at least one night were eligible for inclusion. Patients who were under 18, had an ASA class of 5 or 6, or underwent intracranial, cardiac, carotid, or aortic arch procedures were excluded. Our initial query yielded 838 patients with perioperative stroke. Patient records were inspected to confirm eligibility and clinical or imaging evidence of a stroke within 30 postoperative days. After adjudication, roughly 150 patients with postoperative stroke remained.

This work is in progress. We plan to match each case to 3-5 controls based on potential confounders such as demographic variables, comorbidities, and procedure type using propensity scores. We will measure intraoperative hypotension from blood pressure data by calculating the time-integrated amount of hypotension each patient experienced below predefined thresholds. Finally, multivariable linear regression will be used to test the hypothesis that patients with postoperative stroke experienced a greater degree of intraoperative hypotension than matched controls.

Student Name: Zachary Hudson

Host Department: Emory University

Primary Mentor Name: Andrew Jenkins, PhD

Additional Mentor(s): Paul Garcia, MD, PhD

Title of Research Project: *Isoflurane enhances the function of alpha9/10 nicotinic acetylcholine receptors*

Introduction: Isoflurane is known to modulate the function of many ligand-gated ion channels, including nicotinic acetylcholine receptors (nAChRs). The alpha9/10 nAChR subtype has limited expression in the nervous system (inner ear hair cells for example) and has a unique pharmacology, with nicotine and muscarine both acting as antagonists. The aim of this study was to determine the effect of isoflurane on alpha9/10 nAChR function.

Methods: *Xenopus* oocytes were injected with equimolar concentrations of alpha9 and alpha10 cRNA. Receptor function was assayed 24-72 hours after injection using an automated 8-channel 2-electrode voltage clamp. Oocytes were superfused with buffers containing agonists, antagonists and anesthetics using a robotic solution handler (OpusExpress, Molecular Devices). Data were digitized and stored for offline analysis using pClamp and MATLAB.

Results: As expected, acetylcholine activated the receptors in a concentration dependent manner and these responses were blocked by the addition of nicotine, suggesting these receptors behaved as previously reported. Isoflurane at clinically relevant concentrations potentiated receptor activation, increasing the peak response to acetylcholine EC₂₀ by up to 30%.

Conclusion: The increase in receptor function shown here indicates that in the presence of isoflurane, rather than being inhibited, cholinergic neurotransmission is increased at alpha9/10 containing synapses. Since these receptors act to modulate afferent auditory information, this may explain why hearing is one of the last sensory modalities to be eliminated by general anesthetics.

Student Name: Markus Jackson

Host Department: Stanford University, Department of Anesthesia

Primary Mentor Name: Dr. Brenda Golianu

Title of Research Project: *Acupuncture for the Treatment of Cystic Fibrosis in Teenagers and Young Adults*

Cystic fibrosis (CF) is one of the most common genetic diseases. Significant advances in the treatment and management of CF patients have increased the life expectancy of patients with CF from 18 in 1976 to 37 in 2012. One of the secondary complications of the increased longevity of CF patients is pain. Up to 59% of pediatric patients with cystic fibrosis experience significant pain and discomfort that may decrease their quality of life. Despite the high incidence of chronic pain, many CF patients are not prescribed opioids because the side effects of these medications exacerbate pre-existing gastrointestinal problems. The combination of these and other studies suggest that a more effective treatment strategy is necessary in order to manage chronic pain in CF patients.

Acupuncture has been used for years to help alleviate chronic pain. Medical acupuncture has also been used as an adjunctive therapy to help improve pain in adult CF patients. Our research team aims to investigate whether 4 weekly treatments of acupuncture as compared to sham acupuncture (placing needles at non-points that are anatomically close to the true acupuncture points) is effective in improving pain. Using a randomized placebo-controlled crossover study design, participants will be randomized to either traditional acupuncture (n= 10) or sham acupuncture (n= 10). After the first cycle of treatments, patients will undergo a 2-week wash-out period. Then those receiving sham acupuncture will receive true acupuncture and vice versa. The primary endpoint is the visual analog pain scale as scored by a 0-10 scale.

Student Name: Sonia Jackson Woods

Host Department: University of Alabama at Birmingham

Primary Mentor Name: T.J. Ness, MD, PhD

Title of Research Project: *Inhaled Chlorine Inhibits Locomotion in Mice – Potential Beneficial Effects of Inhaled Local Anesthetics*

The purpose of this study is to examine dose-dependent effects of chlorine gas exposure on locomotion measures and to probe in a preliminary fashion whether there may be an effect of local anesthetics.

The two study hypotheses are [1] Inhaled chlorine gas will produce a dose-dependent inhibition of locomotion in mice, and [2] Inhaled local anesthetics will reverse behavioral effects of inhaled chlorine

Adult C57Bl6 mice had baseline activity measures (15 min) performed using the TruScan locomotion system then were exposed for 30 minutes to either air or 100, 200 or 400 ppm chlorine gas using the UAB Chlorine Gas Exposure Facility. Measures were obtained again immediately after chlorine exposure and at 1,2,4,6 and 24 hours. In separate groups of mice beginning 15 minutes prior to the 1,2,4 and 6 hour post-exposure to 400 ppm Cl₂, the mice received nebulizer treatments with lidocaine (1% or 4%) or 2-chloroprocaine (3%) or saline or no treatment.

The mice treated with nebulized 1% lidocaine (n=8) had statistically significant responses 24 hours post chlorine exposure compared to the mice treated with nebulized 4% lidocaine (n=6) or 3% 2-chloroprocaine (n=15).

In conclusion, inhaled chlorine produces a graded inhibition of locomotion in mice and administration of inhaled local anesthetics (appear to) reduce the hypo locomotion induced by inhaled chlorine exposure. These data, combined with previous findings from our lab, suggest utility of the present model system to study effects on locomotion in mice exposed to less severe lung injury via exposure to 100 ppm chlorine.

Student Name: Benjamin Kwittken

Host Department: Beth Israel Deaconess Medical Center

Primary Mentor Name: Balachundhar Subramaniam MD, MPH Director of Cardiac Anesthesia Research

Additional Mentor(s): Brett A Simon MD, PhD; Vimal Akhouri MD

Title of Research Project: *Assessing lower extremity perfusion following percutaneous revascularization using tissue oxygen monitoring.*

Tissue oximeters measure global tissue perfusion. A sensor is traditionally placed at the thenar eminence or the tongue. Tissue oximetry has never been used to measure the adequacy of lower extremity perfusion after relief of a blockage (i.e. Thrombus). This prospective, pilot, observational study is assessing the ability of the Hutchinson InSpectra StO₂ monitor to measure tissue perfusion at the foot after percutaneous

revascularization interventions (i.e. angioplasty and/or stent placement). Current revascularization tools such as ankle brachial index, toe-to-brachial index, pulse volume recording, duplex ultrasound, near infrared spectroscopy (methods other than StO₂ monitoring such as SpO₂), skin perfusion pressure or physical assessment alone do not allow for rapid evaluation of intervention efficacy, real-time monitoring of improved blood flow, or early warning for rapid intervention in the case of failing stents or compromised limbs during the acute process. The 20 patients included in the study have a disposable tissue oximetry probe placed on the medial eminence of the foot on the intervention side from the beginning of the procedure for the next 24 hours or until discharge. Traditional parameters are being compared to the continuous tissue oximetry readings and patient demographic and clinical data are collected from the medical record for analysis. Pre and post intervention StO₂ data will be analyzed with a paired t test and $p < 0.05$ will be considered significant. This is an ongoing study.

Student Name: Tomas Lazo

Host Department: Stanford University, Dept. of Anesthesia

Primary Mentor Name: Brendan Carvalho, MD

Additional Mentor(s): Alexander Butwick, MD

Title of Research Project: *Hypothermia after Cesarean Delivery: Incidence, predictors, and associated adverse outcomes*

Background: Perioperative hypothermia (PH) is an important adverse outcome, which has been associated with perioperative blood loss, post-operative wound infection, myocardial ischemia, delayed recovery, and increased thermal discomfort. Predictors and adverse outcomes associated with PH have not been adequately elucidated in women undergoing cesarean delivery (CD). The aims of this study are to assess the incidence, predictors and consequences of PH in women undergoing CD.

Methods: This retrospective study, will examine a database of women who have undergone CD at Lucile Packard Children's Hospital, California. Data will be manually abstracted from medical records of patients treated between 2007-2011. We will utilize this database to (i) assess the incidence of PH post-CD, (ii) assess predictors for PH post-CD, and (iii) assess maternal adverse outcomes associated with post-CD PH. We will consider demographic, socioeconomic, obstetric, anesthetic and surgical factors as potential predictors for post-CD PH, as well as the PH-related composite outcome measure. We will construct a composite outcome for adverse maternal outcomes related to post-CD PH, which will include the presence of at least one of the following: postpartum hemorrhage (perioperatively or in recovery), delayed PACU stay (defined as a stay > 90th percentile for PACU duration), pharmacologic treatment for shivering and pain in PACU. Secondary outcomes will include differences in length of PACU and hospital stay, peripartum hemoglobin change, and analgesic consumption between PH and non-PH patients.

Results: Data collection is currently underway, and we plan to present preliminary data at the ASA meeting in October 2012.

Student Name: Cheng-ting Lee

Host Department: Massachusetts General Hospital

Primary Mentor Name: Jianren Mao, MD, PhD

Title of Research Project: *Drug Abuse Patterns in Pain Subjects on Opioid Therapy*

Background: Abuse of prescription opioid and/or illicit drug is a significant challenge in chronic pain management. However, it is unclear whether drug abuse patterns would differ between clinical pain patients and subjects participating in pain research studies.

Methods: We reviewed the results of Random Urine Tests (RUT) conducted between 1/1/2003 and 12/31/2011 in 1) clinical patients treated at the Massachusetts General Hospital (MGH) Pain Clinic (Clinical Group) and 2) study subjects intended to participate in IRB-approved pain studies at the MGH Center for Translational Pain Research (Study Group). Drugs of abuse (DOA) were defined as unprescribed controlled substances and recorded, along with demographic and socioeconomic data, medical history, opioid dose regimen, types and duration of pain.

Results: In the Study Group (n=515), 515 RUT were conducted and 56 (10.9%) showed DOA. Of them, 69.6% were detected in subjects on opioid therapy. Cannabinoids (32.1%), cocaine (32.1%), and benzodiazepam (23.2%) were most commonly abused. In the Clinical Group (n=1,227), 1,067 RUT were conducted and 335 (31%) showed DOA. Of them, 85% were detected in subjects on opioid therapy. Cannabinoids (54%), cocaine (26%), and benzodiazepam (21%) were also the most commonly abused. While both study groups have a larger percentage of females, more males than females showed DOA in RUT.

Conclusions: Both clinical pain patients and study subjects share similar drug abuse patterns. A common factor in both groups appears to be prescription opioid therapy. Details regarding the impact of opioid therapy on drug abuse are currently under investigation.

Student Name: Rosie Li

Host Department: Columbia University

Primary Mentor Name: Robert Whittington, MD, Associate Professor of Clinical Anesthesiology

Additional Mentor(s): Laszlo Virag, MS, Senior Research Staff Associate

Title of Research Project: *Midazolam Induces Tau Hyperphosphorylation Under Normothermic Conditions In Vivo and In Vitro*

In neurodegenerative tauopathies, the microtubule-associated protein tau can undergo aberrant phosphorylation, leading to neurofibrillary pathology development. Anesthetics can induce tau hyperphosphorylation through anesthesia-induced hypothermia and under normothermic conditions, as has been demonstrated with propofol. Hence, we determined the impact of normothermic midazolam administration on tau phosphorylation.

Following institutional approval, male C57BL6/J mice (8-10 week old) received midazolam 10 mg/kg (n=5), 25mg/kg (n=5) or 0.9% saline (n=4) i.p. Mice were sacrificed after 30 min and hippocampi were harvested immediately. Chronically infused mice received 0.8mg/kg/hr midazolam (n=4) or 0.9% saline (n=4) s.c., via osmotic pumps for 24h. SH-SY5Y human neuroblastoma cells, transfected to overexpress tau, were exposed to midazolam 5 uM (n=4), 50 uM (n=4), or vehicle control (n=4) and harvested after 4 or 24h. Normothermia was maintained throughout. Protein levels of phosphorylated tau (p-tau) at the AT8, CP13, and PHF-1 phosphoepitopes and total tau were determined using SDS-PAGE followed by immunoblotting. The tau hyperphosphorylation mechanism was dissected by screening the activation pattern of various tau kinases and phosphatases.

Midazolam significantly increased hippocampal p-tau levels at AT8, CP13, and PHF-1, without a significant change in total tau, 30 min after treatment and after the 24h infusion. A decrease in p-GSK-3b Ser9 protein expression paralleled the p-tau increase in the acute administration study. Midazolam in vitro did not significantly increase p-tau at 4h, while a 24h exposure significantly increased p-tau at all three phosphoepitopes.

These data suggest that midazolam increases tau phosphorylation in vivo and in vitro, possibly via the GSK-3b pathway.

Student Name: Andrew Lohse

Host Department: Regents of the University of Michigan

Primary Mentor Name: Chad M. Brummett, MD

Additional Mentor(s): Jenna Goesling, PhD

Title of Research Project: *The Impact of Centralized Pain on the Analgesic Response to First Diagnostic Medial Branch Block*

Introduction: Prediction of facet intervention response is nearly impossible. A potential explanation may be augmented central nervous system pain processing or “centralized” pain, as is seen in fibromyalgia (FM). We hypothesized that “centralized” pain may be less responsive to a peripheral intervention. The present study investigates the impact of a centralized pain phenotype on response to a first diagnostic medial branch block (MBB).

Methods: Patients status-post MBBs using 0.5% bupivacaine (N=187) were studied retrospectively. Patients were categorized as FM positive or FM negative using the American College of Rheumatology survey criteria for FM.[1] Pain scores (0-10) up to 24 hrs post-MBB were recorded. A linear mixed model was used to study longitudinal effects of MBB on pain responses using R 2.15.0.

Results: FM positive patients described higher pre-procedural pain severity. FM negative female patients experienced a significant pain reduction of -3.59 after 30-min ($p < 0.0001$). The longitudinal response to pain over time varied significantly by FM status ($p = 0.0005$). FM- showed a deeper decline in pain scores followed by gradual return to baseline. This recovery was not present in the FM+ group. FM- pain scores were lower than FM+ by -1.07 (SE=0.37) on average ($p = 0.005$). Gender was not a significant factor ($p = 0.65$).

Discussion: Despite reporting higher preprocedural pain scores, patients with centralized pain showed a blunted initial response to MBB with diminished response over 24-hrs post-MBB. Prospective studies are needed to better understand the impact of centralized pain on facet outcomes.

References

[1] Wolfe F, et al. J Rheumatol. 2011;38(6):1113-1122.

Student Name: Shu Lu

Host Department: University of Pittsburgh

Primary Mentor Name: Jonathan H. Waters, MD

Additional Mentor(s): Gerhardt Konig, MD

Title of Research Project: *Rocking Stored Blood during Acute Normovolemic Hemodilution Impairs Clotting Dynamic and Platelet function*

Introduction: Acute normovolemic hemodilution (ANH) is an intra-operative option for reducing allogenic transfusion. Whole blood(WB) is removed from patients prior to surgery, stored for up to 8 hours un-agitated, and re-infused back to patients after surgery. Normally, platelets are stored agitated to maintain platelet function. The hypothesis of this study was that ANH WB should be agitated continuously to preserve platelet function.

Methods: WB was collected from 8 healthy volunteers(>18yrs) into citrated blood donor bags. Each bag was split into “control”, “rocked”, and “un-rocked” samples. “Rocked” samples were agitated for 8 hrs at room temperature. “Unrocked” samples were stored un-agitated. Prothrombin time(PT), activated partial thromboplastin time(pTT), fibrinogen level(FL), and D-Dimer were measured on “control” samples before storage and “rocked” and “un-rocked” samples post-storage. For platelet function and WB coagulation,

TEG® Platelet Mapping Assay was performed using thrombelastography. Significance was evaluated using paired t-test between “un-rocked” or “rocked” stored samples against un-stored “control” samples.

Results: WB stored for 8 hrs “un-rocked” and “rocked” resulted in no significant changes in Kaolin activated maximum clotting amplitude (UR=64.25;R=56.43;C=63.63), PT(UR=14sec;R=14.8sec;C=14.8sec), pTT(UR=38.65sec;R=41.9sec;C=40.9sec), FL(UR=267mg/dl;R=270mg/dl;C=275mg/dl), and D-Dimer(UR=.23mcg/ml; R=.22mcg/ml; C-.28mcg/ml) compared to “Control”. “Rocked” resulted in increases in clotting time(R=7.55min;C=6.46min;p=.02) and clotting angle(R=54°;C=64°;p=.04) compared to “control” and a decrease in %platelet activation following arachidonic acid platelet agonist activation(R=52%;C=73%;p=.01).

Conclusion: All samples demonstrated similar clotting strength. Only WB stored rocked for 8 hrs resulted in abnormal clotting dynamics, increase clot formation time, and decrease platelet activation compared to un-stored blood. Therefore, blood should be stored un-rocked during ANH.

Student Name: Michelle Mahanian

Host Department: Mount Sinai School of Medicine

Primary Mentor Name: Stacie Deiner, MD

Additional Mentor(s): Jeff Silverstein, MD

Title of Research Project: *Predictors of postoperative delirium in non-cardiac surgery patients*

Background: Postoperative delirium (PD) is an important complication associated with increased mortality, prolonged hospital stay, and functional disability. This study explores the association between PD, preoperative comorbidity, and intraoperative cerebral oxygen desaturation in elderly general surgery patients. Palmberg et al showed decreased incidence of PD when cerebral oximetry is used during cardiac surgery. However, in general surgery patients, the association between cerebral desaturation and PD is not well established. If they are associated, then cerebral oximetry should be routinely monitored in general surgery to guide anesthesiologists’ manipulation of physiology (BP, ETCO₂, FIO₂) and improve outcomes.

Methods: 210 patients over age 68 undergoing major non-cardiac surgery were monitored continually with cerebral oximetry. Regional oxygen saturation was measured as time and area under thresholds of 65%, 60%, and 55% normalized for case hours. Delirium was evaluated in the PACU and on postoperative days 1-3 using the Confusion Assessment Method (CAM).

Results: Patients with PD were more likely to have diabetes (p=0.0293), malignancy (p=0.0141), and lower baseline MMSE (p=0.0030). There was no association between cerebral desaturation and PD at any of the thresholds.

Conclusions: Delirium after general surgery, unlike cardiac surgery, depends on comorbidities rather than cerebral desaturation. Our findings agree with Morimoto et al’s smaller study in abdominal surgery patients, which found that cerebral desaturation is not a predictor of PD. Together these suggest that PD in general surgery occurs via a different mechanism than in cardiac surgery; thus, delirium may be a final common pathway of two etiologically distinct processes.

Student Name: Alex McGaughy

Host Department: Medical University of South Carolina

Primary Mentor Name: Francis X. McGowan, Jr, MD

Additional Mentor(s): Ms. Elizabeth Favre, BS

Title of Research Project: *Isoflurane Reduces Lifespan and Impairs Development in C. elegans*

Introduction: There is increasing concern about deleterious long-term effects of volatile anesthetics, particularly in the very young and very old. Potential mechanisms are poorly understood. Our hypothesis is that anesthetic exposure induces sustained alterations in homeostatic and cell stress signaling networks. Here, we studied effects of isoflurane exposure upon lifespan and development in the model organism *C. elegans*.

Methods: Developing (L4 stage) and mature (9 day) worms (N2 strain) were exposed to an age-specific ED50 concentration of isoflurane for 0, 1, or 4 hours. Survival, body size (length), movement, and brood size were quantified using standard techniques. Lifespan effects were assessed using Kaplan-Meier analysis; other intergroup comparisons used ANOVA with post-hoc correction.

Results: Exposure of L4 worms to an ED50 of isoflurane (7% vol:vol) for either 1 or 4 hours significantly reduced median lifespan ($P < 0.001$ vs. controls) such that survival at 14-16 days was reduced by approximately 50% in both treatment groups. L4-exposed worms also demonstrated significantly reduced size ($P < 0.001$) and movement at maturity. Conversely, isoflurane had minimal effect upon these parameters in mature worms.

Conclusions: These preliminary results suggest that isoflurane exerts significant effects upon complex, multi-component pathways such as lifespan and growth in developing *C. elegans*. Studies including expression microarray, RNA-seq, and genome-wide methylation techniques are ongoing to define the integrative pathophysiology of these effects. We hope to use this efficient and genetically tractable model to identify mechanisms responsible for long-term consequences of cellular stress, anesthesia, and surgery, and thereby focus parallel studies in mammalian systems.

Student Name: Joanna Miller

Host Department: SUNY Downstate Medical Center

Primary Mentor Name: Rebecca Twersky, MD, MPH

Title of Research Project: *Incidence of perioperative dysglycemia in patients with chronic kidney disease undergoing ambulatory surgery*

Introduction: Perioperative blood glucose values are not routinely measured in patients without diabetes; little is known about the incidence of perioperative dysglycemia (hyper- or hypoglycemia) in non-diabetics. Perioperative dysglycemia is associated with increased risk of post-surgical complications. Determining which patients are at risk for developing perioperative dysglycemia, and managing them accordingly, may help improve surgical outcomes.

Because insulin is renally cleared, patients with chronic kidney disease (CKD) are at high risk for dysglycemia. Additionally, these patients require frequent ambulatory procedures to maintain vascular access for hemodialysis. We investigated whether patients with CKD, with or without diabetes, are at high risk for perioperative dysglycemia (day-of-surgery venous blood glucose < 70 or > 180 mg/dl).

Methods: A retrospective chart review was conducted of patients with CKD undergoing ambulatory surgery at Downstate Medical Center from January 2006 through December 2010.

Results: 98 patients (47 diabetics, 51 non-diabetics) undergoing 304 procedures were identified. Of the 304 procedures, 20.7% contained episodes of dysglycemia, (95% CI: 16.5%- 25.7%). Among the 98 patients, 33.7% had at least one episode of dysglycemia (95% CI: 25.1%- 43.5%). Seven out of 51 non-diabetics had at least one occurrence of hypoglycemia. This was not significantly different from the 15% incidence of hypoglycemia in diabetics. There were more episodes of dysglycemia in diabetics than in non-diabetics (51% vs. 17.6%, $p < 0.01$).

These data demonstrate that patients with CKD undergoing ambulatory surgery have high rates of perioperative dysglycemia with an unknown impact on outcomes. Of note is the high incidence of hypoglycemia among non-diabetics with CKD.

Student Name: Leela Mirafzali

Host Department: Regents of the University of Michigan

Primary Mentor Name: Satya Krishna Ramachandran, MD, FRCA

Additional Mentor(s): Kevin Tremper, MD, PhD; Chad Brummett, MD; Michelle Morris, MS

Title of Research Project: *High Risk of Obstructive Sleep Apnea is Associated With Increased Perioperative Pain*

Background: Obstructive sleep apnea (OSA) is estimated to afflict 9-24% of the general population, up to 90% of who have greater risk of developing chronic pain. Anesthesia causes complex changes in sleep architecture with significant reduction of total sleep time and restorative sleep. Given the reciprocal relationship between sleep deprivation and pain, we hypothesized that high-risk OSA patients will present with increased preoperative and postoperative pain, measured by opioid consumption.

Methods: Prospective analysis of patients' chronic pain outcomes of total knee and hip arthroplasty was investigated. Epidural or spinal anesthesia as primary anesthetic was excluded. OSA risk was determined by the PSAP score, using the following: snoring history, hypertension, type II diabetes, BMI > 30 kg/m², age > 43 years, male, Mallampati III or IV, qualitatively assessed thick neck, and reduced thyromental distance estimated < 6 cm. Preoperative and postoperative opioid dosing was converted into single intravenous morphine equivalents. Pearson's Chi-square test and Mann-Whitney-U test were used to compare categorical and continuous data, respectively ($p < 0.05$). The relationship between postoperative opioid requirement and OSA risk factors were evaluated using linear regression.

Results: In 172 patients, high-risk OSA was associated with increased preoperative and intraoperative, but not postoperative opioid dose requirement for comparable pain scores. On linear regression ($r^2 = 0.803$), postoperative opioid consumption was independently associated with preoperative opioid dose (t-statistic 13.5; $p < 0.001$), thick neck (t-statistic 2.1; $p = 0.044$) and hypertension (t-statistic -2.2; $p = 0.031$).

Conclusion: This is the first to demonstrate a relationship between OSA risk factors and clinically relevant measures of perioperative pain sensitivity, pointing to a potential dose-dependent mechanism for increased post-operative respiratory morbidity in OSA patients.

Student Name: Rochelle Molitor

Host Department: Mayo Clinic Rochester

Primary Mentor Name: Carlos Mantilla, MD, PhD

Additional Mentor(s): W. Michael Hooten, MD; Terese Horlocker, MD; Adam Jacob, MD; Sandra Kopp, MD

Title of Research Project: *The Association of Preoperative Heat-Pain Threshold and Tolerance as Determined by Quantitative Sensory Testing on Pain Scores and Postoperative Analgesic Consumption in Patients Undergoing Primary Total Knee Arthroplasty*

Chronic postoperative pain occurs in approximately 20% of patients undergoing total knee arthroplasty (TKA). A strategy is needed to identify pre- or intraoperative risk factors for the development of chronic postoperative pain so that alternative or additional analgesic regimens may be implemented. Quantitative sensory testing (QST) provides precise characterization of somatosensory pathways and may provide insight into a patient's response to injurious stimuli such as surgery. The CASE-IV system represents a subtype of QST technology that specifically quantitates a patient's ability to detect various sensory stimuli, including vibration, cold, and heat-pain in a reproducible fashion. Uniquely, it takes into consideration the variation in sensory thresholds that exist by site, age, gender, height, weight, body mass index and body surface area when reporting results. We hypothesized that preoperative heat-pain sensitivity, as determined by QST, would be predictive of postoperative pain intensity and opioid consumption in patients undergoing primary TKA. Heat-pain thresholds and tolerance will be evaluated in 30 patients scheduled for TKA prior to surgery using the CASE-IV QST system. Patients will also complete a series of preoperative psychological surveys. Postoperative pain assessments (Numeric Rating Scale), opioid consumption, knee range of motion, and ability to perform physical therapy exercises will be monitored. We report a review of the QST method and preliminary results of this ongoing pilot study. Based on the results of the study, we expect to inform the design of a prospective study using QST to identify TKA patients at risk for the development of chronic postoperative pain.

Student Name: Niti Patel

Host Department: Massachusetts General Hospital

Primary Mentor Name: Warren Zapol, MD

Additional Mentor(s): Lorenzo Berra, MD, Riccardo Pinciroli, MD

Title of Research Project: *Identification of subjects with endothelial dysfunction for a human volunteer study of stored blood autotransfusion with inhaled nitric oxide administration*

Background: Transfusion of human packed red blood cells (PRBC) stored for more than 2 weeks is associated with increased morbidity and mortality. During storage, red cells release hemoglobin, which avidly binds nitric oxide (NO). This NO-scavenging mechanism may alter endovascular physiology in subjects with endothelial dysfunction due to disease, like obesity. We hypothesize that 40-day stored PRBC autotransfusion may trigger a pro-inflammatory and vasoconstrictor response in subjects with pre-existing endothelial dysfunction. We further predict that this response may be prevented by the concomitant administration of inhaled nitric oxide (iNO).

Methods: We designed a multiple-crossover, randomized autotransfusion study, for which we screened overweight volunteers (BMI for inclusion: 27-40 kg/m²) to identify subjects with endothelial dysfunction, as defined by a peripheral arterial tonometry (PAT) score of less than 0.6. PAT-score was assessed by an arterial tonometric test (EndoPAT2000). PAT-score is a marker for endothelial function and is partly dependent on NO bioavailability. The enrolled subjects will donate and subsequently be transfused with autologous units stored for 3 or 40 days. Two transfusions of 40-days PRBC will be given, iNO will be administered during one of these transfusions.

Results: Our study population target was reached after screening 57 overweight candidates. We enrolled a cohort of 14 obese (BMI 33.2±4.9 kg/m²), otherwise healthy subjects, 22 to 63 year-old. The average PAT-

score was 0.46 ± 0.12 . Unexpectedly, in our screened population, overweight status did not predict endothelial dysfunction, with non-significant correlation between BMI and PAT-score in a linear regression analysis controlling for age and gender ($p=0.9046$).

Student Name: Cameron Rice

Host Department: UCLA

Primary Mentor Name: Aman Mahajan, MD PhD

Additional Mentor(s): Michael Laks, MD; Wei Zhou, PhD

Title of Research Project: *Sympathetic Innervation of the Ventricular Walls by the Right and Left Stellate Ganglia*

The sympathetic nervous system is believed to be a factor in the genesis of ventricular tachyarrhythmia, one of the most lethal conditions of cardiovascular disease. Autonomic activation of the right and left stellate ganglia (RSG and LSG) can dramatically alter ventricular repolarization leading to arrhythmia genesis and maintenance. However, the contribution of the stellate ganglia to the right and left ventricles (RV and LV) remains unclear. This study evaluated the innervation of the ventricles by comparing T-wave direction during stimulation with the physiological orientation of the ventricles within the porcine chest. A holter monitoring system was used to obtain continuous 12-lead ECG data before and during stimulation of the stellate ganglia by a platinum bipolar electrode connected to a Grass stimulator. Anatomical orientation vectors for the ventricles were calculated using OsiriX image processing application on in-vivo MRI images. When compared with the RV MRI vector, the T-wave vector during RSG stimulation was significantly deviated superiorly in the frontal plane and anteriorly in the horizontal plane ($p < .01$, $p < .01$). Conversely, compared to the LV MRI vector, T-wave vectors during LSG stimulation were significantly deviated inferiorly in the frontal plane and slightly deviated posteriorly in the horizontal plane ($p < .01$, $p = .08$). ECG data in pigs with prior left circumflex infarction showed a slight anterior deviation compared to healthy pigs ($p = .09$). These results suggest that RSG innervates the base and anterior wall of both ventricles with primarily RV innervation and LSG innervates the apex and posterior wall of both ventricles with primarily LV innervation.

Student Name: Giulia Rosanova

Host Department: University of Pennsylvania School of Medicine

Primary Mentor Name: Jeff E. Mandel, MD, MS

Additional Mentor(s): Joshua Atkins, MD, PhD

Title of Research Project: *A pharmacokinetic approach to rapid titration of propofol in a drug induced sleep endoscopy for anatomic diagnosis of sleep apnea*

Obstructive sleep apnea is an important cause of morbidity and mortality. While polysomnography can give an accurate apnea-hypopnea index to qualitatively describe the degree of disease, it cannot elucidate the anatomic sites of obstruction during sleep. Drug induced sleep endoscopy (DISE) is useful in detecting anatomic sites of obstruction, but is difficult to standardize. We describe a novel approach to target controlled infusion (TCI) of propofol to achieve an endpoint of moderate obstruction. We studied 60 patients with a baseline mean AHI of 53.2. This method uses a pharmacokinetic model of propofol which determines the bolus and infusion rates prior to administration, which are continued to an endpoint of moderate obstruction with slow pharyngeal collapse to allow for accurate anatomic diagnosis, which can then be discontinued with rapid recovery. This rapid propofol titration approach permitted diagnosis in all patients. The O₂ desaturation mean for all patients was 79.4% during the polysomnograph and 91.1% during the rapid propofol titration DISE ($P < 0.001$). 88.3% of patients desaturated lower during the polysomnography than during the DISE. In comparison to polysomnography this method makes anatomic diagnosis possible, while exposing the patient to no more risk of desaturation than diurnal sleep. In comparison to bolus dosing of propofol, this approach allows the practitioner to administer propofol in DISE using a protocol. It is the

ability of this method of administration to standardize titration of propofol to the endpoint of moderate obstruction that makes it most valuable for use with DISE as a diagnostic tool.

Student Name: David Rotstein

Host Department: Montefiore Medical Center The University Hospital for the Albert Einstein College of Medicine

Primary Mentor Name: Naum Shaparin, MD

Additional Mentor(s): Singh Nair, MD; Louvonia Boone, MD

Title of Research Project: *A randomized controlled trial evaluating the effectiveness of regional vs local anesthetic technique in creating AV fistulae for dialysis*

Background: Approximately 26-40% of first-time arteriovenous fistula (AVF) creations result in failure. There are few prospective studies investigating how the types of anesthesia (local or regional) can influence AVF maturation. This is a prospective randomized controlled study comparing the three month success rate for AV fistulae created under regional or local anesthesia.

Methods: Following Institutional Review Board approval, patients undergoing a first-time AV fistula creation were randomized into one of the two anesthetic groups; local anesthesia (administered by the surgeon) or regional anesthesia (performed by the anesthesiologist). In the local anesthesia group, patients received 20cc of 1% lidocaine. In the regional anesthesia group, patients received a supraclavicular block with 30cc of a solution that was $\frac{1}{4}$ 0.5% bupivacaine and $\frac{3}{4}$ 2% lidocaine. At the time of PACU discharge, patients completed a short questionnaire assessing their satisfaction with their experience. On the fourth day a blinded researcher called the patients to assess complications and comfort. At three months, the AVF was considered a success if it was being used effectively for dialysis. If the patient had yet to start dialysis, vein mapping was used to assess vessel patency; a mean blood flow \geq 600 ml/min was considered adequate for dialysis.

Discussion: In this ongoing study, analyses of primary endpoints are early. Initial data show no difference between complications among the two groups. However, data projects better postoperative satisfaction and comfort under regional anesthesia. Study limitations include varying teams of surgeons and anesthesiologists and the single-centered study design.

Student Name: Courtney Schilling-Mechling

Host Department: The Children's Hospital of Philadelphia

Primary Mentor Name: Aruna Nathan, MBBS, FRCA

Additional Mentor(s): David Jobes, MD

Title of Research Project: *Obesity and Pediatric Heart Disease in the Kids Inpatient Database: Does obesity affect length of stay and cost of care for children with heart disease undergoing non-cardiac surgery?*

Objective: To determine the influence of obesity on surgical outcomes (length of stay and hospital charges) in children with heart disease undergoing non cardiac surgical procedures (appendectomy, tonsillectomy, cholecystectomy or spinal fusion).

Methods: Subjects were identified using the Kids Inpatient Database (KID) 1997, 2000, 2003, 2006 and 2009. Each admission was evaluated for presence of heart disease, obesity and certain co-morbidities using ICD 9-CM codes. Linear regression was used to assess the effect of these diseases, demographics and hospital characteristics on length of stay (LOS) and hospital charges.

Results: 43 obese children with heart disease underwent the surgical procedures listed above from 1997 to 2009. Multivariate regression analysis was performed using the variables listed. There was no death in obese children with heart disease. The LOS for non-obese children with heart disease was 3.1 days longer than obese children with heart disease.($P=.00001$). There was no difference in LOS between obese children with and without heart disease. There was no difference in total charges between non- obese and obese children with heart disease. The total charge for obese children with heart disease was 34% more than that of obese children without heart disease.

Conclusions: Presence of obesity per se does not appear to increase LOS or hospital charges in children undergoing the above mentioned surgical procedures. However, presence of heart disease seems to increase the total hospital charges for obese children undergoing these procedures.

Student Name: Kiely Schultz

Host Department: University of Colorado Denver

Primary Mentor Name: Breandan Sullivan, MD

Title of Research Project: *Protective Characteristics of Critically Ill Patients against the Development of Delirium*

Delirium is characterized by acute changes in mental status with signs of inattentiveness and either disorganized thought or changes in level of consciousness. In hospital patients, delirium has been linked to increased rates of infection, prolonged mechanical ventilation, and longer length of stay in both the intensive care unit and the hospital. Most of the focus of delirium research has involved identifying drugs that transition patients to delirium. We attempted this pilot study to identify protective characteristics of critically ill patients that consistently protected them from transitioning to delirium. We performed the Confusion Assessment Method for the ICU (CAM-ICU) as our delirium assessment on all patients admitted to our surgical intensive care unit. Patients were excluded if they were comatose or had a language barrier that prevented them from participating in the CAM-ICU. Assessments were performed twice daily for seven weeks by three medical students, for a total of 575 assessments on a total of 163 patients. Twenty-one patients were delirious, for an incidence of 12.88%, with most patients exhibiting hypoactive delirium. Patient information, including demographics, type of surgery, hemodynamic data, oxygenation, creatinine and hemoglobin levels, as well as exposure to certain drugs were collected. Data analysis is ongoing and results of statistical analysis of delirium status and the variables of patient age, type of surgery, hemodynamic data and fentanyl exposure will be presented at the ASA.

Student Name: Kinza Sentissi

Host Department: Beth Israel Deaconess Medical Center

Primary Mentor Name: Balachundhar Subramaniam

Title of Research Project: *The use of endoscopic ultrasound to measure cardiac function and parameters.*

Endoscopic ultrasound is commonly used in gastrointestinal practice for a variety of disorders. It has emerged as the standard of care for the evaluation of mediastinal lymphadenopathy and pancreaticobiliary disease and also plays a prominent role in staging and resection of gastric and esophageal cancers. The purpose of this study is to investigate which cardiac parameters and measures of cardiac function can reliably be seen during the standard EUS examination, using both linear and radial endoscopes. This could potentially allow both gastrointestinal and cardiac organ systems to be evaluated during a single procedure in certain patients. An institutional review board-approved prospective medical record chart review prior to EUS procedure identified 12 patients who were scheduled to undergo EUS for various clinical indications. These patients underwent standard EUS followed by an in-depth cardiac assessment completed by a cardiac anesthesiologist. The results of this study revealed that one can reliably identify the mid-esophageal bicaval view, mitral commissural view,

mid-esophageal long axis view, pericardium, and ascending aorta using the linear scope. Because of the cross-sectional nature of the radial images, a radial endoscope was not able to identify cardiac parameters. Measures of cardiac function requiring Doppler technology were not possible. In conclusion, under the guidance of a qualified ultrasonographer, EUS can be used to readily identify a variety of cardiac parameters, notably views of the left heart, aorta, and pericardium. In patients experiencing acute decompensations during EUS, these parameters may be helpful in quickly identifying potential cardiac etiologies.

Student Name: Janki Shah

Host Department: UMDNJ/NEW JERSEY MEDICAL SCHOOL

Primary Mentor Name: Jean Daniel Eloy, MD

Additional Mentor(s): Steven Shulman, MD; Catherine Schoenberg, BSN

Title of Research Project: *The Effect of Gabapentin on Postoperative Orthopedic Pain and Sleep: A Randomized, Double-Blind, Placebo-Controlled Trial*

Background: Gabapentin, a structural analog of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) has been effective in the treatment of postoperative pain. Gabapentin has also been shown to increase slow wave sleep (SWS), maintain stable REM, and reduce arousals, awakenings, and stage shifts. The purpose of this study is to determine if a single 400 mg dose of gabapentin, when given after orthopedic surgery, decreases postoperative pain and improves sleep.

Methods: In this IRB approved, randomized, double-blind, placebo-controlled trial, fifty patients between the ages of 18 and 70 undergoing total hip arthroplasty, hip fracture repair, or total knee arthroplasty will be recruited. All patients will receive either a lumbar plexus block or a femoral nerve block. Pain will be assessed using the visual analog scale (VAS) and PCA (hydromorphone) use. The primary endpoint will be opioid consumption; subject reported sleep scales and pain scores will also be assessed.

Results: Currently, there are 9 enrolled subjects [gabapentin (G) n=5, placebo (P) n=4]. The mean total opioid consumption over 48 hours was 24% higher with G (14.84 mg \pm 9.68 mg,) than with P (11.95 mg \pm 7.63 mg). The highest pain score within 12 hours of surgery was 18% higher with G (7.4 \pm 2.40) than with P (6.25 \pm 2.99). On postoperative day one, 50% of patients who received P and 60% of those who received G reported very good or fairly good sleep.

Conclusion: There is insufficient data to make a valid conclusion.

Student Name: Andrew Smith

Host Department: Columbia University

Primary Mentor Name: H.T. Lee, MD, PhD

Title of Research Project: *Isoflurane induces interleukin-11 via ERK MAPK in human endothelial cells*

Introduction: Endothelial dysfunction is a major clinical problem that contributes to the development of multi-organ failure and systemic inflammation. We previously demonstrated that volatile anesthetic isoflurane inhibits endothelial apoptosis via activation of extracellular signal-regulated kinase (ERK MAPK). The downstream signaling events occurring in response to isoflurane remain to be elucidated.

Hypothesis: Isoflurane protects against endothelial dysfunction through ERK MAPK-mediated induction of the anti-inflammatory, anti-apoptotic cytokine, interleukin (IL)-11.

Methods and Results: In human endothelial (iHUVEC) cells, isoflurane increased IL-11 mRNA and protein synthesis. The selective ERK MAPK inhibitor, PD98059, but not the Akt inhibitor, Wortmannin, prevented

isoflurane-mediated IL-11 synthesis in iHUVEC. To test the functional relevance of isoflurane-mediated IL-11 induction, we treated iHUVEC with a pathogenic cytokine TNF- α to induce inflammation (5 hr treatment) as well as apoptosis (24-48 hr treatment). RT-PCR results demonstrate that isoflurane-mediated attenuation of pro-inflammatory markers is blocked by an IL-11 neutralizing antibody. Furthermore, isoflurane-mediated attenuation of endothelial apoptosis, as shown by DNA laddering and cleaved caspase formation, is also prevented by IL-11 neutralizing antibody. Finally, treatment with recombinant human IL-11 recapitulates isoflurane-induced endothelial protection against inflammation and apoptosis in iHUVEC.

Conclusions: Isoflurane-induced endothelial protection against apoptosis and inflammation is mediated by ERK MAPK-dependant IL-11 synthesis. Future studies are necessary to determine the relevance of our in vitro findings to an in vivo model of vasculopathy. Human IL-11, already approved for treatment of chemotherapy-induced thrombocytopenia, may potentially become a novel clinical therapy in the management of endothelial dysfunction and systemic inflammation during the perioperative period.

Student Name: Kathryn Steckelberg

Host Department: Mayo Clinic Rochester

Primary Mentor Name: Daryl Kor, MD

Title of Research Project: *Characterization of Use Patterns and Complications associated with Brachial Arterial Catheterization*

Background: Studies have compared the safety and outcomes of radial arterial catheterization (RAC) with other arterial access sites. However, insufficient attention has been placed on brachial artery catheterization (BAC).

Objectives: We aimed to describe use patterns and complications associated with BAC at Mayo Clinic and compare these findings with patients who received RAC. Outcomes to be analyzed include vascular, neurologic, and/or infectious sequelae.

Methods: This single-center, retrospective, matched cohort study analyzed adults undergoing surgical procedures at Mayo Clinic from 2008-2011 who received BAC. This cohort was compared (1:4) to a randomly selected cohort of patients who received RAC. Demographic information, pre-existing medical conditions, pre-operative medications, and ASA status were compared between patients with brachial and radial catheters.

Results: A total of 986 unique patients received BAC over the defined study interval. A second cohort of 3,944 unique patients with RAC was identified. Patients with BAC had a lower body mass index, greater number of preoperative comorbidities, lower serum albumin concentration, and higher ASA status. The BAC cohort was also observed to undergo procedures with longer anesthesia times. Line sequelae are currently under analysis and will be reported at the study's conclusion.

Conclusions: Patients with BAC at Mayo Clinic from 2008-2011 had longer anesthetic exposure times, a higher prevalence of comorbidities, lower serum albumin concentration and higher ASA status than their RAC counterparts. This suggests that these patients are more medically complicated at the time of catheterization. The outcome comparisons between the BAC and RAC cohorts are currently under review.

Student Name: Steven Vanhoy

Host Department: University of Utah

Primary Mentor Name: Harriet Hopf MD

Additional Mentor(s): Matthew Griffiee MD; Timothy Holmberg, MD; Ben Gmelch, MD; Georges Desjardins, MD, FRCC

Title of Research Project: *Rescue Echocardiography Findings are Different Based on Patient Setting*

Background: Many methods are used to evaluate perioperative hemodynamic instability. Echocardiography is a useful diagnostic modality in this clinical scenario. Echocardiography by Level 3 certified anesthesiologists has been available 24 / 7 at our institution since 2009. "Rescue" echocardiography is requested at the discretion of the attending anesthesiologist, usually in response to unexplained hemodynamic instability. We performed a retrospective database analysis to evaluate if findings have different frequencies for intra-operative versus ICU rescue studies.

Methods: With IRB approval, we analyzed the findings of all adult patients who underwent rescue echocardiography in the ICU or OR between February 2010 and June 2012.

Results: 423 rescue echoes were performed: 63% intraoperative; 79.7% during 0700-1900; 60% male; mean (SD) age, 59 (16) years. 97% of studies were readable. Findings more common in the ICU included: reduced LV systolic function ($p=0.0142$; OR 2.41; 95% CI 1.19-4.87); reduced RV systolic function ($p=0.001$; OR 5.31; 95% CI 2.86-9.84); segmental wall motion abnormalities ($p<0.05$; OR 1.18; 95% CI 1.09-1.29); and abnormal diastolic function ($p=0.0143$; OR 1.86; 95% CI 1.13-3.06). Pericardial effusion occurred at about the same rate ($p=0.334$; OR 1.19; 95% CI 0.3-1.49). Hypovolemia appeared more frequently in the OR, although results were often missing from reports.

Conclusions: We found differences between OR and ICU rescue echocardiography findings. These could result from ICU patients having more severe illness and experiencing different stressors; the threshold for service also may be different. Future studies will evaluate the cost and benefits of the service, including outcomes.

Student Name: Alisa Vitkus

Host Department: University of Rochester

Primary Mentor Name: Gail V.W. Johnson, PhD

Additional Mentor(s): Laurent G. Glance, MD

Title of Research Project: *The Effects of Tau on Nrf2 Activity*

Alzheimer's Disease (AD) is the 6th leading cause of death in the US. One of the hallmark features of AD is the accumulation of tau, a microtubule stabilizing protein. AD is associated with oxidative stress and the ability of cells to prevent such damage is compromised. Nrf2, a transcription factor activated by cellular stress, increases expression of antioxidant genes as well as proteins in the autophagy pathway. It has been postulated that deficits in the Nrf2 pathway may contribute to the accumulation of tau. Conversely, increases in tau may negatively impact Nrf2 pathway contributing to a negative feed forward loop. Sulforaphane activates Nrf2 and has been shown to improve cell survival by reducing Reactive Oxygen Species (ROS) generation and increasing clearance of pathological proteins. Basally, Nrf2 is rapidly degraded when bound to Keap1 which causes Nrf2 to be polyubiquitinated and targeted to the proteasome. When Keap1 encounters oxidative stress or electrophiles, NRF2 degradation pathway is inhibited and Nrf2 responsive genes increase. Sulforaphane is an electrophilic molecule that acts on Keap1 and thus is a Nrf2 agonist. The study focused on understanding how tau affects Nrf2 activity. To examine how specific phosphorylated forms of tau may affect Nrf2 we transfected cells with different tau constructs and incubated in the absence or presence of sulforaphane. NRF2 activity was subsequently measured. These studies begin to elucidate the relationship

between select processes that are contributing to AD neurodegeneration, and how aberrant tau might compromise the cells' ability to prevent such damage.

Student Name: Deva Wells

Host Department: University of Washington

Primary Mentor Name: Karen Domino, MD, MPH

Additional Mentor(s): Karen Posner, PhD; Linda Stephens, PhD

Title of Research Project: *Patterns of injury and liability in neurosurgical anesthesia: A closed claims analysis*

Introduction: Neuroanesthesia is commonly recognized as a high-liability subspecialty of anesthesia care, given the potential for serious adverse outcomes. We examined injuries, damaging events, and liability outcomes of neurosurgical claims in the ASA Closed Claims database.

Methods: Claims involving craniotomies (n=41) and procedures on the cervical spine (n=72) and thoracic and lumbar spine (T-L spine, n=213) were compared to other surgical procedure claims (other claims, n=2,016) for injuries occurring between 1995 and 2009. Proportions were compared by chi-square, Fisher's exact test and payments by Mann-Whitney U test.

Results: Permanent and severe injuries were more common among neurosurgical claims (38% vs. 18% other claims, $p < 0.001$). Eye injuries were more common among T-L spine claims (22% vs. 3% of other claims, $p < 0.001$). Severe nerve injury occurred more often in cervical spine claims (21% vs. 3% in other claims, $p < 0.001$). T-L claims had a higher proportion of hemorrhage and/or fluid management events (18%) and positioning events (24%) than other claims (6% and 4%, $p < 0.001$). More central venous catheter related-events occurred in craniotomy claims (20% vs. 4% of other claims, $p < 0.001$). Twenty-one percent of cervical spine claims involved difficult airway management. Payments for neurosurgical claims were greater (median=\$385,000) than those for other claims (\$262,000, $p < 0.05$).

Conclusions: Neurosurgical claims frequently involved costly, debilitating injuries. Eye injury occurred in nearly a quarter of T-L spine claims, reflecting the increased risk of ischemic optic neuropathy during prone spine surgery. Adequate fluid replacement during hemorrhage and careful positioning in the prone position may improve patient safety.

Student Name: John Williams

Host Department: Oregon Health & Science University

Primary Mentor Name: Kirk Lalwani, MD, FRCA

Title of Research Project: *Patient and Family Centered Care in Pediatric Sedation*

Patient and Family Centered Care (PFCC) is a burgeoning topic of interest in the healthcare field. When patients and families are involved in the care provided by the healthcare team outcomes and satisfaction have been shown to improve. The Institute for Patient- and Family-Centered Care defines the components of PFCC as 1) Dignity and Respect, 2) Information Sharing, 3) Participation, and 4) Collaboration. What defines these concepts is likely to be different in each setting and certain to vary between patients. However a number of assessment tools have been developed and validated for use in a variety of settings with both adult and pediatric patients. According to the Society for Pediatric Sedation (SPS) there is a need to assess a number of issues in how we approach the planning and delivery of health care and how can we measure and improve patient and family centered care in pediatric sedation. There are currently no instruments available to assess PFCC in pediatric sedation. To be able to properly provide a patient and family centered experience and ultimately improve care, outcomes, and satisfaction of both families and providers, we propose the

development of a survey instrument to assess what constitutes patient and family centered care in the setting of pediatric sedation.

Student Name: Brittany Winckler

Host Department: University of California Irvine

Primary Mentor Name: Zeev N. Kain, MD

Title of Research Project: *Behavioral Recovery after Tonsillectomy and Adenoidectomy: The Proximal-Distal Model*

Background: Previous literature examining predictors of children's postoperative recovery from tonsillectomy and adenoidectomy (T&A) has focused on state (proximal) variables and neglected trait (distal) variables. In order to fully understand behavioral postoperative recovery, distal personality characteristics must also be considered. The purpose of this study was to evaluate distal trait predictors of both immediate and long-term behavioral recovery in children following T&A.

Procedure: Participants included 241 children ages 5-12 scheduled to undergo general anesthesia and outpatient T&A. Parents completed baseline psychosocial measures of state and trait variables such as the Child Behavior Checklist (CBCL). Throughout the first two weeks after surgery and at postoperative months 3 and 6, parents completed the Post-Hospitalization Behavior Questionnaire (PHBQ). Hierarchical linear regressions controlled for demographics, pain, and state variables to determine trait predictors of behavior.

Results: On the first postoperative day, 94% of all parents reported new-onset maladaptive behavioral changes, decreasing to 16% at postoperative month 6. Child temperament (sociability) and parental coping style influenced early behavioral recovery with regard to general anxiety ($p=0.02$) and separation anxiety ($p=0.01$). Children with fewer baseline behavior problems (delinquent and withdrawn behavior-CBCL) were more likely to have persisting new-onset maladaptive behaviors across several PHBQ behavioral domains (separation anxiety, general anxiety, apathy/withdrawal, sleep anxiety) at postoperative months 3 and 6 ($p_s < 0.03$).

Conclusions: This study highlights which children may be most at risk for behavioral changes after surgery. These findings give parents and healthcare providers information about what recovery pattern to expect from T&A given certain distal trait variables.

Student Name: Valerie Wong

Host Department: State University of NY (SUNY) Stony Brook

Primary Mentor Name: Peggy Ann Seidman, MD

Title of Research Project: *Penile Tumescence as a Measure of Caudal Block Efficacy*

The caudal block has been used for decades in Pediatric Anesthesia to administer analgesia below the infraumbilical region. Despite its widespread use, no "gold standard" exists for evaluating its efficacy due to obstacles in working with the indicated population. When neuroaxial local anesthetics are administered, sympathetic stimulation is inhibited allowing for unopposed parasympathetic activity. In males receiving caudal block, this may manifest as tumescence. This study was performed to evaluate the potential use of penile tumescence as a marker of caudal block efficacy.

Five male patients between the ages of six to 18 months undergoing circumcision were recruited. Several physiologic parameters were measured in relation to the caudal block. Prior studies have shown transient temperature changes in the lumbar dermatomes compared to cervical regions with caudal onset(1). Temperature was measured from skin probes at L2 and C4. Penile tumescence pressures were measured

directly via needle manometry from within the penis cavernosa. In addition, a tactile score given by the surgeon, and a visual score given by the surgical technician or nurse, were used to evaluate tumescence on a scale from zero, no observable tumescence, to three, very firm tumescence.

Preliminary results indicate that penile tumescence may be used as a measure of caudal block efficacy. However, further studies must be performed to determine whether such a physiologic response is reproducibly reliable with adequate sensitivity.

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Student Name: Tian Xia

Host Department: UMDNJ/New Jersey Medical School

Primary Mentor Name: Rex Ponnudurai, MD

Additional Mentor(s): Heidi Brehm, MD; Amy Davidow, PhD; Catherine Schoenberg, RN; Alex Bekker MD, PhD

Title of Research Project: *A Prospective Study to Establish a Correlation between Infusion Rate of Propofol and Bispectral Index in Patients Receiving Total Intravenous Anesthesia*

Background: The use of Total Intravenous Anesthesia (TIVA) with propofol has increased and demonstrated improved recovery characteristics. However, propofol with a short half life can pose risks on intraoperative awareness and recall. An anesthetic depth monitor, the Bispectral Index (BIS XP) device by Aspect, has been used with inhalation anesthesia and can be beneficial for patients undergoing TIVA. This study aims to look at the correlation between infusion rates of propofol and BIS values.

Methods: This was a prospective, observational, IRB approved study with a goal of recruiting 40 patients both genders, ASA I-III, between the ages of 18 to 65 undergoing elective gynecological or orthopedic surgery longer than 180 minutes. With BIS sensor placed on the forehead, standardized induction protocol was administered. After tracheal intubation, continuous propofol infusions with varying dosages at 30 minute intervals was administered at 120, 140, 160, and 180 mcg/kg/min. Vital signs and BIS were recorded during TIVA at 5 minute intervals.

Results: 16 patients were recruited. BIS values ranged from 13 to 67 with a high frequency in the 20s. After controlling for BIS values within 30 minutes of induction, BIS values decreased showing a trend toward statistical significance ($p=0.0536$) per 20 mcg increase in propofol infusion rates.

Discussion: There was a negative correlation between infusion rates of propofol and BIS values. The BIS was a valuable monitor when using TIVA. More patients will be recruited for further analysis.

Student Name: Katie Yang

Host Department: Duke University Medical Center

Primary Mentor Name: Tong-Joo Gan, MD, MHS

Additional Mentor(s): Ashraf Habib, MB BCh

Title of Research Project: *Memantine for Postoperative Analgesia Following Radical Retropubic Prostatectomy*

The use of certain non-opioid analgesics alongside traditional opioids to treat acute postsurgical pain has been associated with decreased postoperative pain scores, opioid requirements, and incidence of opioid-related adverse effects. This ongoing double-blind randomized controlled trial investigates the role of the NMDA receptor antagonist memantine in the treatment of acute postsurgical pain. Following IRB approval, 57 patients scheduled to undergo radical retropubic prostatectomy were consented and enrolled in the study. Patients were randomized to receive either 40 mg oral memantine or placebo perioperatively, split into three doses. All patients underwent a standardized anesthesia regimen during surgery and received postoperative analgesia via morphine PCA. Pain was assessed at various intervals up to 6 months postoperatively using opioid consumption and pain score. Presence of opioid-related adverse effects was also elicited. Area of wound hyperalgesia was measured 24 h postoperatively.

Data were available on 40 patients. The memantine group had lower mean 24 h-postoperative opioid consumption and nausea incidence, although differences were not statistically significant. Memantine patients had a statistically lower rate of rescue antiemetic administration. They also reported statistically higher pain scores within one week postoperatively, but generally lower scores after one month. These preliminary data suggest that although perioperative memantine decreases postoperative nausea and opioid consumption 24 h postoperatively and acute postsurgical pain one month postoperatively, the drug increases pain scores within one week after surgery. This drug may show promise in the treatment of chronic pain, but is likely of limited utility in the treatment of acute postoperative pain.

Student Name: David Zacharias

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Primary Mentor Name: Simon C. Body, MB, ChB, MPH

Additional Mentor(s): Nicholas T. Longford, PhD; Dr. Kevin Lilly, MD

Title of Research Project: *Clinical assessment and utility of near-infrared cerebral oximetry in cardiac surgery*

Background: Near-infrared cerebral oximetry is becoming common in cardiac surgical monitoring, even as a standard of care at many institutions. Yet the scientific basis for incorporating this technology into clinical practice and standard diagnostic and treatment algorithms for using it are lacking. We hypothesized that clinicians' choices of action would lack consensus given a clinical cardiac surgery scenario in which cerebral oximetry is used.

Methods: We surveyed the Society of Cardiac Anesthesiologists and the online Cardiovascular Perfusion Forum using a series of 11 case questions assembled from real patient scenarios, asking what subsequent clinical action the practitioner would take. Demographic and cerebral oximetry utilization data were collected. An index of dispersion was used to assess response heterogeneity overall and within demographic subgroups.

Results: Of 880 respondents, 65% of Anesthesiologists and 81% of Perfusionists reported that cerebral oximetry was either an essential or useful monitor. Our main findings were 1) dispersion indices were lower, indicating greater consensus for therapeutic choice, in scenarios characterized by mild ScO₂ changes and 2) dispersion indices were higher, indicating lower consensus of therapeutic choice, in scenarios characterized by larger ScO₂ changes.

Conclusions: Although practitioners find that cerebral oximetry is useful, published treatment guidelines do not exist. We observed greatest consensus in therapies when smaller changes in cerebral saturation were observed and least consensus when severe changes in oxygen saturation were observed. We interpret this as indicating that practitioners need evidence-based guidelines for therapies based on cerebral oximetry and outcome studies quantifying its therapeutic benefit.

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