39th ANNUAL SHIELDS RESEARCH DAY

ANNUAL SHIELDS LECTURER
PROFESSOR IRENE TRACEY
MA (Oxon), D.Phil., FRCA, FMedSci

7 Hart House Circle
University of Toronto
HART HOUSE
7:45am - 3:30pm
07:45 AM Breakfast and Registration
Location: The Great Hall

08:30 AM Welcome
Location: The Great Hall
Dr. Beverley Orser, Chair, Anesthesia
Dr. Zeev Friedman, Chair, Annual Shields Research Day 2018

08:45 AM Session A – Oral Presentations
Location: The Great Hall
Moderators: Drs. Keyvan Karkouti and Brian Cuthbertson

A1 The Effect of Anesthetic Technique on Mortality and Major Morbidity Following Hip Fracture Fixation
Sarah Tierney - Fellow

A2 Inflammation and Anesthetic Drugs Synergistically Interact to Impair Cognition in Mice
Shahin Khodaei – Graduate Student

A3 Development of a Head-Mounted Holographic Needle Guidance System for Enhanced Ultrasound Guided Regional Anesthesia
Julian Wiegelmann - Fellow

A4 Prognostic Impact of Preoperative Ambulatory Blood Pressure on Mortality Following Major Elective Noncardiac Surgery
Ashwin Sankar - Resident

A5 Vascular Permeability Associated with Modelled Traumatic Brain Injury is Reduced by Administration of Human Umbilical Cord Perivascular Cells
Tanya Barretto – Graduate Student

A6 Innervation of the Posterior Capsule of Knee Joint: A Cadaveric Study
John Tran – Graduate Student

A7 Canadian Consensus Guidelines for the Perioperative Management of Patients on Buprenorphine
Akash Goel - Resident
09:30 AM Session B - Poster Session
Location: East Common Room

B1 Neurocognitive Functioning Following CPAP Treatment in Elderly Patients with Obstructive Sleep Apnea: A Metaanalysis of Randomized Controlled Trials
Talha Mubashir – Research Assistant

B2 Sensing Tissue Stiffness: New Therapies for Heart Failure and Cardiac Fibrosis
Julia Plakhotnik – Graduate Student

B3 Effect of Internal Jugular Vein Compression on Intracranial Volume: A Transorbital Ultrasound Study of the Optic Nerve
Michael Dinsmore - Fellow

B4 Optimizing Discharge Opioid Prescription for Major Joint Replacement Surgery: A Longitudinal Quality Assurance Survey
Rakhi Talak – Research Assistant

B5 Effects of human umbilical cord perivascular cell conditioned media in a model of traumatic brain injury in adult
Eileen Liu – Graduate Student

B6 Development of a High-Fidelity Novel Training Model for Dynamic Trans-orbital Ultrasonography of Optic Nerve Sheath Diameter
Zakir Hajat - Fellow

B7 Preoperative anemia increases the risk of blood product transfusion in children undergoing spine surgery.
Montserrat Fontanals - Fellow

B8 The Pattern and Distribution of Body Fluid During Pregnancy: A Systematic Review and Meta-Analysis
Julia Pasquale – Medical Student

B9 Systematic Review of the saddle block for perianal ambulatory patients
Carla Todaro - Fellow

B10 Differential cardiovascular response following hemodilution with colloid versus crystalloid
Nikhil Mistry – Research Assistant

B11 Incidence and recovery of recurrent laryngeal nerve injury in children with biventricular physiology following aortic arch surgery: a retrospective cohort study
Minako Sano - Fellow

B12 Adverse Heart-Lung Interactions in Ventilator-Induced Lung Injury
Bhushan Katira - Fellow

B13 Relative efficacy of TIVA and adjuvant intraoperative dexmedetomidine in reducing emergence delirium in children: a network meta-analysis
Maria-Alexandra Petre - Resident

B14 Extubation in the operating room and use of healthcare resources after pediatric cardiac surgery: A retrospective cohort
Mehr Jain – Medical Student

B15 Seasonal Variation Amongst Incidence Of Hypothermia in Severely Ill Trauma Patients
Kennedy Ninh Hao – Medical Student

B16 Sleep Study Parameters for Predicting Perioperative Complications in Patients with Obstructive Sleep Apnea: A Review
Colin Suen - Resident
B17  Differential effect of dexmedetomidine on intracranial EEG recordings from human hippocampus and neocortex
Joshua Bennitz - Fellow

B18  Comparison of cost and outcomes for minimally invasive percutaneous versus surgical paddle lead implantation for spinal
Pranab Kumar - Fellow

B19  A clinical comparison of two bronchial blockers versus double-lumen tubes for one-lung ventilation
Serena Shum - Fellow

B20  Survey on associated symptoms and morbidities in carriers of RYR1 genetic variants
Carlos Alberto Ibarra Moreno - Fellow

B21  Surface Ultrasound as Screening Tool for Diagnosis of Obstructive Sleep Apnea (OSA): A Systemic Review of Literature
Arvind Tuteja – Research Assistant

B22  Opioid medication errors and resultant harm in pediatric practice: five years’ experience of adverse event reporting in a quaternary pediatric hospital.
David Greaney - Fellow

B23  Evaluation of iPACK Block - A Cadaveric Study
Laura Giron-Arango - Fellow

B24  Pre-operative biomarkers and Imaging Tests as predictors of post-operative delirium in non-cardiac surgical patients
Farrah Ayob - Fellow

B25  Integration of Virtual and Augmented Reality to the Operating Room via the Microsoft
Stephen Szeto – Medical Student

B26  Virtual Reality and Pain Management: An Evidence Based Review
Elizabeth Maxwell - Fellow

B27  A Systematic Review of Paresthesia-Free Spinal Cord Stimulation Modes for Complex Regional Pain Syndrome
Yasmine Hoydonckx - Fellow

B28  Twitter Hashtags for Anesthesiologists
Nan Gai - Fellow

B29  Evaluation of sleep health in interventional clinical trials for patients with chronic neuropathic pain: A systematic review
Aidan McParland – Medical Student

B30  Pain, Agitation and Delirium in Cardiovascular Intensive Care Unit; Barriers for implementation
Victoria Postnikova – Graduate Student

B31  A Retrospective Analysis of the Incidence and Treatment of Hypothermia in Pediatric Trauma Patients
Grahme Weisgerber – Fellow

B32  Transient paraplegia following Epidural Blood Patch
Chaminda Wijeratne - Fellow

B33  Evaluation of sleep health in pain questionnaires used in the chronic pain population: A systematic review of literature.
Shreya Desai – Research Assistant

B34  Case report – Supraclavicular Brachial Plexus Neurolysis for a Malignant Peripheral Nerve Sheath Tumor
Weiyang Christopher Liu - Fellow
10:00 AM Session C – Oral Presentations  
Location: The Great Hall  
Moderators: Drs. Greg Hare and Hannah Wunsch

C1 Elevated Red Cell Distribution Width (RDW) is an Adverse Prognostic Indicator in Elective Noncardiac Surgery: A Retrospective Cohort Study  
*Justyna Bartosko - Resident*

C2 A Carbon Nanotube Sensor to Develop Precision Therapies for Heart Failure  
*Manpreet Malhi – Graduate Student*

C3 Competency By Design: A Mixed Methods, Ethnographic Study  
*Gianni R. Lorello – Faculty*

*C4* The Risk of Severe Aortic Stenosis in Elective Non-Cardiac Surgery  
*Jay S. Han - Resident*

*C5* Ketamine Prevents a Persistent Increase in L-Aminobutyric Acid Type-A Receptor Function In Hippocampal Neurons After General Anesthesia  
*Winston Wenhuan Li – Graduate Student*

C6 Mental Illness After Intensive Care: A Population Based Cohort Study  
*Lavarnan Sivanathan*

C7 Comparison of the North American Caffeine Halothane Contracture Test and The Japanese Calcium-Induced Release Test for Diagnosis of Malignant Hyperthermia Susceptibility  
*Carlos Alberto Ibarra Moreno - Fellow*

11:15 AM Session D – Oral Session  
Location: The Great Hall  
Moderators: Drs. David Mazer and Duminda Wijeysundera

D1 Risk Factors for Opioid Induced Respiratory Depression in Surgical Patients: A Systematic Review and Meta-Analysis  
*Kapil Gupta - Fellow*

D2 Anesthetic Activation of GABA (A) Receptors in Astrocytes Triggers a Persistent Increase in a Tonic Inhibitory Current in Hippocampal Neurons  
*Arsene Pinguielo – Graduate Student*

D3 Weeding Out The Problem: The Impact of Preoperative Cannabinoid Use on Pain in The Perioperative Period  
*Weiyang Christopher Liu - Fellow*

D4 Morphine Alters Cancer Metabolic Pathways  
*Doorsa Tarazi – Graduate Student*

D5 Using Patient-Reported and Wearable-Technology Date to Assess Outcomes of Spinal Cord Stimulation Trials for Neuropathic Pain Syndromes  
*Nimish Mittal - Fellow*

D6 Heart Rate Variability can Predict Post-Induction Hypotension in Patients with Cervical Myelopathy  
*Sujoy Banik - Fellow*
12:00 PM Lunch Break and Poster Viewing
Location: The Great Hall

1:00 PM  **Faculty Guest Speaker:**
Dr. David Mazer, Professor of Anesthesia
“Trials and Tribulations of Clinical Trials – What I’ve Learned from TRICS”

1:15 PM  **Annual Shields Lecture:**
Professor Irene Tracey, Head of Department of Nuffield Chair Anesthetic Science
“Advanced Neuroimaging of Pain, Analgesia and Anesthesia Induced Altered States of Consciousness”

2:15 PM  **Anesthesiologist & Philanthropist**
Dr. Hal Marryatt
Contributions to the Department of Anesthesia

2:25 PM  **Former Chair, Department of Anesthesia (2003-2006)**
Dr. David Bevan
Tribute to Dr. Arthur Scott

2:40 PM  **Academic Faculty Promotions**
Dr. Beverley Orser, Chair, Department of Anesthesia

2:50 PM  **Shields Day Awards Presentation Session**
Bateman, Hammell, Rothbart, Byrick, Bryan and Bevan  Awards, Residents and Fellows Tuition Awards, Laws Travel Award, and Clinical Excellence Award

3:15 PM  **Closing Remarks**
Location: The Great Hall
Dr. Beverley Orser, Chair, Anesthesia
Dr. Zeev Friedman, Chair, Annual Shields Research Day 2018

3:20 PM  **Departure**
ANNUAL SHIELDS LECTURE – PROFESSOR IRENE TRACEY

“Advanced Neuroimaging of Pain, Analgesia and Anesthesia Induced Altered States of Consciousness”

Professor Irene Tracey holds the Nuffield Chair of Anaesthetic Science and is Head of the Nuffield Department of Clinical Neurosciences at the University of Oxford – a 550-person world-leading basic and clinical research department. Irene did her undergraduate and graduate studies at the University of Oxford from 1985-1993 and then held a postdoctoral position at Harvard Medical School until 1996. In 1997, Irene helped to co-found the now world-leading Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB) at the University of Oxford and was its Director from 2005 until 2015. She was also Head of the Nuffield Division of Anaesthetics and an Associate Head of the Medical Sciences Division at Oxford prior to taking up her current post. Over the past 18 years her multidisciplinary research team has contributed to a better understanding of pain perception, pain relief and nociceptive processing within the injured and non-injured human central nervous system using advanced neuroimaging techniques. More recently, they have been investigating the neural bases of altered states of consciousness during anaesthesia.

Alongside senior leadership roles within the University, Irene has served and continues to serve on many national and international committees, such as the International Association for the Study of Pain (IASP), REF2014, British Neuroscience Association and Lundbeck Brain Prize Committee. She is currently appointed to the Council of the MRC. She is a passionate advocate for women in science and is involved in several mentorship schemes. In 2008 she was awarded the triennial Patrick Wall Medal from the Royal College of Anaesthetists and in 2009 was made an FRCA for her contributions to the discipline. In 2015 she was elected a Fellow of the Academy of Medical Sciences and in 2017 won the Feldberg Foundation Prize. In September 2019, she will become the Warden of Merton College, Oxford – one of Oxford’s oldest undergraduate and graduate colleges dating back to 1264.

She is married to Professor Myles Allen, a climate physicist, and they have three children: a daughter and two sons.
THE AWARDS

Dr. Evelyn Bateman Award
Named in honor of Dr. Evelyn Bateman, Chief of Anesthesia at the Women's College Hospital from 1956-1972, this award recognizes excellence in anesthesia at the undergraduate level.

Dr. David Bevan Award
The Dr. David Bevan Award is awarded to the presenter of the best overall research poster at the Annual Shields Research Day.

Dr. A.C. Bryan Award
The A.C. Bryan Award is awarded to a graduate student judged to have presented the best research project at the Annual Shields Research Day.

Dr. R.J. Byrick Award
The R.J. Byrick Award recognizes the best fellow's research paper presented at the Annual Shields research Day. Dr. Byrick was the Department's 6th Chair of Anesthesia, serving from 1993-2003. He was then Vice-Dean of Clinical Affairs for the Faculty of Medicine, University of Toronto, until 2007. Dr. Byrick is currently a clinician at St. Michael's Hospital.

Dr. Thomas Donald Hammell Award
The Thomas Donald Hammell Memorial Award in Anesthesia recognizes outstanding contributions to the Residency Program (as chosen by other residents).

Dr. Alan K. Laws Travel Fellowship Award
The Laws Travel Fellowship Award is one of two awards given by the Department of Anesthesia in honor and memory of Dr. Alan Laws. This award provides travel support for senior residents or fellows to advance their research programs in anesthesia.

Dr. Hynek Rothbart Award
The Dr. Hynek Rothbart Award is awarded to the best paper presented by a resident at the Annual Shields Research Day.

UT Anesthesia Resident and Fellows Tuition Awards
Awarded to meritorious Anesthesia residents and/or fellows who are engaged in graduate studies that are clearly integrated into their existing residency/fellowship program, and are linked with their overall career plan.

Awards for Clinical Excellence
For excellent clinical skills (Anesthesia and Critical Care Medicine) and consistent demonstration of exemplary patient service.
ABSTRACTS

A1 ♦ The Effect of Anesthetic Technique on Mortality and Major Morbidity Following Hip Fracture Fixation

Sarah Tierney – Fellow
UHN – Toronto Western Hospital

Background
Spinal anesthesia has proven physiologic benefits over general anesthesia but there is insufficient evidence regarding a mortality benefit after hip fracture surgery[1]. We performed a retrospective, single-center, propensity-score matched cohort study to evaluate the association of anesthetic technique and mortality in patients undergoing hip fracture fixation over a 13-year period.

Methods
Following approval from the University Health Network Research Ethics Board, electronic databases were used to identify patients who underwent hip fracture fixation from January 1st, 2003 to December 31st, 2015. Clinical, laboratory and outcome data were subsequently extracted. Mortality data were obtained from the hospital discharge database. Principal exposure was spinal versus general anesthetic and the primary outcome was 90-day in hospital mortality. Secondary outcomes were 30 and 60-day mortality, hospital length-of-stay, pulmonary embolism, major blood loss and major acute cardiac events. A propensity score-matched-pair analysis was performed using a non-parsimonious logistic regression model.

Findings
Two thousand five hundred and ninety-one patients were identified. Of these, 883 patients in the spinal anesthesia group (SA) were matched to patients in the general anesthesia group (GA). Patients who received GA had a greater 90-day mortality (8.6% vs. 6.3%, p=<.001) (Figure 1), and a higher incidence of both pulmonary embolism (2.3% vs 0.5%, p=<.001) and major blood loss (7.7% vs 4.8%, p=<.001). There was no difference on the hospital length-of-stay or major cardiac events (Table 1).
Conclusions
This observational propensity-score, matched-pairs, cohort study suggests a strong association between spinal anesthesia and lower 90-day mortality, as well as reduced rates of pulmonary embolism, major blood loss and a shorter hospital length-of-stay. The propensity score model included 29 independent variables which are either proven to influence, or are very likely to influence, mortality and morbidity. This minimizes the extent of treatment selection bias which is inherent of all retrospective studies. The year the surgical procedure was performed was also taken into account which minimized the potential confounding from unmeasured and unknown effects of changes in processes of care over the study period.

References

Collaborator(s): Dr. Anahi Perlas, Dr. Laith Malhas, Dr. Vincent Chan, Dr. Scott Beattie

A2 ± Inflammation and Anesthetic Drugs Synergistically Interact to Impair Cognition in Mice

Shahin Khodaei – Graduate Student
Sunnybrook Health Sciences Centre

Background
Cognitive deficits such as delirium occur frequently in the postoperative period and are associated with poor long-term outcomes, increased healthcare costs, and increased mortality (Anesthesiology, 2008). The causes of such cognitive impairments are poorly understood but emerging evidence suggests that both inflammation and anesthetic drugs are important contributing factors. In laboratory animals, inflammation prior to surgery worsened postoperative cognitive performance (PLoS One, 2017). Treatment with an anesthetic drug such as etomidate or
Isoflurane resulted in cognitive deficits that persist long after the drug has been eliminated (J ClinInvest, 2014). Based on these findings, we sought to determine how these factors interact to affect cognition. Specifically, we hypothesized that inflammation and an anesthetic drug interact synergistically to impair cognitive function.

**Methods**
Experiments were approved by the local animal care committee and experimenters were blinded to treatment groups (Fig. A). Adult male mice were injected with a proinflammatory endotoxin lipopolysaccharide (LPS; 1 mg/kg, i.p) to induce inflammation. Twentyfour hours later, mice were treated with an anesthetizing dose of etomidate (etom; 20 mg/kg, i.p). The duration of loss of righting reflex (LORR) was assessed, and starting 48 hours after the etomidate injection, problem-solving abilities were assessed using a three-day puzzle box assay (Fig. B). Statistical analysis was performed using GraphPad Prism 7. Data are presented as mean +/- SEM.

**Results**
LPS injection alone did not cause LORR but increased the duration of etomidate-induced LORR by 43% (etom: 18.1 +/- 1.3 min vs. LPS + etom: 25.9 +/- 2.1 min, p < 0.001). Mice treated with LPS + etomidate showed deficits in problem-solving that were not observed in mice treated with either etomidate or LPS alone. Specifically, mice treated with LPS + etomidate exhibited longer latencies to complete an easy task on Day 2, as well as the more difficult plug task on Day 4, of the puzzle box assay (Fig. B).

**Conclusion**
Our findings suggest that inflammation and etomidate interact synergistically to impair performance on problem-solving tasks. Such deficits lasted for 4 days after anesthetic treatment. A similar mechanism may account for persistent cognitive deficits seen in patients after anesthesia and surgery.

**Collaborators:** Yu-Feng Xie, Dian-Shi Wang, Beverley Orser
Inflammation and etomidate interact to impair cognition in mice. (A) Timeline of the experimental procedure. (B) Top: Schematic diagram of the PB assay. Bottom left: Summarized data showing impaired performance in the initial task and the plug task of the PB assay only in mice treated with LPS + etomidate. * p < 0.05, ** p < 0.01, compared with control. Bottom right: Kaplan-Meier plots showing performance of mice, showing that mice treated with LPS + etomidate took longer to complete these tasks.
Development of a Head-Mounted Holographic Needle Guidance System for Enhanced Ultrasound Guided Regional Anesthesia

Julian Wiegelmann - Fellow
Sunnybrook Health Sciences Centre

Background
The use of emerging mixed reality technology for enhancing needle-based procedures is a novel development. Currently image guided therapies are performed by simultaneously visualizing an anatomic target and needle using ultrasound (US). However, procedures that may benefit from real time image guidance, such as challenging neuraxial procedures (spinal or lumbar/thoracic epidural), are can be difficult to perform in this manner. US guidance, in the context of neuraxial procedures, typically involves pre-procedural US scanning to identify relevant anatomy, estimate the intended needle pathway, and create surface markers to help guide needle insertion points. The procedure is then carried out by the operator, recreating from memory, the location and angulation of the ultrasound as a path for the needle. Previous studies have shown that this method can reduce procedure time and needle passes, and therefore potentially reduce patient discomfort and morbidity (Chin et al., 2011). However, little is known about the accuracy with which operators replicate an ideal needle trajectory once identified by US. The Microsoft Hololens is the first self contained, head-mounted, holographic computing device. It allows users to experience mixed reality – the combination of spatially stable holograms with the real world.

Methods
We have created software for the Hololens which precisely registers the position of an ultrasound transducer by affixing an optical tracking marker, allowing for a spatially stable hologram to be projected into the user's visual field depicting the ideal needle path. Operators may then use this hologram to precisely guide the needle angulation and location (see Figure 1). We hypothesize this will reduce procedure time and the number of needle passes.

Results
Preliminary work with models of the lumbar and thoracic spine has demonstrated that a range of operators (novices to experienced regional anesthesiologists) can rapidly learn to use holograms to successfully perform neuraxial anesthesia.

Conclusions
Further study is required to quantify the potential benefit of holographic guidance on procedural accuracy. While this may have wide ranging implications for many image guided therapies outside of anesthesia, a randomized control trial is planned to quantify its effect on thoracic epidural placement.

References
Figure 1: Holographic Guidance of Needle Placement

This figure depicts a Hololens user’s view of aligning a Tuohy needle with a hologram representing an ideal needle path (white line) into an ultrasound phantom. The difference between the Tuohy and Hologram positions is due to a recording artefact, and is not perceived by the user.

Collaborators: Clyde Matava, Paul McHardy, Stephen Choi, Oskar Singer, Shelly Au

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A4 ♦ Prognostic Impact of Preoperative Ambulatory Blood Pressure on Mortality Following Major Elective Noncardiac Surgery

Ashwin Sankar - Resident
UHN – Toronto General Hospital

Background
Blood pressure (BP) is routinely measured during preoperative evaluation for surgery. The association of preoperative BP profiles with mortality after major elective noncardiac surgery remains unclear.

Methods
After institutional ethics approval, we conducted a retrospective cohort study of consecutive patients undergoing major elective noncardiac surgery at University Health Network (Toronto, Canada) between 2008 and 2015. Institutional databases linked preoperative clinic assessments (patient characteristics) with the operating room registry (surgical details) and electronic inpatient records (outcomes). The primary exposure was the resting ambulatory BP measured in preoperative clinic, characterized as the mean arterial pressure (MAP) and pulse pressure (PP). The primary outcome was 30-day in-hospital mortality. A priori, we expected possible nonlinear relationships between the exposures (i.e., MAP, PP) and outcome. The exposures were therefore expressed as 4-knot restricted cubic splines that allowed for flexible modeling of their relationship with outcome. In unadjusted analyses, the association of each of MAP and PP with 30-day mortality were graphically examined, and exposure thresholds associated with 30-day mortality were established. In adjusted analyses, a multivariable logistic regression model evaluating the association of MAP and PP with 30-day mortality was constructed that adjusted for demographics,
body mass index, comorbidities and surgical procedure. We verified underlying model assumptions and tested for a statistical interaction between MAP and PP.

Results
The cohort included 40,289 patients, with a median MAP of 97 mm Hg (IQR 89 - 105) and PP of 52 mm Hg (IQR 44 - 63). In total, 1.7% (n=673) of patients died within 30-days of surgery. Non-linear relationships were observed between MAP, PP and mortality in unadjusted and adjusted analyses. In unadjusted analyses, a MAP less than 90 mm Hg (OR 1.24 per 5-unit decrease; 95% CI, 1.17 – 1.31), PP less than 40 mm Hg (OR 1.32 per 5-unit decrease; CI, 1.18 – 1.47) and PP greater than 60 mm Hg (OR 1.08 per 5-unit increase; CI, 1.04 – 1.12) were associated with increased odds of mortality. After risk-adjustment, the probability of mortality versus both MAP and PP are graphically represented in Figure 1. A MAP less than 90 mm Hg (OR 1.16 per 5-unit decrease; CI, 1.09 – 1.23) and PP less than 40 mm Hg (OR 1.26 per 5-unit decrease; CI, 1.11 – 1.42) were associated with increased odds of mortality. There was no statistically significant interaction between MAP and PP (p=0.14).

Conclusions
Low preoperative MAP and PP were associated with increased postoperative mortality in this large cohort of patients undergoing major elective noncardiac surgery. Future research is needed to explore mechanisms underlying this association, and to test interventions to mitigate risks in patients with low MAP and PP.

Collaborators: Kevin E. Thorpe, Karim S. Ladha, Gordon Tait, W. Scott Beattie, Duminda N. Wijeysundera
A5 ♦ Vascular Permeability Associated with Modelled Traumatic Brain Injury is Reduced by Administration of Human Umbilical Cord Perivascular Cells

Tanya Barretto – Graduate Student
St. Michael's Hospital

Background
Traumatic Brain Injury (TBI) is the leading cause of morbidity and life-years lost in North America and without any clinical therapeutic treatments for TBI, advancement in this area is an urgent issue. The direct impact to the skull is followed by a delayed secondary injury that is composed of cellular and molecular mechanisms that result in the breakdown of the blood brain barrier (BBB) and white matter among other events. This prolonged time frame of secondary injury suggests a window of opportunity for intervention. The BBB is composed of the neurovascular unit (NVU), which is integral for regulated transport of nutrients and gases between the blood and brain. Following injury, the NVU is damaged therefore disrupting controlled gas and nutrient transport. Human umbilical cord derived perivascular cells (HUCPVCs) isolated from full term cords have been shown to express mesenchymal, neurotrophic and vascular factors, making them a potential candidate to rescue BBB breakdown. The pleiotropic activity of these factors may potentially protect the neurovascular unit and rescue white matter damage after TBI.

Methods
A moderate TBI was modeled using a rat fluid percussion injury (FPI) device. Rats were systemically infused with 1.5 x 10^6 cells 1.5 hours post injury, and survived for 24h, 48h or 7 days. Vascular leakage was assessed using an Evan’s blue assay. Immunohistochemistry (IHC) for RECA-1 at 24h and 48h was performed to assess vascular density and NF200 for axonal integrity in brain sections. Cortical tissue at the injury site was extracted at 24h and 48h for Western blot analysis to examine the expression of tight junction proteins complexes and neurofilament breakdown.

Results
Vascular leakage was expressed in mg of Evans Blue per gram of tissue. At 24h and 48h vascular leakage was 6.4 ug and 15.5 ug vs. 1.7 ug in sham rats. HUCPVC infused leakage values were 5.5 ug and 3.3 ug at 24 and 48 hours, respectively. Western blot analysis demonstrates NF200 is increased in injured animals relative to sham and cell infused animals, a similar trend was observed in a particular tight junction protein, occludin. Investigation into some of the mechanism of modulation of vascular permeability by HUCPVCs is underway.

Conclusions
This model demonstrated quantifiable outcome of vascular leakage. The infusion of HUCPVCs following injury was associated with less vascular leakage and is thus a potential therapeutic strategy to address neurovascular injury after TBI.

Collaborators: Eugene Park, Elaine Liu, Denis Gallagher, Andrew Baker
A6 • Innervation of the Posterior Capsule of Knee Joint: A Cadaveric Study

John Tran – Graduate Student
UHN – Toronto Western Hospital

Background
Postoperative pain following total knee arthroplasty (TKA) can limit early mobilization and recovery. Ultrasound (US) guided peripheral nerve blocks (PNBs) have been utilized to provide non-opioid postoperative analgesia following TKA. More recently, novel approaches targeting the nerve supply of the posterior capsule have been suggested as a supplement to the commonly used femoral nerve and adductor canal blocks. However, the effectiveness of these novel approaches requires a detailed understanding of the innervation of the posterior capsule of the knee joint. Previous cadaveric studies of nerve supply to the posterior capsule are scarce and have not been related to landmarks visible with US. Therefore, the objectives of this cadaveric study were to 1) document the course and frequency of the nerves innervating the posterior capsule, and 2) define anatomical landmarks visible with US to localize the nerves.

Methods
In 15 semi-embalmed specimens, the terminal articular branches of nerves supplying the posterior knee joint capsule were meticulously dissected under 3.5X magnification. The origin of the terminal articular branches was identified, the quantity recorded, and course documented in relation to landmarks visible with US. A frequency map of the nerve supply to the posterior capsule was generated. This study was approved by the University of Toronto Health Sciences Research Ethics Board.

Results
Terminal articular branches from the posterior division of obturator (PON), and tibial (TN) nerves were found to supply the posterior capsule in all specimens. Additionally, terminal articular branches from the common fibular nerve (CFN) and sciatic nerve (SCN) were found in 8 and 3 specimens, respectively. The capsular distribution of TN covered the entire posterior capsule. PON supplied the superomedial posterior capsule overlapping with TN. The superolateral posterior capsule was innervated by TN and, when present, the CFN/SCN. US landmarks to localize these terminal articular branches include the superior border of the femoral condyles, intercondylar fossa, adductor hiatus, and popliteal artery and vein.

Conclusions
The relationship to US landmarks and frequency map of the course and distribution of terminal articular branches, supplying the posterior capsule, provide an anatomical basis for improving the precision of supplemental PNBs targeting the posterior knee joint.

Collaborator: Anne M.R. Agur
Canadian Consensus Guidelines for the Perioperative Management of Patients on Buprenorphine

Akash Goel – Resident
UHN – Toronto General Hospital

Background
Given that there is a surge in buprenorphine prescriptions for patients with chronic pain and addiction, it is inevitable that more patients maintained on buprenorphine will present for surgery and peri-operative management by Anesthesiologists. Therefore, it is imperative that we provide guidance to perioperative health care providers in order to optimize the care provided to this patient population.

Methods
A panel of clinician scientists with expertise in perioperative management of patients maintained on Buprenorphine for chronic pain and/or substance use disorders was convened with a charge to prepare a consensus statement on optimal management of these patients in the perioperative period. The aims of these guidelines are to: (a) provide the rationale and scientific basis for the management of patients taking buprenorphine prior to surgery; (b) Specify the need for perioperative guidelines in this context; (c) and offer a set of recommendations for the perioperative management of these patients. The pharmacology of Buprenorphine, existing guideline documents, and a systematic review conducted by a sub-group of the panel formed the basis for these guidelines.

Conclusion
The panel believes that whenever a buprenorphine maintained patient arrives for emergent or elective surgery, that they should be maintained on their dose of buprenorphine until at least post-operative day (POD) 1. Ideally, the buprenorphine maintenance dose should first be evaluated on POD1, at which point the provider may choose to halve the maintenance dose if the patient is adjudged to be experiencing inadequate analgesia. Patients should ideally be discharged on some dose of buprenorphine. The panel also recommends that the patient and outpatient buprenorphine provider ought to be engaged early in the perioperative period. Where possible, neuraxial techniques, regional techniques, and analgesic adjuncts should be used. While pain management is an important facet of the perioperative management in these patients, perioperative buprenorphine treatment retention and harm reduction should be equally important, particularly in the post-operative period. The panel acknowledges that publishing this statement per se will not result in its spontaneous acceptance, adherence to its recommendations, or change in routine practice. Implementation of these strategies will require a shift in the rationale behind management of these patients, and strong champions amongst the addiction and pain societies will be required to change perioperative practitioner behaviour. Finally, the panel recognizes that further research is required on this topic in order to implement meaningful change in practitioner behaviour for this highly marginalized patient group.

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<tr>
<th>Domain</th>
<th>Recommendation</th>
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<td>Basis of Management</td>
<td>1. Pain management, perioperative addiction treatment retention, and harm reduction should form the basis of management</td>
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Engagement of outpatient provider

1. The outpatient provider should be engaged early and throughout the process, especially at discharge

2. Determine if your patient is at special risk of relapse and other complications of re-exposure to agonist therapy

Engagement of patient

1. Providers should engage the patient early to outline strategies, manage expectations about their perioperative course and the importance of treatment retention.

Buprenorphine Therapy

1. Determine current indication and duration of buprenorphine therapy

2. Buprenorphine SL should be maintained until POD1 irrespective of expected pain or type of surgery. All other formulations of buprenorphine should be maintained indefinitely.

3. POD1 should be the first point in the perioperative period during which change in management is considered, one of which is to reduce the dose of buprenorphine, perhaps by half

4. Patients should be discharged on some dose of buprenorphine.

Adjunct Therapies

1. Multimodal Analgesia (i.e. NSAIDs, Acetaminophen, membrane stabilizers, opioids, NMDA-antagonists) should be considered.

2. Neuraxial and Regional techniques are strongly recommended in the perioperative period for surgeries that warrant this

Table 3: Recommendations by the Canadian Consensus Guidelines Group on management of patients taking buprenorphine therapy in the perioperative period.

Collaborators: Saam Azargive, Karim Ladha, John Hanlon, Philip Peng, David Flamer, Wiplove Lamba, Joel Bordman, Collin Clarke, Meldon Kahan, Sanjho Srikandarajah, Harsha Shanthanna, Scott Dugan, Tania Di Renna, Hance Clarke

B1  Neurocognitive Functioning Following CPAP Treatment in Elderly Patients with Obstructive Sleep Apnea: A Metanalysis of Randomized Controlled Trials

Talha Mubashir – Research Assistant
UHN – Toronto Western Hospital

Background
Obstructive sleep apnea (OSA) is a common sleep breathing disorder that is associated with an increased risk of cognitive impairment in the elderly (1). A number of meta-analyses and review
studies have demonstrated a partial reversibility in cognitive dysfunction with continuous positive airway pressure (CPAP) therapy. Previous meta-analyses have included mostly middle-aged adults with OSA and assessed more specific components and processes of cognitive function, such as processing speed and verbal fluency (2-4). Our objective was to provide a quantitative synthesis of RCTs to determine if CPAP improves neurocognitive functioning in elderly individuals with OSA.

Methods
We searched PubMed, Embase, Cochrane Central Registry of Controlled Trials and electronically available conference abstracts to identify relevant studies with a publication date limit up to March 31, 2017. Inclusion criteria included: (1) RCTs, (2) elderly population (mean age≥60 years) with OSA, (3) CPAP as study intervention, and (4) the use of standardized neurocognitive assessment tools to measure performances in Complex Attention (CA), Executive Function (EF), Language (LA), Learning & Memory (LM) and Perceptual Motor Function (PMF). The primary outcome measure was the ratio of mean (RoM) between treatment and control groups (3) sham CPAP and 9 usual care) reflecting the change in neurocognitive outcome scores from baseline to the end of the trial. We performed stratified meta-analyses and meta-regression specified a priori.

Results:
Twelve RCTs totaling 879 elderly individuals with moderate-severe OSA were included. Seven studies had an elderly population with concomitant neurological comorbidities: stroke, Alzheimer's, or Parkinson's diseases. Our meta-analysis showed significant improvements in CA (1.42,95%CI 1.15-1.76,I2=39%), EF (1.80,95%CI 1.01-3.19,I2=88%) and PMF (1.75,95%CI 1.39-2.20,I2=59%) with CPAP treatment independent of the neurological comorbidities. Significant positive effects on neurocognitive functioning were also observed with longer nightly CPAP use (≥4h), severe OSA and obese populations. Those treated for 5-12 vs. 1-4 weeks demonstrated a positive dose-response relationship on EF. Finally, meta-regression analyses demonstrated CA (1.83,95%CI 1.25-2.70,meta-regression p=0.688), EF (1.63,95%CI 1.00-2.68,meta-regression p=0.62) and LM (2.16,95%CI 1.16-4.04,metaregressiop=0.834) improved significantly in individuals with OSA and stroke following CPAP therapy.

Conclusions
CPAP is effective in improving several components of neurocognitive function in elderly individuals with moderate-to-severe OSA, independent of the neurological comorbidities. Our findings provide an important framework for future studies to investigate the effect of CPAP on elderly OSA individuals in conjunction with various confounders, including treatment duration, CPAP adherence, BMI status, disease severity and co-morbidities.

References
1. JAMA. 2011; 306:613-619
Collaborators: Talha Mubashir, Jayadeep Patra, Elizaveta Oulman, Jean Wong, Clodagh M. Ryan, David F Tang-Wai, Sheila Riazi, Mandep Singh, David T. Wong, Frances Chung
**B2  Sensing Tissue Stiffness: New Therapies for Heart Failure and Cardiac Fibrosis**

**Julia Plakhotnik – Graduate Student**
The Hospital for Sick Children

**Background**
In the failing heart, contractility and relaxation are both impaired by stiffening of the tissue, resulting from progressive fibrosis. This tissue stiffening strains cardiac myocytes, further compromising mechanical function, and accelerating organ failure. The integrin-linked kinase (ILK) protein improves cardiac contractility by forming large protein complexes responsible for force-sensing. In tissue from highly stiff, failing hearts, we showed a depletion of key ILK interactions, notably, with the cell adhesion protein beta-parvin (parvB). We hypothesize that the ILK:parvB complex modulates cardiac myocyte function in response to pathologic stiffness, where cell strain is high, and that restoring this protein complex would improve heart function.

**Methods**
To model healthy and failing heart stiffnesses, human stem cell-derived cardiac myocytes were cultured as a 2D tissue on scaffolds of 5 (healthy adult) and 100 (failing, fibrotic) kPa. ILK:parvB complexes were quantified in-situ using the DuoLink proximity ligation assay. To evaluate the effect of parvB on myocyte function, contractile parameters were calculated from video particle tracking of spontaneous contractions with simultaneous recordings of intracellular calcium changes, via the cytosolic calcium dye FLIPR5.

**Results**
Stiff tissue scaffolds (100 kPa), mimicking heart failure, decreased ILK:parvB interactions by 41 ±6% (p value <0.05), which was reversed by increasing parvB cellular levels (p value 0.001). Pathologic stiffness adversely affected cardiomyocyte function, decreasing beat rate by 12 ±2% (p value <0.01), and increasing arrhythmogenicity (p value <0.05), which were corrected by parvB expression (p values <0.01). This cardiac-protective effect was in part due to parvB-dependent mediation of inotropic and lusitropic kinetics. 100 kPa stiffness delayed contraction kinetics and calcium-contraction coupling (inotropy) by 20 ±4% and 41 ±11%, respectively (p values < 0.001), which were mitigated by 9 ±4% and 50 ±10% (p values <0.01) via parvB expression. Moreover, 100 kPa stiffness delayed relaxation and calcium decay (lusitropy) by 32 ±2% and 23 ±6%, which were corrected by parvB expression (p values <0.01).

**Conclusions**
We showed how the ILK:parvB complex was decreased in models of fibrotic heart failure, consistent with our previous findings in human heart failure samples. Moreover, pathologic tissue stiffness diminished cardiac myocyte beat rate and rhythm, which was mitigated by the restoration of ILK:parvB complexes. This cardiac-protective effect was in part due to parvB-dependent mediation of contraction and relaxation kinetics at pathologic stiffness. This indicates that the ILK:parvB complex can modulate cardiac myocyte function at pathologic heart stiffness, presenting a novel therapeutic target for heart failure.

**Collaborators:** Henry Mah, Manpreet Malhi, Kyu Kim, Yousef Shafieyan, Alexandra Traister, Sarvatit Patel, Rachana Patel, Boris Hinz, John Coles, Jason Maynes
Effect of Internal Jugular Vein Compression on Intracranial Volume: A Transorbital Ultrasound Study of the Optic Nerve Sheath Diameter

Michael Dinsmore - Fellow
UHN- Toronto Western Hospital

Background
Concussions have become a growing epidemic in both competitive sports and recreational activities and incur significant personal and socio-economic costs [1]. It has been shown that mild jugular venous compression causes an increase in intracranial blood volume which may have a protective effect by minimizing brain “sloshing” within the cranium [2, 3]. A recent study on competitive football players has shown that wearing a neck collar reduces harmful microstructural brain changes following a concussion [4]. However, the effect of wearing a cervical neck collar on intracranial volume has not been demonstrated in the upright position. Therefore, the aim of this study was to investigate the effect of IJV compression on intracranial volume using transorbital ultrasound of the optic nerve sheath diameter (ONSD) as a surrogate of changes in intracranial volume [5].

Methods
Following Research Ethics Board approval and informed consent, healthy adult (>18 years) volunteers were recruited for a prospective observational study. Ultrasound measurements were performed on the right IJV cross-sectional area, and the change on right eye ONSD before and after application of IJV compression. Compression was achieved with a neck collar comprising two rectangular sponge pads (2 cm x 3 cm) designed to sit over the IJV’s. A 100 mL saline bag was attached to a calibrated pressure transducer, which was placed between the collar and the back of the volunteer’s neck, and the transducer was zeroed at the level of the pads. The neck collar was tightened by traction of the Velcro elastic straps until a pressure of 20 mmHg was achieved. All volunteers were in the sitting position and ultrasound of the IJVs was performed at the level of the cricoid cartilage cephalad to the neck collar. Statistical analysis was performed using a paired t-test with Bonferroni correction.

Results
Two independent investigators performed ultrasound measurements on ten healthy volunteers. Mean (SD) cross-sectional area for the right IJV at the level of the cricoid was 0.10 (0.05) cm² at baseline with a corresponding ONSD of 4.6 (0.5) mm. After application of the neck collar, IJV cross-sectional area increased to 0.66 (0.40) cm² with a corresponding increase of ONSD to 4.9 (0.3) mm which was significant when compared to the baseline value (P = 0.041) (Figure 1).

Conclusions
We present the first study to demonstrate that mild IJV compression in subjects in the sitting position increases the intracranial volume as demonstrated by an increase in ONSD. Therefore, our finding may support the use of a neck collar in minimizing the harmful effect of concussions.
References

Collaborators: Dr. Zak Hajat, Dr. Joseph Fisher, Dr. Lashmi Venkatraghavan
Optimizing Discharge Opioid Prescription for Major Joint Replacement Surgery: A Longitudinal Quality Assurance Survey

Rakhi Tilak – Research Assistant
St. Michael’s Hospital

Background
Opioid prescriptions for surgical procedures are generally standardized, despite differences in analgesic requirement. Prescriptions also vary between surgeons. As a result, some patients experience difficulties in achieving adequate pain control due to under-dosing, while others are left with unused opioid medications by the end of the treatment period. Some physicians may use immediate post-surgical opioid requirement to gauge the prescription needed after discharge. However, it is unclear if short-term increased requirements predict higher requirement post-discharge. This survey aims to examine current surgical prescription practices, assess whether we underprescribe or over-prescribe post-operative opioids and generate evidence to inform practice improvement.

Methods
Following institutional approval, opioid use in adult patients undergoing elective unilateral total hip arthroplasty (THA) or total knee arthroplasty (TKA) at St. Michael’s Hospital was assessed. Patients were followed prospectively for 12 weeks postoperatively. No changes were made to the management and opioid prescription practice by surgeons and surgical residents. The primary outcome was prescribed quantity and potency (calculated as oral morphine mg equivalent; MME) and amount of opioid medication left unused (MME). Secondary outcomes included patient satisfaction, duration of opioid prescription, and patients requiring additional opioid management. All data are presented as mean ± standard deviation.

Results
Postoperative opioid requirement and prescription data has been collected on 459 patients within 24 hours, 253 patients at 2 weeks, 219 patients at 4-6 weeks, and 149 surveys at 12 weeks postoperatively. Discharge MME was 515±281 mg, with no difference between THA (513±275 mg) and TKA (512±279 mg). Patient satisfaction score for the opioid pain prescription in the 2-week surveys was 7.28/10. On average, 22.7 tablets (MME = 311mg) remained unused per patient (28 for THA and 14 for TKA). However, 25.8% of patients were already completely out of medication (15% of THA and 42% of TKA) but only 15.8% of patients got additional prescription opioid when they ran out of medication.

Conclusion
Risk of over and under prescribing opioids postoperatively continues to challenge clinicians. These data indicate that a large amount of postoperative opioid prescriptions remains unused (MME = 330 mg). While about 20 % of patients required none or 1-2 days of opioid treatment after TKA and THA, over 40% of patients still require opioid analgesic 2 weeks after surgery. TKA patients required a longer period and higher dose of opioid analgesics, suggesting that THA patients generally require lesser amount of opioid analgesic than TKA patients. Reducing the amount of opioid prescribed for THA coupled with use of non-opioid analgesic may be an effective for postoperative pain management.
B5 • Effects of human umbilical cord perivascular cell conditioned media in a model of traumatic brain injury in adult

Eileen Liu – Graduate Student
St. Michael’s Hospital

Background
Traumatic brain injury (TBI) is a leading cause of mortality and morbidity worldwide. The pathophysiology of TBI is classified into primary injury, the initial external physical impact to the head, followed by secondary injury, which involves a cascade of biological events that can further neuronal damage. A novel, closed-head model of mild TBI (mTBI) was developed using adult zebrafish and targeted, pulsed high-intensity focused ultrasound (pHIFU) as a medium- to high-throughput system to evaluate therapeutic candidates. Stem-cell-based therapies have been demonstrated to have the potential to directly target the cascades of secondary brain injury. In the current study, we evaluate mesenchymal stem cells (MSC) derived from the human umbilical cord perivascular cells (HUCPVC). HUCPVCs are a progenitor cells that can be isolated from umbilical waste material after birth and have a greater proliferation capacity when compared to the other MSCs. A proteomic analysis demonstrated that the secretome of HUCPVCs include antiapoptotic, antioxidative, antiexcitotoxic, and neurite growth factors.

Methods
All experiments were approved by the St. Michael’s Hospital Research Ethics Board and complied with the guidelines established by the St. Michael’s Hospital Animal Care Committee and Canadian Council on Animal Care. Adult zebrafish were grouped into four treatment groups: sham, pHIFU
injury, pHIFU injury with basal media, and pHIFU injury with HUCPVC conditioned media. Injuries were induced under anesthesia by targeted pHIFU at the zebrafish brain at an intensity of 11MPa and 50msec in duration. The basal media and HUCPVC conditioned media were delivered retro-orbitally 1-hour post-injury. Behavior recordings and tissue extractions were performed at 6-, 12-, and 24-hours post-injury. The behavior was evaluated with the Novel Tank Test to measure their stress and anxiety levels. Western blot and immunohistochemistry were performed to observe and quantify for cellular and morphological changes.

**Results**

Injury induced by the pHIFU has significantly altered the behavior of the adult zebrafish on their total distance traveled (p<0.01), mean velocity (p<0.01) and percent immobile (p<0.01). Further quantitative data regarding the impact of HUCPVC conditioned media on the adult zebrafish mTBI model will be available for presentation at Shields Day.

**Conclusions**

This study investigates the potential of the adult zebrafish mTBI model for the rapid evaluation of different therapeutic options on the cascades of secondary brain injury. Additionally, this study also investigates the potential of the HUCPVC conditioned media as a potential therapeutic option for secondary brain injury. This is a work in progress.

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**B6 • Development of a High-Fidelity Novel Training Model for Dynamic Trans-orbital Ultrasonography of Optic Nerve Sheath Diameter**

**Zakir Hajat - Fellow**

UHN – Toronto Western Hospital

**Background**

Transorbital ultrasound measurement of optic nerve sheath diameter (ONSD) has been shown to be a bedside, non-invasive technique for measurement of raised intracranial pressure (ICP). This technique can be quickly learned by novice operators; however, achieving competency requires numerous practice scans on patients (1, 2). To avoid the theoretical risk to patients, training models can be an effective educational tool. However, the current training models are unrealistic and can only providesingle static ONSD measurements (3). Therefore, the aim of this study was to develop a high-fidelity training model for measuring ONSD, and to test the reliability and reproducibility over a wide range of simulated ICP values.

**Methods**

Research Ethics Board approval was exempt for this study as there were no human subjects. A dynamic ONSD model was designed and constructed using a hemispherical table-tennis ball, mounted onto a 3.0 mm pediatric micro-cuffed endotracheal tube (ETT), to represent the globe of the eye attached to the optic nerve. The saline-filled cuff was attached to a 1.0 mL syringe allowing the user to manipulate the ONSD in real-time by inflating the cuff to 0.1, 0.2, and 0.3 mL representative of normal, borderline, and raised ICP (Figure 1A). Statistical analyses were performed using SPSS Software.
Results
Two independent investigators each performed 10 randomized and blinded ONSD measurements at 0.1, 0.2, and 0.3 mL ETT cuff volumes. Mean (SD) measurements for investigator 1 were 4.7 (0.2), 5.7 (0.1), and 6.4 (0.2) mm (Figure 1B). Investigator 2 measurements were 5.1 (0.3), 5.9 (0.2), and 6.8 (0.3) mm. Combined investigator 95% confidence interval (P < 0.05) was 4.8-5.0, 5.7-5.9, and 6.5-6.8 mm, respectively. Intra-class correlation coefficient (Cronbach’s Alpha) were 0.89, 0.89, and 0.91. The median ONSD inter-observer difference was 0.3 mm (IQR 0.3-0.4 mm).

Conclusion

Collaborators: M. Dinsmore, L. Venkatraghavan, A. Niazi
Preoperative anemia increases the risk of blood product transfusion in children undergoing spine surgery.

Montserrat Fontanals - Fellow
Hospital for Sick Children

Background
Anemia has been identified as an important modifiable risk factor for transfusion in a variety of adult surgical populations. The objective of our study was to assess a potential association between preoperative anemia, transfusion, and outcome in children and adolescents undergoing spine surgery.

Methods
After ethics approval, we performed a retrospective analysis of children and adolescents included into the American College of Surgeons National Quality Improvement Program pediatric database who underwent spine surgery between January 1st 2012 and December 31st 2016. We used the reference values for children and adolescents published in the textbook Nathan and Oski’s Hematology of Infancy and Childhood to define anemia. Patients with bleeding/hemostasis disorders were excluded, as well as children transfused preoperatively. We reviewed demographic and surgical characteristics, the incidences of blood product transfusion and postoperative complications (postoperative mechanical ventilation, infection, readmission, hospital length of stay (LOS), 30-day mortality). Uni- and Multivariable logistic regression analysis were used to identify independent predictors for transfusion and postoperative complications associated with anemia and transfusion.

Results
We included 9,095 patients in our analysis. 81% of the patients were 12 years old or older, and 70% were female. Preoperative anemia was observed in 14% of the population and 67% of the patients included were transfused. Our multivariable logistic regression showed that anemia, surgical time >350 min, more than 7 vertebral levels fused, neuromuscular disease and cerebral palsy were independent predictors of blood product transfusion (Table 1). After adjustment for confounding variables, anemia was independently associated with prolonged LOS (Adjusted OR: 1.31, 95%CI: 1.11-1.54, p=0.001). The incidences of postoperative mechanical ventilation (p<0.001), infection (p=0.001), hospital readmission (p=0.01) and 30-day mortality (p=0.03) were increased in patients transfused.

Table 1. Multivariate Analysis of factors associated with blood product transfusion

<table>
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<th>Odds Ratio</th>
<th>95% Conf. Interval</th>
<th>P value</th>
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<tbody>
<tr>
<td>Anemia</td>
<td>1.52</td>
<td>1.32</td>
<td>1.75</td>
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<tr>
<td>Neuromuscular disease</td>
<td>1.52</td>
<td>1.34</td>
<td>1.74</td>
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<tr>
<td>Cerebral palsy</td>
<td>1.62</td>
<td>1.32</td>
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Conclusions
In our study, preoperative anemia was associated with an increased risk for blood product transfusion and prolonged LOS in children and adolescents undergoing spine surgery. Transfusion was also associated with higher incidences of postoperative complications. Further studies are needed to determine if preoperative treatment of anemia could help reduce the need for intraoperative transfusion.

Collaborators: James O’Leary, Christian Zaourour, Teresa Skelton

B8 •  The Pattern and Distribution of Body Fluid During Pregnancy: A Systematic Review and Meta-Analysis

Julia Pasquale – Medical Student
UHN – Toronto Western Hospital

Background
Weight gain during pregnancy has been associated with plasma volume expansion, increased cardiac output and retention of sodium and water [1]. Total body water (TBW) increase is likely to be greater in women with pregnancies complicated by gestational hypertension and preeclampsia; in addition increased fluid states and rostral fluid shift have been associated with sleep disordered breathing [2]. In this systematic review and meta-analysis, we aimed to evaluate the pattern and distribution of body water during pregnancy in healthy women and those with hypertensive disorders of pregnancy (HDP).

Methods
Electronic literature search of Medline, Embase, Cochrane Database of Systematic Reviews databases and conference abstracts was conducted for the period of 1946 to March 2017. We included studies that used bioelectrical impedance analysis to investigate TBW, extracellular water (ECW), intracellular water (ICW) and thoracic fluid content (TFC) during pregnancy in healthy women and those with HDP. Meta-analysis for longitudinal changes in healthy pregnancies was performed by fitting a random effect model, accounting for variations between studies. The pooled slope of TBW change over time was estimated by Markov Chain Monte Carlo method. Meta-analysis for the comparison of TBW, ECW, ICW and TFC values during third trimester in healthy pregnancies and HDP was performed by pooling the standardized mean differences (Cohen’s d) from each study and fitting a random effect model.

Results
A total of 1784 articles were screened, of which 21 studies were included in this meta-analysis (healthy pregnancies 17 studies [n=1759 patients] HDP 7 studies [n=759 patients]). We found that TBW increased across studies from pre-pregnancy period until delivery in healthy women. The pooled estimate of the slope of TBW change was statistically significantly increased by 0.168L (95% highest posterior density 0.038-0.307L) for every 1-week increase in gestational age (Fig 1a). The
pooled estimates for mean TBW (Cohen's d=0.351; 95%CI -1.504-2.207), ECW (Cohen's d=0.375;95%CI -4.347-3.597), ICW (Cohen's d=0.156;95%CI -0.671-0.983) and TFC (Cohen's d = 1.001;95%CI -0.219-2.220) were not significantly different between healthy and HDP patients. However, the mean TBW (Cohen's d=1.049;95%CI 0.270-1.828]) and ECW (Cohen's d=0.823; 95%CI 0.25-1.395) in women with HDP were significantly higher than healthy pregnancies when patients with gestational hypertension and no edema were excluded (Fig 1b).

Figure 1a. Forest plot indicating changes in total body water (TBW) slope, across each study (Fig 1a) in healthy pregnancies. The pooled estimates were statistically significant, as the 95% highest posterior density estimates did not include zero. Figure 1b. Forest plot indicating difference in TBW between healthy and hypertensive pregnancies (Fig 1b). The pooled estimates for Cohen’s d were statistically significant (the 95% CI did not include zero), after exclusion of patients with HDP and no edema (see text for explanation).

Conclusion
Our study shows that TBW increases with increasing gestational age in uncomplicated pregnancies. Furthermore, pregnancies complicated by hypertensive disorders with edema show increased TBW and ECW compared to those with uncomplicated pregnancies. This may explain in part a higher incidence of complications such as pulmonary edema and sleep disordered breathing seen in some women with HDP.

Collaborators; Eugene Yoon and Sally Hu

B9 • Systematic Review of the saddle block for perianal ambulatory patients

Carla Todaro • Fellow
UHN – Toronto Western Hospital

Background
The use of low dose spinal anesthesia for ambulatory perianal surgery has gained popularity in recent years. The patients undergoing perianal ambulatory surgery require a rapid onset of action of spinal anesthesia (saddle block) with adequate sensory block and a rapid recovery from the motor block postoperatively. 1 The primary objective was to define a minimum low dose of local
anesthetic to achieve successful saddle block. The secondary outcomes were mean onset time, duration of sensory block, mean motor regression time and void time.

Methods
The literature search was performed according to PRISMA guidelines 2 by an expert librarian familiar with literature search. The inclusion criteria in our review were: 1) adult surgical patients (>18 yr), 2) ASA physical status I-III, 3) undergoing perianal surgery, 4) under saddle block, 5) only English articles. The block was considered successful when the surgery was conducted only under saddle block, without need for GA or additional local anesthetics or analgesics. The secondary objectives were: evaluation of the mean onset time of sensory block and motor block, time to void postoperatively, evaluation of readiness to discharge and discharge time from the hospital.

Results
The initial search yielded 1396 citations. After deduplication and screening of the abstracts and titles, 67 articles were reviewed. After reading full texts and removing all case reports, 13 studies were found suitable to be included for this systematic review. All the studies were clinical trials (12 randomized and 1 not randomized). According to the studies analyzed we found that 9 out of 13 studies clearly defined the condition of "block success" as the ability to have surgery without the requirement for additional analgesia or conversion to GA. Using this criteria, we found a 97 % success rate using low dose local anesthetics. The mean onset time, duration of sensory block, mean motor regression time and void time are summarized in Table 1 and 2. The reported causes of block failure were: inadequate analgesia, adverse anatomical conditions and impossible dural puncture. The forest plot (Figure 1) suggests that low-dose of both long-acting and short-acting local anesthetics similarly expedite discharge compared to high doses of long-acting and short-acting local anesthetics a dosage of 5 mg for long acting low dose and 20 mg for short intermediate acting low dose are reliable for a successful saddle block.

Conclusion
This study suggests that the use of low dose local anesthetics for saddle block is reliable, in particular by using long acting low dose local anesthetic, the mean void time and mean motor regression time are significantly faster than in the other categories. Based on the available literature, we found that a saddle block, using bupivacaine 5 mg can achieve reliable surgical anesthesia with a favorable recovery profile for ambulatory perianal surgery.
Bibliography


Collaborators: Carla Todaro, Andrew Grant, Faraj Abdallah Richard Brull,
B 10 † Differential cardiovascular response following hemodilution with colloid versus crystalloid

Nikhil Mistry – Research Assistant
St. Michael’s Hospital

Background
Controversy exists as to the optimal fluid for intravascular volume resuscitation during acute blood loss in critical care settings. Results from recent trials have limited colloid and red blood cell utilization, leaving crystalloid as the primary intraoperative resuscitation fluid (1-3). We assessed both colloid and crystalloid resuscitation protocols in terms of their impact on cardiovascular parameters and tissue perfusion. We hypothesize that hemodilution with colloid will be no different than crystalloid in maintaining cardiac output, mean arterial pressure (MAP), and tissue perfusion following acute hemodilution.

Methods
Following institutional animal care committee approval, Sprague Dawley rats (400-600g) were block-randomized to either 40% isovolemic hemodilution with colloid (1:1 hydroxyethyl starch or albumin), vs. crystalloid (3:1 saline), or a sham procedure (control) (n=4 for all). Anesthetized rats (2% isoflurane) underwent hemodilution by exchanging blood for infused solution via the tail artery and vein over a 10 minute period. Heart rate, MAP, and core temperature were monitored continuously. Hemoglobin concentration, arterial/venous blood gases, and echocardiogram data were measured at baseline, 30, and 60 minutes post-hemodilution. Echocardiogram outcomes were evaluated in a blinded fashion.

Results
Hemoglobin levels were lower following hemodilution with colloid versus crystalloid (69±9g/L vs. 85±11g/L; p<0.001). Post-hemodilution MAP was comparable between both groups (66±11mmHg vs. 74±8mmHg; p=0.46). At 60 minutes, lactate values were higher in the colloid group (2.2±0.4mmol/L) relative to the crystalloid group (1.6±0.3mmol/L; p<0.03). Hemodilution with colloid increased left ventricular mass (p<0.05 vs. crystalloid), fractional shortening (p=0.03 vs. control), and cardiac output (p=0.01 vs. crystalloid). There were no differences in other cardiovascular parameters.

Conclusions
Both resuscitation protocols maintained blood pressure. Following hemodilution with colloid, the relative increase lactate suggests that there was inadequate tissue perfusion despite the increase in cardiac output. By contrast, crystalloid resuscitation resulted in maintenance of cardiac output and no increase in systemic lactate, suggesting that tissue perfusion was adequate. These data argue against our hypothesis and suggest significant differences in cardiac output and tissue perfusion following hemodilution with colloid and crystalloid. These findings suggest that resuscitation to hemodynamic targets (cardiac output) may not be indicative of adequate microvascular tissue perfusion.

Study support: AHSC AFP (SMH-17-014 to GMTH)

References
B 11+ Incidence and recovery of recurrent laryngeal nerve injury in children with biventricular physiology following aortic arch surgery: a retrospective cohort study

Minako Sano - Fellow
Hospital for Sick Children

Objective
Recurrent laryngeal nerve (RLN) injury can cause vocal cord paralysis (VCP) or dysfunction, contributing to swallowing dysfunction and increased risk of aspiration. The primary aims of this study were to examine the incidence, characteristics, and recovery of RLN injury after aortic arch surgery in children with biventricular physiology; secondary aim was to examine the direct cost of RLN injury in this population during the same hospital admission.

Methods
With Research Ethics Board approval, all children (aged <18 years) with biventricular physiology who underwent aortic arch surgery with cardiopulmonary bypass from 2005 to 2016 at The Hospital for Sick Children, Toronto, were included in this retrospective cohort study. VCP was defined as complete immobility of a vocal cord during awake flexible fiberoptic laryngoscopy. Between group analyses were performed using Wilcoxon rank sum test for continuous data and Fisher’s exact test for categorical data. Direct costs (adjusted for inflation) were modeled using generalized linear models with a Gamma distribution for the dependent variables.

Results: A total of 226 patients were included in the analysis. The incidence (95%CI) of VCP was 26.2 (20.6% to 32.5%). Fifty one percent of patients with long-term follow-up (n =19 /37) did not have functional recovery of vocal cord function. Children with VCP had a lower weight, increased duration of intubation, and longer postoperative ICU and hospital lengths of stay (LOS) compared with children without VCP. The VCP group had a higher risk of aspiration (86.4% vs. 12.1%; P<0.001) and alternative feeding regimen requirements (93.2% vs. 21.1%; P<0.001) compared with the non-VCP group. Unadjusted direct hospital costs were higher in the VCP group ($75,139 vs. $54,149; P<0.001), but after adjusting for pre-operative confounding factors (gestational age at birth, age on day of surgery, pre-operative ventilation, pre-operative ICU LOS) there was no statistical difference between groups (P=0.06). The predicted mean (95%CI) direct cost for children with and without VCP was $99,303 ($79,187 to $119,420) vs. $78,600 ($66,889 to $90,311), respectively.

Conclusions
For children with biventricular physiology who underwent aortic arch surgery, over a quarter of children developed VCP and more than half of these did not have long-term recovery. Low weight at surgery was associated with increased risk of VCP, and children with VCP had increased risks of aspiration and feeding difficulties. VCP is a common complication after aortic arch surgery, these data will contribute to future strategies for risk mitigation and management.

Collaborators: Minako Sano, James D. O’Leary, Christoph Haller, Chavisa Rassameehirun, Evan J. Propst, Priscilla Chi, Samuel Fung, Michael-Alice Moga, Osami Honjo
B 12+  Adverse Heart-Lung Interactions in Ventilator-Induced Lung Injury

Bhushan Katira - Fellow
Hospital for Sick Children

Background
The original in vivo study of ventilator-induced lung injury by Webb and Tierney (1974) showed that high VT (or driving pressure) with zero PEEP caused overwhelming lung injury, thought to be due to lung shear stress resulting in high permeability edema. The precipitous nature of the edema (in 45/0); prompted us to wonder about a cardiac contribution. We therefore reproduced the experiments and determined the effect and contribution of ventricular function in this model of VILI.

Objective
To reproduce the lung injury and edema in the ‘Webb and Tierney’ study and investigate the underlying mechanism thereof.

Methods
Study was conducted in 5 series of experiments. In Series 1, Sprague-Dawley rats (≈400 g) received mechanical ventilation for 60 min according to the protocol of Webb and Tierney (Groups as per airway pressure; 14/0, 30/0, 45/10, 45/0 cmH2O). Additional experimental series were conducted for groups 45/0 and 45/10 only (20 min duration, to ensure survival of all animals survived), to assess microvascular permeability (Series 2; 4/group), echocardiography (Series 3; 4/group); and right (Series 4; 5/group) and left ventricular pressure (Series 5; 4/group). MEASUREMENTS AND MAIN RESULTS: In Series 1, the original Webb & Tierney results were replicated in terms of lung/body weight ratio (45/0 > 45/10 ≈ 30/0 ≈ 14/0; P<0.05), and histology. In 45/0, pulmonary edema was overt and rapid, and survival <30 min. Microvascular permeability and lung water increased in 45/0 (not in 45/10; Series 2). In 45/0, there was cyclical abolition of pulmonary blood flow (Series 3) and significant reduction of right ventricular systolic pressure (Series 4) with each breath. Over 20 min. there was progressive right ventricular dilation and reduction in ventricular function (Series 3, 4; Figure 1). The left ventricular end-diastolic pressure (effective transmural) progressively increased in 45/0 (not in 45/10; Series 5, Figure 2).

Collaborators: RE Giesinger, D Engelberts, D. Zabini, A Kornecki, G Otulakowski, T Yoshida, WM Kuebler, PJ McNamara, KA Connelly, BP Kavanagh
Conclusions
In a classic model of ventilator-induced lung injury, high peak pressure (and zero positive end-expiratory pressure) causes respiratory swings (obliteration during inspiration) in right ventricular filling and pulmonary perfusion, ultimately resulting in right ventricular failure and dilation. Pulmonary edema was due to increased permeability, which was augmented by a modest (approximately 40%) increase in hydrostatic pressure. The lung injury and acute cor pulmonale is likely due to pulmonary microvascular injury, the mechanism of which is uncertain, but likely due to cyclic interruption and exaggeration of pulmonary blood flow.

B 13+ Relative efficacy of TIVA and adjuvant intraoperative dexmedetomidine in reducing emergence delirium in children: a network meta-analysis
Introduction
Emergence delirium (ED) occurs in 12-18% of pediatric general anesthetics (GA) and is associated with adverse effects including injury to the child and surgical site, parental anxiety and dissatisfaction, increased nursing care and additional healthcare costs. The use of a total intravenous anesthetic (TIVA) technique and the intraoperative use of dexmedetomidine as an adjuvant to a gas-based anesthetic have each been shown to reduce the incidence of ED compared to sevoflurane, but no studies have directly compared their relative efficacy. The aim of the current study is to conduct a systematic review and network meta-analysis of existing randomized controlled trials (RCTs) to compare the effect of TIVA to that of intraoperative dexmedetomidine as an adjuvant to a sevoflurane-based GA on the incidence of ED in a pediatric population.

Methods
REB approval was not required for this study. We conducted a systematic search of 11 databases. Inclusion criteria were RCTs of pediatric patients < 18 yo undergoing GA for surgery or diagnostic procedures using sevoflurane, sevoflurane with intraoperative use of adjuvant dexmedetomidine, or TIVA. Data extracted from eligible RCTs were analyzed according to network metaanalysis methodology using a Bayesian Markov Chain Monte Carlo approach. Odds ratios (OR) and 95% credible interval (Crl) were calculated. Secondary outcomes included postoperative nausea and vomiting (PONV) and time to emergence and extubation.

Results
The systematic literature search returned 57 studies comprising a total of 945 patients in the dexmedetomidine group, 1195 in the TIVA group and 1978 in the sevoflurane group. TIVA and sevoflurane with intraoperative use of adjuvant dexmedetomidine were both associated with significantly less ED than sevoflurane alone (OR = 0.25, 95% Crl 0.16-0.39; high quality of evidence, OR = 0.17, 95% Crl 0.11-0.24; high quality of evidence, respectively). Indirect comparison of the primary outcome showed that sevoflurane anesthetic with intraoperative use of adjuvant dexmedetomidine seemed to be superior to TIVA in the incidence of ED, but it was not statistically significant (OR = 0.66, 95% Crl 0.36-1.17; low quality of evidence).

Conclusion
The results of the study indicate that the intraoperative use of dexmedetomidine as an adjuvant to sevoflurane-based general anesthetic and TIVA are equivalently effective as prophylaxis against ED and PONV in children. We suggest that children undergoing general anesthesia may be better to receive intraoperative dexmedetomidine as an adjuvant to sevoflurane, to decrease incidence of ED. However, these findings are limited by the overall low quality of evidence (conditional recommendation). For future research on this topic, direct comparison and cost-effectiveness analyses of these two interventions may be appropriate.

Collaborators: Marina Englesakis, Jason Maynes, Petros Pechlivanoglou, Kazuyoshi Aoyama
Exubation in the operating room and use of healthcare resources after pediatric cardiac surgery: A retrospective cohort

Mehr Jain – Medical Student
Hospital for Sick Children

Background
Early extubation after pediatric cardiac surgery is being used increasingly by healthcare providers with the aim of improving postoperative outcomes and use of healthcare resources[1]. Recent advances in anesthesia management, such as the use of ultra-short-acting opioids, have allowed anesthesiologists to consider extubation in the operating room (OR) as feasible[2], while still minimizing the stress response to surgery[3]. The aim of this study was to examine the association between extubation in the OR and use of healthcare resources (primary outcome: postoperative length of hospital stay (LOS); secondary outcome: hospital cost).

Methods
With REB approval, data (demographic, perioperative, and direct hospital costs [inflation adjusted]) were collected for 307 eligible children who underwent cardiac surgery between 2009 and 2016 at the Hospital for Sick Children, Toronto, who were either extubated in the OR (n = 152) or within 24 hours of ICU admission (n = 155). Postoperative LOS (primary outcome) was modeled as an over-dispersed Poisson variable using a negative binomial regression model and reported using an incident rate ratio (IRR); direct cost was modeled using a generalized linear regression model with a Gamma distribution. Statistical significance was defined as (two-tailed) P < 0.05. All statistical analyses were performed using STATA 13 (STATAcorp LP, Texas, USA).

Results
Characteristics of children included in the cohort are described in the Table. After adjusting for confounding factors, (age, RACHS [risk adjustment for congenital heart surgery] score, operative time, and cardiopulmonary bypass time), postoperative LOS was significantly lower in children who were extubated in the OR (IRR 0.74; 95%CI, 0.61 to 0.88; P = 0.001) and predicted mean [95%CI] direct costs were also lower in children who were extubated in the OR compared with children who were extubated within 24 hours of ICU admission, $23,663 ($19,784 to $27,542) vs. $34,902 ($30,336 to $39,468) (P<0.001).

Table. Characteristics of children (n = 307) included in the cohort, classified by time of extubation.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Extubated in the OR</th>
<th>Extubated in ICU within 24hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (interquartile range), unless specified</td>
<td>N = 152</td>
<td>N = 155</td>
</tr>
<tr>
<td>Age (days)</td>
<td>1,572 (420 to 3533)</td>
<td>201 (150 to 741)</td>
</tr>
<tr>
<td>Male, n(%)</td>
<td>93 (61.2)</td>
<td>87 (56.1)</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>15.8 (8.9 to 27.5)</td>
<td>6.7 (5.5 to 10.5)</td>
</tr>
<tr>
<td>RACHS category, n(%)</td>
<td>1</td>
<td>22 (14.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 (1.9)</td>
</tr>
</tbody>
</table>
2 90 (59.2) 103 (66.5)
3 36 (23.7) 39 (25.2)
4 1 (0.7) 4 (2.6)
5 0 (0.0) 0 (0.0)
6 0 (0.0) 2 (1.3)
Uncategorized 3 (2.0) 4 (2.6)

Previous cardiac surgery 55 (36.2) 50 (32.3)
CPB time (min) 78 (62 to 102) 108 (79 to 138)
Cross-clamp time (min) 51 (25 to 72) 73 (48 to 102)
DHCA, n(%) 5 (3.3) 9 (5.8)
Dexmedetomidine, n(%) 57 (37.5) 17 (11.0)
Reintubation in the OR 4 (2.6) n/a

ICU, intensive care unit; RACHS, risk adjustment for congenital heart surgery; CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest; OR, operating room

Conclusions
After adjusting for covariates, extubation in the OR was associated with decreased healthcare use (postoperative LOS and direct hospital costs) compared with children who were extubated within 24 hours of ICU admission. This approach can be cost effective and should be considered for select patients undergoing cardiac surgery to improve access to hospital resources.

References

Collaborators: Anne-Marie Leo, Sayaka Nakamura, David Faraoni, Osami Honjo, Alejandro Floh, Vannessa Chin, James O’Leary

B 15+ Seasonal Variation Amongst Incidence Of Hypothermia in Severely Ill Trauma Patients

Kennedy Ning Hao – Medical Student
Sunnybrook Health Sciences Centre

Background
Major trauma is the leading cause of death in up to 10% of all deaths worldwide. The morbidity and mortality of acute severe trauma has been shown to be exacerbated by hypothermia (<36 °C) in the severely ill trauma patients. When compared to normothermic patients with similar ISS, injured
patients with hypothermia have significantly increased mortality. Early prevention and management of hypothermia is crucial as reducing the severity and duration of hypothermia has also been shown to result in an increased possibility of successful resuscitation and survival. Currently, however, it is unknown whether a pattern of seasonal hypothermia exists for severely injured trauma patients which may affect hypothermia recognition and management.

Methods
Time series were constructed from retrospective data on critically ill trauma patients collected between 2010 and 2015 inclusively at Sunnybrook Health Sciences Centre. Patients who had missing temperature data or who had their first temperature taken in the trauma bay (TB) past two hours of admission were excluded; 718 of all 1153 patients were included in the study. Temperature data taken upon initial admission to the TB was used to study hypothermia incidence over time; summary metrics were derived over monthly periods. We conducted statistical decomposition using a moving average model to estimate trend, and used this model to estimate seasonal trends for hypothermia across the studied time period. Data were normalized to adjust for monthly differences in patient intake.

Results
The mean age of the included patients was $\mu \pm SD = 41.31 \pm 18.57$. The mean temperature of the patients was $\mu \pm SD = 35.31 \pm 1.03$, and 53.6% of patients were hypothermic upon arrival to TB. We used the constructed time series in order to estimate patterns of seasonality in hypothermia instances. There were slightly increased hypothermic events per patient per month in the summer compared to winter in the estimated seasonal trends. However, there was no significant difference seen in the normalized counts of hypothermia patients between winter and summer months ($p = 0.467$).

![Decomposition of Normalized Hypothermia Events](image-url)
Conclusion
Early prevention and treatment of hypothermia is critical in severely ill trauma patients regardless of the season. The importance of managing hypothermia in the summer tends to be underestimated, and increased awareness is necessary for better patient outcomes.

Collaborators: Hao, Kennedy; Au, Shelly; Callum, Jeanie; Pannell, Dylan; Tien, Homer; Alam, Asim

Sleep Study Parameters for Predicting Perioperative Complications in Patients with Obstructive Sleep Apnea: A Review

Colin Suen - Resident
UHN – Toronto Western Hospital

Background
Obstructive sleep apnea (OSA) is a common sleep-breathing disorder. In the perioperative setting, OSA is a challenging diagnosis as it has been associated with an increased risk of post-operative complications including cardiac and pulmonary complications, difficult intubation, increased resource utilization and in rare instances, death. For perioperative risk stratification, it is unclear whether specific parameters in polysomnography (PSG) or pulse oximetry are associated with postoperative complications in patients with OSA. The objective of this narrative synthesis is to evaluate the literature on the practical interpretation of parameters in polysomnography or pulse oximetry to assess the severity of OSA for perioperative risk stratification.

Methods
For this narrative synthesis, we obtained pertinent articles from Ovid MEDLINE®, Ovid MEDLINE® In-Process & Other Non-Indexed Citations in the past ten years (2008 to December 2017) and EMBASE, using a search method designed by an information specialist and manual searches. The comprehensive search included terms for ‘Obstructive Sleep Apnea’ and “Sleep Assessment” and ‘Postoperative and Adverse Effects”. The search was restricted to English language articles, and studies involving adults. To supplement our database searches, a citation search of references from primary or review articles was also performed. Irrelevant papers were excluded by title and abstract review.

Results
The search yielded 1,810 papers, of which 21 were included in the review. Preoperative apnea hypopnea index (AHI) and measurements of nocturnal hypoxemia such as oxygen desaturation index (ODI), cumulative sleep time percentage with SpO2 < 90% (CT90), minimum SpO2, mean SpO2, and longest apnea duration were associated with perioperative complications. Newer parameters being studied are total apnea duration and obstruction severity, which are potentially useful in identifying patients with high arousal threshold who may be at increased risk.

Conclusion
OSA is an important risk factor for perioperative complications in the surgical population. Significant association between AHI and postoperative adverse events exists. Complications may be more likely to occur in the category of moderate-to-severe OSA (AHI ≥ 15). Other sleep study parameters such as ODI, CT90, mean and minimum SpO2, and longest apnea duration have been shown to be associated with post-operative complications and may provide additional values in
risk stratification. Further research is necessary to validate the utility of existing and new sleep study parameters in the perioperative setting.

Collaborators: Lusine Abrahamyan and Jean Wong

B 17* Differential effect of dexmedetomidine on intracranial EEG recordings from human hippocampus and neocortex

Joshua Bennitz - Fellow
UHN – Toronto Western Hospital

Background
Dexmedetomidine (DEX), a selective α2 receptor agonist, produces sedation similar to natural sleep with minimal respiratory depression.1 DEX has been shown to have a neuroprotective effect with decreased incidence of postoperative delirium and cognitive dysfunction.2 Currently, knowledge about the effects of DEX on brain activity is derived from scalp EEG with little known about its effects on subcortical structures, especially the hippocampus.3 Understanding the intracranial EEG (iEEG) effects of DEX may provide important information regarding its unique properties. The aim of our study was to compare the effects of DEX on the iEEG spectrum from the temporal lobe neocortex and hippocampus.

Methods
After REB approval and informed patient consent, patients who had bilateral insertion of intracranial electrodes for epilepsy were recruited. This study was conducted during removal of electrodes under DEX sedation (1μg/kg bolus over 10 minutes). All patients had unilateral epilepsy and iEEG data were collected from the non-epileptogenic side. Continuous iEEG recordings were acquired at 5 kHz (0.05-1kHz band pass filter) from 10 minutes before to 10 minutes after the DEX bolus. Baseline spectra were compared to spectra obtained after DEX bolus from hippocampal and neocortical electrodes. Data were analyzed using MATLAB (Natick, MA, USA).

Results
Power spectra were computed from a total of 209 electrodes in 5 patients. Compared to baseline, there was a qualitative increase in power in the 0-10Hz ranges with DEX and a peak difference at 8Hz. DEX significantly increased the iEEG power in the delta (0-4Hz; p=<0.001), theta (4-8Hz; p=0.02) and alpha/spindle (8-16Hz; p<0.001) frequency ranges (Figure 1). There were no differences in the power spectrum in the neocortex (p=0.88) and hippocampus (p=1.0) with DEX compared to baseline. More importantly, there were no changes in the theta power in the hippocampus with DEX.
Conclusion
This is the first study to look at the effect of DEX on the human hippocampus. The hippocampus is important in cognition and memory formation, and is active during REM sleep. In the hippocampus, theta waves are known to coordinate memory, spatial navigation, and behavior. Most anesthetic agents are known to abolish theta and increase alpha waves. Our study showed that DEX preserves the theta waves in the temporal neocortex and hippocampus. This finding might explain the unique properties of DEX on memory and cognition.

References
3. Anesthesiology. 2014;121:978-989

Collaborators: Pasarikovski CR, Valiante TA
**Comparison of cost and outcomes for minimally invasive percutaneous versus surgical paddle lead implantation for spinal**

**Pranab Kumar - Fellow**
UHN – Toronto Western Hospital

**Background**
Spinal cord stimulation (SCS) is used to treat intractable chronic pain with an exponential increase in use of SCS over the last two decades. Two approaches - surgical paddle lead implantation involving laminotomy (SurgSCS) and minimally invasive implantation of cylindrical leads (MISCS) – are used for SCS implants. While the laminotomy paddle lead implantation is the commonest approach in Canada, our centre is now using the MISCS approach performed by pain physicians for most SCS implants.

**Methods**
After obtaining Institutional Review Board approval, a retrospective chart review of outcomes of SCS procedures performed at the Toronto Western Hospital using the two approaches (SurgSCS and MISCS) from January 2015 to February 2018 was performed. The data extracted and compared included demographics, indications for SCS, length of hospital stay, procedural and care costs, and analgesic outcomes at three months after the procedure.

**Results**
The study cohort had 51 patients with 29 patients in SurgSCS (mean age: 54.7 ± 13.2 years with 14 females) and 21 patients (mean age: 46 ± 8.7 years with 9 females) in MISCS groups. The most common indication for SCS was Failed Back Surgery Syndrome with neuropathic pain in both groups (13 patients in the SurgSCS group and 16 patients in the MISCS group). Procedural costs were significantly lower in the MISCS group because all patients in SurgSCS group received a single wide paddle lead (average cost 3170 dollars) whereas majority of patients in the MISCS group received one or two cylindrical leads (average cost 1360 dollars). Health-care costs were significantly lower in the MISCS group because the median (range) length of in-hospital stay in the SurgSCS group was 7 (6.5 ± 1.5) days while it was 0.25 (0.2-0.3) days in the MISCS group with all patients in the MISCS group being discharged on the same day (Figure 1). No patients in MISCS group required overnight hospital stay. Analgesic outcomes were similar in both groups at three months (over 90% patients had 50% or greater reduction in pain at three months after the implant) and there were minimal complications in both groups.

**Figure 1.** Comparison of health-care costs for equipment (SCS leads) and hospital stay between the surgical laminotomy and minimally invasive SCS implant groups.
Conclusions
This observational study shows cost-benefits of MISCS compared with the surgical laminotomy approach. This, and published literature,\(^1\),\(^2\) has led to change in practice at our centre with most patients receiving SCS implants through the minimally invasive route. However, decisions regarding the SCS technique are made collaboratively between Anesthesia and Pain Medicine, Neurosurgery, and Physiatry and some patients with prior extensive spine surgery require the surgical approach. Longer follow-ups are required to compare complication rates (lead migration, infections) and analgesic efficacy between the two groups.

References

B 19• A clinical comparison of two bronchial blockers versus double-lumen tubes for one-lung ventilation
Serena Shum - Fellow
UHN – Toronto General Hospital

Introduction
One-lung ventilation (OLV) is commonly achieved through the use of a double lumen endotracheal tube (DLT) or the placement of a bronchial blocker (BB) via a single lumen endotracheal tube. A systematic review and meta-analysis showed BBs took longer for initial placement and were more prone to malpositioning than DLTs.\(^1\) More recently, however, Bussieres et al.\(^2\) demonstrated quicker placement and superior lung collapse in favor of BBs over DLTs. This study compares the EZ blocker (EZB), Uniblocker and DLT with respect to ease of placement, incidence of intra-operative malpositioning, and quality of lung collapse.
Methods
67 patients undergoing elective thoracotomies or video-assisted thoracoscopic surgery (VATS) requiring OLV for > 30 minutes were randomized to receive a DLT, Uniblocker or EZB. The time and number of attempts required to achieve lung isolation with the device was measured. Furthermore, the quality of lung collapse as assessed by the surgeon using the Lung Collapse Score (LCS) was obtained at the time of pleural opening and 10 and 20 minutes after pleural opening. The LCS is a 11-point rating scale with 0 being no lung collapse and 10 being the best lung collapse. The number of repositions required throughout the procedure was also recorded. Finally, the patients were assessed for postoperative complications.

Results
There were 19 patients randomized to receive a DLT, 23 to an EZB, and 25 to a Uniblocker. The mean time to lung isolation for the DLT, EZB, and Uniblocker were 183.84, 211.78, and 178.68 seconds, respectively, with no significant difference between devices. Mean LCS for the DLT, EZB, and Uniblocker groups at pleural opening and 10 and 20 minutes after pleural opening were not significantly different. Device failure occurred in one case (5.3%) with a DLT and two cases (8.7%) with the EZB. No cases of failure were reported with the Uniblocker. Difficult placement, defined as requiring more than two passes to achieve acceptable placement, occurred on one occasion with the DLT (5.3%), three occasions (13.0%) with the EZB, and twice (8.0%) with the Uniblocker. Table 1 shows the incidence of repositioning, the number of cases requiring greater than two repositions, and the average number of repositions by device. Post-operative sore throat and/or hoarseness occurred 21.1% (n=4) of patients who received a DLT, 21.7% (n=5) of EZB patients, and 12.0% (n=3) of Uniblocker patients.

<table>
<thead>
<tr>
<th>Device</th>
<th>Number of cases requiring repositioning (%)</th>
<th>Number of cases requiring &gt; 2 repositions</th>
<th>Mean number of repositions</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLT</td>
<td>3 (15.8%)</td>
<td>0</td>
<td>0.16</td>
</tr>
<tr>
<td>EZ Blocker</td>
<td>8 (34.8%)</td>
<td>3</td>
<td>0.70</td>
</tr>
<tr>
<td>Uniblocker</td>
<td>10 (40.0%)</td>
<td>0</td>
<td>0.48</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td></td>
<td>0.12</td>
</tr>
</tbody>
</table>

Discussion
There is no significant difference across groups with regards to time required to achieve lung isolation, number of repositions, as well as the quality and timing of lung collapse. Difficult initial placement and subsequent repositioning occurred most frequently with the EZB. Post-operative sore throat
throat and/or hoarseness occurred least frequently with the Uniblocker and occurred at similar rates between the DLT and EZ

References


Collaboratior: Lusine Abrahamyan and Jean Wong

B 20• Survey on associated symptoms and morbidities in carriers of RYR1 genetic variants
Carlos Alberto Ibarra Moreno - Fellow
UHN – Toronto General Hospital

Background
RYR1 gene is associated with malignant hyperthermia (MH) susceptibility. Patients with MH susceptibility show hypermetabolic reaction with exposure to volatile anesthetics and depolarizing muscle relaxants. While a majority of MHS patients are asymptomatic in the absence of anesthesia, some of the patients who carry RYR1 variants may show a variety of symptoms, such as exertional heat illness, myopathy and increased risk of bleeding. Our aim was to explore and identify any symptoms (in the absence of anesthesia) that carriers of RYR1 variants may experience during their daily life. Methods: Following institutional ethics board approval, a questionnaire was sent to patients who carried RYR1 variants, and to any family member who was tested genetically. The questionnaire included an inquiry of fatigue, heat intolerance, heat stroke, bladder and bowel complaints; assessment of chronic pain (as per Short-Form McGill Pain Questionnaire – SF-MPQ-2); assessment of general health (as per EQ-5D-5L and EQ VAS); assessment of mood (as per modified Hospital Anxiety and Depression Score – HADS); and assessment of bleeding tendency (as per modified Condensed Molecular and Clinical Markers for the Diagnosis and Management of Type 1 Von Willebrand’s Disease Bleeding Questionnaire – MCMDM-1). Responders were pooled into two groups: carriers of RYR1 variants (Group 1), and non-carrier family members (Group 2). Each questionnaire item was compared between the two groups. Statistical significance was determined using Mann-Whitney U test, t-test, chi-square, or Fisher’s exact test, where appropriate.

Results
Over the course of 17 months, 97 questionnaires were sent. Out of 40 questionnaires received to date, 27 subjects are in Group 1, and 12 are in Group 2. There were no significant differences in age or gender. Self-rated general health status was worse in Group 1. There was no statistically significant difference between the study groups’ fatigue, heat intolerance, bladder or bowel complaints, anxiety, depression, and pain scores. The occurrence of heat stroke and abnormal bleeding scores were seen exclusively in Group 1. Results are summarized on the table.
**Conclusion**: Carriers of RYR1 variants appeared “less healthy” compared to non-carrier family members, and they share similar symptoms and signs during daily life and in the absence of anesthetics. However, drawing conclusions on specific associations is currently hampered by lack of sufficient study power.

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**B 21** • Surface Ultrasound as Screening Tool for Diagnosis of Obstructive Sleep Apnea (OSA): A Systemic Review of Literature

**Arvind Tuteja – Research Assistant**

UHN – Toronto Western Hospital

**Background**

Obstructive sleep apnea (OSA) is a common sleep disordered breathing condition that leading to upper airway obstruction, oxygen desaturation and postoperative complications. Ultrasound (US) is a portable, non-invasive tool with potential for screening for obstructive sleep apnea (OSA). The objective of this systematic review is to evaluate the correlation of surface US measurements with OSA diagnosis.

**Methods**

Electronic literature search was performed in Medline, Medline In-Process, Embase, Cochrane Database of Systematic Reviews databases, and international conference abstracts. We included case series, cohort studies and randomized controlled trials of patients with known or suspected OSA using sleep study (Reference test), who underwent a surface US measurement (Index test). US parameters, scanning technique, and OSA diagnosis were recorded. The risk of bias for diagnostic tests was assessed using the QUADAS-2 tool. Screening, data extraction and summarization were conducted by two independent reviewers (AT and AG), and final consensus obtained by supervising authors (MS and VC).

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**TABLE: Comparison of gender, age, occurrence of symptoms (upper), and rater’s scores (lower) between the two groups.**

<table>
<thead>
<tr>
<th>Group</th>
<th>Gender</th>
<th>Age (Mean ± SD)</th>
<th>Heat stroke*</th>
<th>Heat intolerance</th>
<th>Fatigue</th>
<th>Bladder Symptoms</th>
<th>Bowel Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M 13</td>
<td>41.5 ± 2.6</td>
<td>9</td>
<td>10</td>
<td>9</td>
<td>3</td>
<td>6</td>
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<tr>
<td></td>
<td>F 14</td>
<td>16.0 ± 2.4</td>
<td>24</td>
<td>24</td>
<td>25</td>
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<td>24</td>
</tr>
<tr>
<td>2</td>
<td>M 6</td>
<td>33.8 ± 2.4</td>
<td>0</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>F 6</td>
<td>18.4 ± 2.4</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>11</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>EQ-5D-5L INDEX*</th>
<th>EQ VAS</th>
<th>SF-MPQ-2 Pain</th>
<th>HADS Anxiety</th>
<th>HADS Depression</th>
<th>MCMIDM-1 bleeding score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.87 [0.81-1.00]</td>
<td>80 [74.25-90]</td>
<td>8.50 [0.25-29.00]</td>
<td>4.00 [3.00-5.50]</td>
<td>2.00 [1.00-4.50]</td>
<td>4</td>
</tr>
<tr>
<td>N</td>
<td>26</td>
<td>24</td>
<td>26</td>
<td>27</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>2</td>
<td>1.00 [0.94-1.00]</td>
<td>90 [75-66]</td>
<td>0.00 [0.0-25.50]</td>
<td>5.50 [2.00-9.25]</td>
<td>1.50 [0.0-5.00]</td>
<td>0</td>
</tr>
<tr>
<td>N</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>

*Age is expressed as mean ± standard deviation. Heat stroke and abnormal bleeding score occurrence are highlighted. n = number of observations. Rater's scores are expressed as median [Interquartile range]. Generic health indices are based on EQ-5D-5L and EQ VAS. Short Form McGill Pain Questionnaire (SF-MPQ-2) used as chronic pain index. Hospital Anxiety and Depression Score (HADS) is used for mood assessment. The modified Condensed Molecular and Clinical Markers for the Diagnosis and Management of Type 1 von Willebrand's Disease Bleeding Questionnaire (MCMIDM-1) is used for bleeding tendency assessment. *P < 0.05
Results: Our search generated 2030 articles, of which 15 studies (13 prospective cohort and 2 cross-sectional studies) evaluating 1,948 patients met the inclusion criteria. The studies were conducted in Europe, Asia, Middle East and USA. Patients visited sleep medicine (42%), cardiology (35%), and respiratory (16%), and community clinics (7%). Using the QUADAS-2 tool, four studies were judged low risk of bias across all four domains. Of these, there was good to moderate correlation between OSA diagnosis and US parameters including carotid intimal media thickness, coronal tongue area, distance between lingual arteries, dynamic tongue base thickness during Mueller maneuver (MM), hyoid bone to hard palate length, lateral pharyngeal wall thickness, retro-palatal diameter during MM, and tongue base width, (p<0.05) (Table 1). No correlation was found with anterior neck, umbilical and mesenteric fat thickness and brachial artery diameter flow index (p>0.05) (Table 1).

Table 1: Summary of findings

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Study Design</th>
<th>Sample Size &amp; Setting</th>
<th>Ultrasound Variable</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aklin et al (2005)</td>
<td>Cohort Prospective</td>
<td>N=70 (Turkey) - Outpatient clinic</td>
<td>IMT (Intima Media Thickness) – CCA, ICA, Bulb and plaque</td>
<td>Strength of correlation with OSA; Good; p value: p&lt;0.01 for RCCA, LCCA, Lbulb; p=0.001 for LICA &amp; Rbulb; p=0.05 for RICA</td>
</tr>
<tr>
<td>Andonova et al (2012)</td>
<td>Cohort Prospective</td>
<td>N=54 (Bulgaria) - 27 with OSA and 27 controls</td>
<td>CCA- IMT and Plaque</td>
<td>Strength of correlation with AHI; Good cIMT with AHI: r=+0.43, p&lt;0.05</td>
</tr>
<tr>
<td>Apaydin et al (2013)</td>
<td>Cohort Prospective</td>
<td>N=87 (Turkey) - Habitual simple snoring (HSS) / OSAS: AHI &gt;5</td>
<td>CCA-IMT</td>
<td>Strength of correlation with OSA; Moderate p value=0.03 (OSAS and HSS); No correlation between severity of OSAS and CCA-IMT (Mild-Moderate OSAS : Severe OSAS p=0.55)</td>
</tr>
<tr>
<td>Bague et al (2005)</td>
<td>Prospective</td>
<td>N=83 (France) - Sleep clinic</td>
<td>Carotid IMT &amp; Plaque</td>
<td>Strength of correlation with OSA; Moderate: p value: p 0.04 - carotid IMT/ p 0.05 - plaque formation and nocturnal oxygen desaturation</td>
</tr>
<tr>
<td>Ciccone et al (2011)</td>
<td>Cohort Prospective</td>
<td>N=156 (Italy)</td>
<td>Carotid IMT</td>
<td>Strength of correlation with OSA; Good; Positive relationship between IMT and OSAS duration (r=0.34;p&lt;0.001) and between AHI and IMT (r&lt;0.51;p&lt;0.001).</td>
</tr>
<tr>
<td>Ciccone et al (2014)</td>
<td>Cohort Prospective</td>
<td>N=120 (Italy) - 80 OSA (newly diagnosed, AHI &gt;=5); 40 controls</td>
<td>Carotid IMT</td>
<td>Strength of correlation with OSA; Good Significantly elevated cIMT in OSA compared to non-OSA and in moderate-severe OSA compared to mild OSA or control; p value: p&lt;0.01</td>
</tr>
<tr>
<td>Chen et al (2014)</td>
<td>Cohort Prospective</td>
<td>N=40 (Taiwan) - recent diagnosed sleep apnea and AHI &gt;= 5 ; Controls: AHI&lt;5</td>
<td>Dynamic TBT (Tongue Base Thickness)</td>
<td>Strength of correlation with OSA; Moderate 1.5BT with MM (Mueller Manœuvre) - (odds ratio: 2.11, 95% confidence interval: 1.15–3.87, p&lt;0.05)</td>
</tr>
<tr>
<td>Lahav et al (2009)</td>
<td>Cohort Prospective</td>
<td>N=41 (Israel) Sleep clinic Only men.</td>
<td>DLA (distance between lingual arteries), tongue base width &amp; height</td>
<td>Strength of correlation with OSA; Good A correlation of 0.557 between DLA &amp; AHI; p value: p&lt;0.001</td>
</tr>
<tr>
<td>Shu et al (2013)</td>
<td>Cohort Prospective</td>
<td>N=105 (Taiwan) - Sleep laboratory</td>
<td>RP (retropalatal) &amp; RG (retroglossal) diameter under FI (Forced Inspiration) &amp; MM</td>
<td>Strength of correlation with AHI; Good Factors correlated with AHI: 1. RP diameter on MM (c=-0.624, p&lt;0.001), 2. UAL (c= 0.581), 3. % RP shortening on MM (c= 0.584, p&lt;0.001)</td>
</tr>
<tr>
<td>Wang et al (2009)</td>
<td>Cohort Prospective</td>
<td>N=90 (Taiwan) - Patients suggestive of OSA; Setting not mentioned</td>
<td>Tongue thickness (TT), CTA, HH Length, RG &amp; RP diameter under FI &amp; MM</td>
<td>Strength of correlation with OSA; Good Significant correlation of RP Diameter, RP shortening on MM, CTA, TT &amp; HH Length with AHI; p value: p&lt;0.001</td>
</tr>
</tbody>
</table>
**Conclusion**

Our review shows that surface ultrasound may be a useful tool for evaluation of OSA. However, large prospective studies are needed to validate and establish this tool as a screening method for OSA.

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**B 22** Opioid medication errors and resultant harm in pediatric practice: five years’ experience of adverse event reporting in a quaternary pediatric hospital.

**David Greaney - Fellow**
Hospital for Sick Children

**Background**

Opiate therapy in pediatric practice is particularly error prone due to variations in age, weight, dosing, dilution, pharmacokinetic and pharmacodynamic variations. An institutional review 2004-2008 at Sick Kids identified opioids as a significant source of harm. Subsequently, a medication safety committee was created and entrusted with the responsibility of identifying, reporting, and addressing all medication related harm. We report on the first 5 years of this committee successes in decreasing opioid related harm, particularly prescribing error in surgical and PICU patients.

**Procedures**

A medication safety database is maintained and updated on a monthly basis to reflect medication related harm, opioid errors, error related context, and contributory factors across all departments in the hospital. Concomitantly, a number of initiatives were implemented under the auspices of the medication safety committee including: drug/ error identification, promotion of hospital-wide
reporting, orientation programme for new staff (e.g. prescribing related videos and lectures), and increased accountability on consultants for higher risk specialties (e.g. surgical).

The following data represents a five-year interim analysis of the medication safety database. Variables analysed include error type (NCC-MERP), error characteristics, drug type and class, contributing factors, outcome, and other important variables related to opiate related medication events.

Results

November 2012 - September 2017: 8752: medication safety reports- 671 opioid related (7.5%) [Figure 1]. Opioid related harm persists. Careless handling / disposal errors carry clinical risk and, in the current climate, risk of diversion or suspicion thereof. Efforts to improve prescriber error may lead to a downstream increase in administration error. IV dosing is disproportionately highly represented, and carries a unique risk for life threatening complications.

<table>
<thead>
<tr>
<th>Location</th>
<th>count</th>
<th>Phase</th>
<th>count</th>
<th>Route</th>
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<th>Harm</th>
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<tr>
<td>Morphine</td>
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<td>18</td>
<td>Infusion</td>
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<td>PCA</td>
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<tr>
<td>Hydromorphone</td>
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<td>136</td>
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<td>IV</td>
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<td>Surgical wards</td>
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<tr>
<td>Fentanyl</td>
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<td>Mild</td>
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<tr>
<td></td>
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<td>IV</td>
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<td>Other</td>
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</tr>
</tbody>
</table>

Conclusions

Immediate and future medication safety initiatives should focus on increasing systematic resilience towards opiate reconciliation, and intravenous prescribing/ administration.

Collaborators: Renu Roy and Conor McDonnell

**B 23** Evaluation of iPACK Block - A Cadaveric Study

Laura Giron-Arango - Fellow
UHN – Toronto Western Hospital

Introduction

Total knee replacement (TKR) is a procedure associated with severe pain.1 Interest is growing in motor sparing regional anesthetic techniques to enhance early rehabilitation.2 The recently described iPACK block for posterior knee pain relief involves ultrasound guided local anesthetic infiltration of the interspace between the popliteal artery and the posterior knee capsule.3 It is believed that this block
targets only the terminal nerve branches involved in posterior knee pain, without causing motor block. This cadaveric study aims to evaluate dye spread distribution in the popliteal fossa and the nerves affected following an iPACK block injection.

Materials and methods
After IRB approval, 6 lightly-embalmed cadaveric specimens were injected with 10 mL of a methylene blue solution, using the ultrasound-guided iPACK block technique originally described by Dr. Sanjay Sinha. With the thigh in neutral position, a 22-G 8-cm echogenic block needle was inserted into the medial aspect of the knee approximately 1 finger breadth above the patella under ultrasound guidance using a curved 2-5 MHz probe. A fine guide wire was passed into the popliteal artery, the movement of which helped identify the artery’s location in the ultrasound image. The needle was advanced in plane to the level of the artery. Dye was injected in 1 mL increments while the needle was gradually withdrawn. During dissection, the sciatic, common peroneal (fibular) and tibial nerves and their articular branches, posterior branch of the obturator nerve, and superior medial and superior lateral genicular nerves were identified. In each specimen, nerves stained with methylene blue and staining frequency were recorded (Figure 1).

![Diagram](image)

**FIGURE 1:** Dissection of knee joint assessing dye spread distribution and staining of articular branches supplying the capsule.
A: Posterior view of knee showing dye distribution deep to popliteal vessels and staining of superior medial genicular nerve, and articular branches of posterior branch of the obturator nerve
B: Medial view of knee showing dye spread into anteromedial compartment between vastus medialis muscle and surface of the femur and staining of superior medial genicular nerve
ADM, adductor magnus muscle; ADMT, adductor magnus tendon; BF, biceps femoris muscle; CFN, main common fibular (peroneal) nerve; F, femur; P, patella; PV, popliteal vessels; S, sartorius muscle; TN, main tibial nerve; VM, vastus medialis muscle.

Results
In all specimens, posterior branch of the obturator nerve and superior medial genicular nerve were stained. However, superior lateral genicular nerve was stained in 67% of specimens, the main common fibular nerve in 67%, and the main tibial nerve in 33%. Articular branches of the tibial nerve were found in all specimens with a 50% (n=3) stain rate. Articular branches of the common fibular nerve were found in 4 of 6 specimens with staining occurring only in 2. In all specimens, dye
was found anterior to the popliteal vessels with spreading through the adductor hiatus into the anterior compartment of the thigh, between the vastus medialis muscle and the surface of the femur. Lateral dye spread did not extend into the anterior compartment.

**Discussion**
Our preliminary data suggest that an iPACK block injection can reach both the articular branches of the sciatic nerve and posterior branch of the obturator nerve, as well as the superior medial genicular nerve. It also reaches the adductor canal through back diffusion through the adductor hiatus. This block potentially provides relief for both posterior and anterior knee pain but the clinical relevance requires evaluation in future studies.

**References**

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**B 24** Pre-operative biomarkers and Imaging Tests as predictors of post-operative delirium in non-cardiac surgical patients

**Farrah Ayob - Fellow**
UHN – Toronto Western Hospital

**Introduction**
Post-operative delirium is emerging as a significant health and financial burden. The usefulness of biomarkers and imaging tests to predict POD may facilitate preventative measures to reduce its incidence. Our objective was to summarize the evidence of pre-operative and imaging tests to predict POD in non-cardiac surgery and to inform further research in this topic.

**Methods**
A systematic search of English articles in MEDLINE (1946 to January 2018), Medline (up to January 2018), EMBASE (1947 to January 2018), Cochrane Central Register of Controlled Trial (up to January 2018), Cochrane Database of Systematic Reviews (2005 to January 2018), PsychINFO (1806 to January 2018), CINAHL, Web of Science, Scopus, Pubmed and ClinicalTrials.Gov. Search included preoperative biomarkers or imaging tests used to predict POD and a validated POD assessment tool. Paediatric, cardiac surgery and nonhuman studies were excluded. Risk of bias was assessed using the Quality In Prognosis Study Tool (QUIPS).

**Results**
Thirty-six prospective cohort studies involving 5201 patients were included. Seventeen studies described serum tests (Interleukin-6, Insulin like growth factor-1, C-Reactive Protein, cholinesterases, apoE genotype, leptin, thioredoxin, hypovitaminosis, hypoalbuminaemia, GABA), 9 studies described cerebral-spinal fluid tests (CSF barrier dysfunction, monoamine precursor, melatonin, inflammatory mediators, S100B and neurofibrillary tangles) and three studies described imaging test; magnetic resonance imaging of cerebral blood flow and brain microstructure and computed tomography of total psoas area. CRP appears to be the most promising biomarker associated with POD with four out of six positive studies.

Table 1: Summary of result

<table>
<thead>
<tr>
<th>Biomarkers</th>
<th>Number of studies with Positive predictive finding</th>
<th>Studies [Author, Year, Country]</th>
<th>Number of studies with No predictive finding</th>
<th>Studies [Author, Year, Country]</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-6</td>
<td>4 (2 post-operative tests)</td>
<td>Capri et al., 2014, Italy</td>
<td>1</td>
<td>Lenstra, 2008, Netherlands</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vavulaschou et al., 2017, USA</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Westhoff et al., 2013, Netherlands</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Lin, 2013, China</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRP</td>
<td>4</td>
<td>Vavulaschou et al., 2017, USA</td>
<td>2</td>
<td>Lenstra, 2008, Netherlands</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Xiang et al., 2017, China</td>
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<td></td>
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<td>Dillon, 2017, Israel and UK</td>
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<td></td>
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<td>Neerland, 2016, Norway &amp; UK</td>
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</tr>
<tr>
<td>IGF-1</td>
<td>1</td>
<td>-Shen, 2016, China</td>
<td>2</td>
<td>Yen, 2016, USA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lenstra, 2008, Netherlands</td>
</tr>
<tr>
<td>Reduced Cholinesterase activity</td>
<td>2</td>
<td>Cerejeira et al., 2011, Portugal</td>
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<td></td>
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<td>Cerejeira, 2012, Portugal</td>
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</tbody>
</table>

Conclusion
We are still in the early stages in identifying biomarkers and imaging tests; larger studies with more variety of surgical populations and aligning POD assessment and confounding factors are required to identify the significance of these biomarkers to predict POD.

Collaborators: George Ho, Enoch Lam, Hossam El-Beheiry, Frances Chung, Jean Wong

B 25 • Integration of Virtual and Augmented Reality to the Operating Room via the Microsoft

Stephen Szeto – Medical Student
Hospital for Sick Children

Background
The advancement of technology and innovation in medicine has drastically grown in both the scientific and mainstream media world. From tissue engineering to 3D printing, medicine is quickly evolving to the needs of society. In particular, the field of reality manipulation (virtual, augmented,
and mixed reality) has garnished much attention for its potential to improve efficiency within the healthcare, especially in the operating room (OR). As of now, image guided procedures in the OR are spatially and technically challenging as users must balance their view on an imaging screen (e.g. ultrasound), the patient/working space, and other key monitors such as the vitals machine. Here, we suggest a potential solution using reality manipulation. Currently, there is no research that has validated a function for reality manipulation in the OR. The purpose of this project is to demonstrate the effectiveness of mixed reality (blending virtual and augmented reality) during image guided procedures in the OR.

**Methods**

We integrated an ultrasound machine and an OR vitals machine into two simultaneous holographic screens through the Microsoft HoloLens via a secured network conducted over a signal transducer (Epiphan VGADVI Broadcaster).

**Results**

Real time streaming of ultrasound and a patient’s vitals were projected into space through the Microsoft HoloLens. There was a time lag of seconds between the ultrasound/vitals and the respective projections. Screen manipulation was possible to adjust the size and location of each screen separately to suit the user’s preference.

**Conclusions**

In this preliminary project, we demonstrated the potential for a functional purpose (image guided procedures) of mixed reality in the operating room. Future works will track efficacy and feasibility to operate with the Microsoft HoloLens.

**Collaborator:** Rushil Chaudhary, Dr. Fahad Alam, Dr. Clyde Matava

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**B 26+ Virtual Reality and Pain Management: An Evidence Based Review**

Elizabeth Maxwell - Fellow
Sunnybrook Health Sciences Centre

**Background**

Virtual Reality (VR) technology presents computer-generated images and sounds to patients, imitating a stimulus that would usually be presented through the physical environment. While it is not clearly understood how VR influences pain perception, the mechanisms may be related to activation of the descending inhibitory pathways of the pain-modulation system. Participants are distracted by the virtual environment through multisensory cues, diverting their attention from an unpleasant stimulus. This review builds on the current literature to evaluate whether VR is useful for pain management and adds an in depth look at what specific types of pain it is useful for, in an attempt to propose a treatment algorithm.

**Methods**

155 had relevance to the search topic – the abstracts of the 155 papers were screened and 37 full-text articles were included in the review. Studies were included if a Virtual Reality intervention was used and pain was measured as an endpoint.

**Results**
24 of the 37 studies reviewed reported an improvement in pain scores when VR was utilised, however, there were variable results in the effectiveness of VR. In the acute pain subgroup, VR was shown to be useful for burns, musculoskeletal, ischaemic, thermal, postsurgical and some procedural pain. It was not useful for cystoscopy, lumbar puncture or paediatric port insertion. In the chronic pain subgroup, VR was shown to be useful for phantom limb pain, neuropathic pain secondary to spinal cord injury and chronic headache, however it was not found to be effective for CRPS or fibromyalgia.

**Conclusions**
In a time when we are increasingly exploring non-pharmacologic options for pain management it is encouraging to see the benefit VR may offer. We have developed an algorithm which provides an evidence based guide for VR treatment by identifying which type of pain VR is useful for. Further studies are required to evaluate the optimum prescription for VR content, dose and duration.

**Collaborator:** Fahad Alam
**A Systematic Review of Paresthesia-Free Spinal Cord Stimulation Modes for Complex Regional Pain Syndrome**

Yasmine Hoydonckx - Fellow  
UHN – Toronto Western Hospital

**Background**

Tonic spinal cord stimulation (T-SCS) is often used for the treatment of complex regional pain syndrome (CRPS). However, many patients are refractory to T-SCS or experience attenuation of the analgesic effect over time due to tolerance development. Paresthesias is another reason of T-SCS failure. Paresthesia-free SCS (PF-SCS) modes including high frequency (HF), BurstTM, and high density (HDTM) stimulation were introduced recently for the treatment of failed back surgery and neuropathic pain syndromes but these may also have a role in the treatment of CRPS.2 This systematic review was conducted to summarize the evidence on the role of PF-SCS for CRPS.

**Methods:** We searched MEDLINE, Embase, Cochrane, Google Scholar, Prospero, proceedings of annual meetings of pain societies and clinicaltrials.gov (up to September 21, 2017) for studies including adult patients with refractory CRPS treated by PF-SCS modes (HF, BurstTM and HDTM) compared to placebo, medical or conventional T-SCS. We determined the post-treatment intensity of pain (up to 24 months after intervention) and changes in CRPS-associated symptoms and associated domains (functional outcomes, quality of life, medication usage, and patient satisfaction). Sustainability and adverse effects were also assessed.

**Results**

We identified 13 studies (7 case series, 5 conference abstracts, 1 randomized controlled trial) including 62 patients with upper or lower limb CRPS. Ten papers reported the outcome of HF, 2 papers the outcome of BurstTM and 1 paper the outcome of HDTM. Pretreatment pain intensity was severe (NRS > 6/10) in all studies. Follow-up was up to 2 years after initiation of PF-SCS. In 59 patients, pain intensity with PF-SCS was reduced by 30% to 100% with reduction in medications to treat neuropathic pain. PF-SCS also attenuated CRPS-associated symptoms (swelling, color and temperature changes). Six papers reported significant improvement of quality of life. PF-SCS modes were commonly reported to provide "rescue" analgesia in patients with failure of T-SCS. The adverse effects profile of PF-SCS was similar to T-SCS. Possible drawbacks of PF-SCS for some patients were inability to feel paresthesias and the 'recharge burden'. No paper reported negative results for PF-SCS, probably reflecting publication bias.
Figure 1. Traditional spinal cord stimulation waveforms associated with paresthesia (a); Newer paresthesia-free waveforms (b. Burst (internal pulse frequency 500 Hz and burst repetition rate 40 Hz; c. High Frequency – 10 kHz; d. High Density – 400 Hz with pulse width of 400 microsec). [Adapted from Linderoth B, Foreman RD. Conventional and novel spinal stimulation algorithms: hypothetical mechanisms of action and comments on outcomes. Neuromodulation 2017:20:525-533.]

Conclusions
Paresthesia-free SCS modes have the potential to increase analgesic success rates in CRPS. CRPS-associated symptoms are also attenuated. Further research is warranted involving prospective comparative effectiveness studies.

References

Collaborators: Matteo Costanzi and Anuj Bhatia
**B 28: Twitter Hashtags for Anesthesiologists**

**Nan Gai - Fellow**  
UHN – Toronto Western Hospital

**Background**  
Twitter is a social media platform that has been encouraged for use among anesthesiologists as a way to stimulate conversation, distribute research, enhance conference experiences, and expand journal club sessions. The purpose of this study was to identify the most popular and relevant anesthesia hashtags and provide recommendations on the best hashtags for anesthesiologists.

**Methods**  
This study was exempted from ethics approval. Systematic searches were performed on Twitter to identify actively used anesthesia-related hashtags. A variety of web-based hashtag tracking services were then used to collect specific tweet data over the previous 30 days (ie total number of tweets, number of retweets and replies, number of users using the hashtags). All data were entered into an Excel™ spreadsheet and were analyzed using descriptive statistics.

**Results**  
The most frequently used general anesthesia hashtags were #anesthesia and #anaesthesia, with 1,618 and 845 tweets, respectively (Table 1). The #anesthesia hashtag had the greatest potential reach (2,187,495) and impressions (6,332,537). The most popular and relevant hashtags within anesthesia subspecialties or interest groups include #pedsanes (1,009 tweets), #anesJC (358 tweets), #obanes (261 tweets), #intubation (219 tweets), #regionalanesthesia (101 tweets), #neuroanesthesia (18 tweets), and #cardiacanesthesia (5 tweets). Most of the tweets utilizing anesthesia-related hashtags originated from North America.
Conclusions
We have identified the most popular anesthesia-related hashtags on Twitter to help anesthesiologists increase the reach and degree of discussions in anesthesia-related social media. For anesthesiologists new to the social media world, we hope to assist in learning to navigate Twitter for anesthesia-related content.

<table>
<thead>
<tr>
<th>Table 1 Tweets and Impressions of most active anesthesia-related hashtags</th>
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<td>anesthesiologist</td>
</tr>
<tr>
<td>regionalanesthesia</td>
</tr>
<tr>
<td>anaesthesiology</td>
</tr>
<tr>
<td>airwaymanagement</td>
</tr>
<tr>
<td>difficultairway</td>
</tr>
<tr>
<td>neuroanesthesia</td>
</tr>
<tr>
<td>cardiacanesthesia</td>
</tr>
<tr>
<td>anesthesiologist</td>
</tr>
<tr>
<td>intubate</td>
</tr>
</tbody>
</table>

Conclusions
We have identified the most popular anesthesia-related hashtags on Twitter to help anesthesiologists increase the reach and degree of discussions in anesthesia-related social media. For anesthesiologists new to the social media world, we hope to assist in learning to navigate Twitter for anesthesia-related content.

B 29* Evaluation of sleep health in interventional clinical trials for patients with chronic neuropathic pain: A systematic review

Aidan McParland – Medical Student
UHN – Toronto Western Hospital

Introduction
Sleep and pain are two of the most important protective and regulatory biological processes with a bidirectional relationship. It has been shown that lack of sleep promotes the development of hyperalgesia, a common manifestation of neuropathic pain (NP) syndromes. We hypothesized that sleep health domains are assessed inadequately or under-reported in interventional clinical trials in patients with chronic NP. In this systematic review, we evaluated the reporting trends and impact on sleep health in clinical trials involving interventions for treatment of chronic NP.

Methods
An electronic literature search of Embase, Medline, Cochrane Controlled Trials Register, Cochrane Database of Systematic Reviews, Biosys, Web of Science, and Scopus was conducted between January of 1995 up to April, 2017. Inclusion criteria were randomized controlled trials of studies investigating an intervention other than pharmacological therapy for the treatment of chronic neuropathic pain (duration longer than 3 months). Outcome measures included the five critical sleep domains, sleep quality (the subjective assessment of good or poor sleep), alertness (the ability to maintain attentive wakefulness), sleep timing (the placement of sleep within 24 h), sleep efficiency (the ease of falling asleep and returning to sleep) and sleep duration (the total amount of sleep over 24 h). In addition, the impact of the pain intervention on sleep health was also recorded. Screening of articles, data extraction, and summarization were conducted by two independent reviewers, and consensus obtained from supervising investigators.

Results
Our search yielded 3531 studies, of which 576 were screened for full-text review. Of these, 18 clinical trials met inclusion criteria for this abstract. A total of 1311 patients were enrolled across these trials. Painful diabetic neuropathy (PDN) was the most common NP state studied (50%) (Table 1), followed by post-herpetic neuralgia (PHN) (28%), and general neuropathic pain (17%) (Table 2). Quality of evidence was good to moderate for the included studies. Only four studies (22%) used validated sleep questionnaires to record sleep changes, and none of the studies captured sleep. Of the five sleep domains analyzed, sleep efficiency was the most reported domain (72% of studies), followed by sleep quality (56%), alertness/sleepiness (28%), sleep duration (28%), and sleep timing (22%). Ten trials reported some improvement in sleep health (global or one sleep health domain), no improvement in 6 studies, and unclear in 2 trials.
### Conclusion

Sleep health is often under-reported in trials on interventions for NP, but it is an important quality of life metric. More than 50% trials reported some improvement in sleep health following an intervention for chronic NP. Future trials should use validated measures and tools to report the impact of interventions for NP on sleep.
B 30+ Pain, Agitation and Delirium in Cardiovascular Intensive Care Unit; Barriers for implementation

Victoria Postnikova – Graduate Student
UHN – Toronto General Hospital

Introduction
International guidelines recognize pain, agitation and delirium (PAD) as priorities in adult cardiac surgery patients. Pain is common but frequently poorly treated; lighter levels of sedation are associated with shorter duration of mechanical ventilation and shorter ICU length of stay; delirium is associated with prolonged ICU stay, increased mortality, and post-operative cognitive dysfunction. Several validated tools are recommended to assess PAD including Critical Care Pain Observation Tool (CPOT), Numerical Pain Rating Scale (NRS), Sedation Agitation Scale (SAS) and Confusion Assessment Method for the ICU (CAM-ICU).

Objective
To investigate possible barriers in the diagnosis and treatment of PAD in the Cardiovascular Intensive Care Unit at Toronto General Hospital.

Methods
Between June and November 2017 multiple surveys (electronic and paper) and in-person interviews were conducted with ICU physicians, nurses, respiratory therapists, and physiotherapists. Baseline performance data of CAM/SAS/CPOT was obtained using practice audit over 2 consecutive weeks. Thematic analysis was performed on material gathered from interviews conducted using standardized questions. Responses were collected and analyzed using Microsoft Excel.

Results
63 surveys were returned. Response rate cannot be calculated because distribution and replies were anonymized as per management request. Survey results are shown in Table 1.
<table>
<thead>
<tr>
<th>Question</th>
<th>Strongly disagree (%)</th>
<th>Disagree (%)</th>
<th>Neither agree or disagree (%)</th>
<th>Agree (%)</th>
<th>Strongly agree (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain, Agitation and Delirium are important issues in our unit</td>
<td>0.0</td>
<td>1.6</td>
<td>0.0</td>
<td>33.3</td>
<td>65.1</td>
</tr>
<tr>
<td>Pain, Agitation and Delirium are well addressed in our unit</td>
<td>3.2</td>
<td>20.6</td>
<td>15.9</td>
<td>55.6</td>
<td>4.8</td>
</tr>
<tr>
<td>CPOT (Critical Care Pain Observation Tool) is useful to recognize pain in patients who are unable to communicate</td>
<td>3.3</td>
<td>13.3</td>
<td>31.7</td>
<td>43.3</td>
<td>8.3</td>
</tr>
<tr>
<td>CPOT is easy to use</td>
<td>6.7</td>
<td>13.3</td>
<td>28.3</td>
<td>46.7</td>
<td>5.0</td>
</tr>
<tr>
<td>SAS (Sedation Agitation Scale) is useful to describe the level of sedation/agitation</td>
<td>1.6</td>
<td>1.6</td>
<td>3.2</td>
<td>73.0</td>
<td>20.6</td>
</tr>
<tr>
<td>CAM-ICU (Confusion Assessment Method for the ICU) is useful to assess presence of delirium</td>
<td>1.6</td>
<td>14.8</td>
<td>24.6</td>
<td>44.3</td>
<td>14.8</td>
</tr>
<tr>
<td>All members of medical staff are familiar with CPOT, SAS and CAM-ICU</td>
<td>9.7</td>
<td>17.7</td>
<td>27.4</td>
<td>33.9</td>
<td>11.3</td>
</tr>
<tr>
<td>The amount of importance paid to the neurological part of the report is greatly staff dependent</td>
<td>1.6</td>
<td>11.1</td>
<td>12.7</td>
<td>61.9</td>
<td>12.7</td>
</tr>
</tbody>
</table>

**Discussion**

Based on results of the survey, one of the barriers was lack of confidence and uncomfortability with CPOT and CAM-ICU. Another common barrier is staff related, including low prioritization and inconsistency when addressing PAD. Possible limitations of this study could include response bias due to voluntary participation.

**Conclusion**

Although CVICU clinicians recognize the importance of PAD, only 45% reported being familiar with these scales. While SAS score was considered easy to use and useful, CPOT and CAM-ICU were viewed less favorably. Future steps include a systematic approach using education and mandatory utilization of these tools during rounds.

**Collaborators:** Dr. Marcin Wasowicz and Dr. Warren Luksun

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**B 31**: A Retrospective Analysis of the Incidence and Treatment of Hypothermia in Pediatric Trauma Patients

**Grahme Weisgerber – Fellow**
Hospital for Sick Children

**Background**
Traumatic injury is a leading cause of pediatric death in the United States and Canada. Children are at increased risk of hypothermia for multiple reasons including a high body surface area to mass ratio and higher metabolic rate. Hypothermia is an important predictor of morbidity and mortality in pediatric trauma patients admitted to hospital. They are at increased risk of coagulopathy and bleeding and thus may require a higher rate of transfusion, which is also a predictor of mortality in trauma patients.

**Methods**
Local Research Ethics Board approval was obtained. We performed a retrospective chart review to document the incidence of hypothermia (temperature <36.5°C) and how often warming interventions are performed during the initial resuscitation of pediatric (age 0-18) trauma activations at a pediatric tertiary trauma centre. Logistic regression was performed to determine predictors of hypothermia in pediatric trauma patients. Multivariate analysis was done using purposeful selection.

**Results**
During the pilot study period a total of 41 patients were analyzed. Results are reported as mean (SD). Of the trauma activations, age was 10.6 (4.3) years, Injury Severity Score (ISS) was 14.8 (18.7), lowest Glasgow Coma Scale (GCS) in the trauma bay was 12.8 (4.4), elapsed time in the trauma bay was 63.1 (39.9) minutes, BIG score was 9.2 (10.7) (BIG score is a mortality predictor in pediatric trauma calculated as admission base deficit + (2.5 x INR) + (15 – GCS)), and volume of crystalloid received in the trauma bay was 7.2 (12.4) ml/kg. Fifty-eight percent of activations were male, 17% of patients required intubation, 14% required transfusion and warming initiatives were used in 12%. Predictors analyzed for inclusion in multivariate analysis, at a p value of < 0.2 included ISS score, GCS at the scene, GCS in the trauma bay, transfusion and BIG score. Patient age and weight were forced into the model. The final multivariate logistic regression model included patient age, patient weight and BIG score with reasonable predictive ability (c = 0.6) and good model discrimination.

**Conclusions**
Of the trauma activations reviewed, blunt trauma was the predominant mechanism with penetrating trauma comprising a small minority. The use of warming initiatives was poorly documented in the charts reviewed. More severe trauma requiring intubation, transfusion, and institution of warming initiatives correlated with hypothermia. Identifying patients who are hypothermic and instituting warming initiatives early in these patients’ management may help improve patient care and outcomes. Further evaluation of predictors of hypothermia is required and may help in identifying these patients. Once identified the development of a specialized pediatric hypothermia algorithm may improve temperature management and mitigate some of the potential adverse outcomes of hypothermia in trauma patients.

**Collaborator:** David Goodick, Suzanne Beno, Paul Wales, Teresa Skelton

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**B 32** Transient paraplegia following Epidural Blood Patch

**Chaminda Wijeratne - Fellow**

Sunnybrook Health Sciences Centre

**Introduction**
Spontaneous Intracranial Hypotension is a neurological condition caused by spontaneous spinal cerebrospinal fluid (CSF) leaks characterised by orthostatic headache and a variety of atypical neurological symptoms. Imaging techniques including magnetic resonance (MRI) are fundamental in locating the precise anatomical site of the CSF leak. Management strategies include epidural infusion of crystalloids, colloids, fibrin glue or hematic blood patch (EBP), before a surgical repair is warranted. We report a case in which a patient treated with EBP developed transient paraplegia for 90 minutes following the procedure.

Material and Methods
Patient informed consent was obtained for submission of a case report.

Results
37-year-old male with clinical and radiological findings diagnostic of spontaneous intracranial hypotension presented for a planned epidural blood patch at T11-12 to be followed by an infusion via epidural catheter with colloid. He had a past history of two epidural blood patches with partial and temporary benefit. MRI showed a possible CSF leak at T11 and also noted epidural lipomatosis along the length of the thoracic and lumbar spine with extradural compression most prominent from T4-T7 levels with mild flattening of the cord with no change in cord signal. L5-S1 disc protrusion was also noted without any compression. Other past medical history included treated obstructive sleep apnoea, obesity and hypertension. Epidural blood patch was performed with autologous blood from forearm in sterile condition under fluoroscopy guidance. The patient complained of crescendo back pain up to 7/10 on visual analogue scale (VAS) after only 14ml injection via epidural catheter. Epidural catheter was removed due to the discomfort. 25 minutes following procedure, patient became paraplegic at the level of T8 dermatome with sensorial and motor deficit and deep tendon hyperreflexia. Vital signs were stable including a blood pressure of 170/90mmHg. Patient was transferred for urgent MRI and Neurosurgical assessment. 90 minutes post event, the patient returned to his baseline neurological status except for back pain VAS 4/10. MRI at this time demonstrated evidence of recent epidural blood patch, but no other changes from his baseline MRI. Cord signal was normal.
Discussion
This case illustrates a transient paraplegia following EBP in a patient with pre-existing epidural lipomatosis. Spinal Epidural lipomatosis is a rare cause of spinal cord compression and neurological deficits. We postulate that compression by the EBP may have unbalanced the cord transmural perfusion pressure. The increase in venous pressure may have been exacerbated by the pre-existing epidural lipomatosis. Resolution was likely due to redistribution of blood in the epidural space. This rare case highlights the importance of evaluating the epidural space anatomical target and anatomical variances including spinal stenosis, disc protrusion, spondylolisthesis and in this case spinal epidural lipomatosis. Infusion or injection of foreign material in the neuraxial space could alter the fine perfusion balance of the spinal cord structures. Injection in aliquots and assessment of pain/pressure during the procedure may not be sufficient to prevent the catastrophic misadventure of spinal cord ischemia as seen with epidural hematoma.

Collaborator: Arsenio Avila

Evaluation of sleep health in pain questionnaires used in the chronic pain population: A systematic review of literature.

Shreya Desai – Research Assistant
UHN – Toronto Western Hospital

Background
The sleep poll of the 2015 National Sleep Foundation found that adults experiencing chronic pain attributed 35-55 % of their problems in mood, daily activities, relationships and work to sleep
difficulties. Using a theoretical framework of sleep health by Buysse, sleep domains have been independently associated with adverse long-term health outcomes. The complex interaction between chronic pain and sleep is not well understood. We hypothesized that sleep domains are not comprehensively evaluated in chronic pain studies. The aim of this systematic review was to evaluate whether the commonly used pain questionnaires assess sleep quality and important sleep health domains.

Materials and methods
A literature search was conducted using the Ovid Medline database from 1946 to May 7, 2017. The titles, abstracts and full text screening were done by two independent reviewers. Additional independent searches were also conducted in PubMed, Google Scholar and the NIH PROMIS network. The inclusion criteria were: 1) Studies involving chronic pain patients (duration longer than 6 months); 2) Validated pain assessment tools were used to evaluate impact on pain and sleep; 3) Human studies and 4) Publications in English. The exclusion criteria were pediatric population. Sleep health was assessed using Buysse’s definition of sleep quality (the subjective assessment of good or poor sleep), alertness (the ability to maintain attentive wakefulness), sleep timing (the placement of sleep within 24 h), sleep efficiency (the ease of falling asleep and returning to sleep) and sleep duration (the total amount of sleep obtained per 24 h). The extent and quality of capture for the five main sleep domains were reported.

Results
A total of 1338 citations were identified, of which 423 abstracts were selected. We identified 54 validated questionnaires of which, 22.2 % (12/54) pain questionnaires included some aspects of sleep domains as part of a global sleep assessment. Sleep efficiency measured as the ease of falling asleep or returning to sleep was the most reported sleep domain (66.7%), followed by sleep quality (16.7%), duration (16.7%) and alertness (8.3%). None of the questionnaires reported sleep timing (Table 1). The Pain and Sleep Questionnaire (PSQ) assessed 3 sleep domains in addition to global assessment.
Table 1: Summary of important findings

<table>
<thead>
<tr>
<th>Pain Questionnaires</th>
<th>Study Reference</th>
<th>Global sleep assessment</th>
<th>Quality</th>
<th>Alertness</th>
<th>Timing</th>
<th>Efficiency</th>
<th>Duration</th>
<th>Reported by</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Pain Society Patient Outcome Questionnaire revised (APS-PQXR) Assessment of Discomfort in Dementia (ADD)</td>
<td>Gordon 2010, McNell 2001</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td>Self</td>
</tr>
<tr>
<td>DOLOPLUS-2 Scale</td>
<td>Fio 2014</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nurse</td>
<td></td>
</tr>
<tr>
<td>Geriatric Pain Measure (GPM)</td>
<td>Block 2007</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>Self</td>
<td></td>
</tr>
<tr>
<td>Global Pain Scale (GPS)</td>
<td>Gentile 2011</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>Self</td>
<td></td>
</tr>
<tr>
<td>Non-Communicative Patient’s Pain Assessment Instrument (NP-PAIN)</td>
<td>Fio 2014</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nurse</td>
<td></td>
</tr>
<tr>
<td>Pain and Sleep Questionnaire (PSQ) Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACS-LAC)</td>
<td>Feather 2012</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>Self</td>
<td></td>
</tr>
<tr>
<td>Rheumatoid Arthritis Pain Scale (RAPS)</td>
<td>Anderson 2001</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
<td>Self</td>
<td></td>
</tr>
<tr>
<td>The Chronic Pain Sleep Inventory (CPS)</td>
<td>Kasinskas 2007</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td>Self</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion**

Sleep health is an under-reported component in the chronic pain population, of which sleep efficiency was the most reported domain. Future studies should report all sleep domains as part of the clinical assessments of patients with chronic pain.

**Collaborators:** Mandeep Singh MD, Anuj Bhatia MD, Frances Chung MBBS, Dinesh Kumbhare MD, Jean Wong MD, Jayadeep Patra PhD
Case report – Supraclavicular Brachial Plexus Neurolysis for a Malignant Peripheral Nerve Sheath Tumor

Weiyang Christopher Liu - Fellow
UHN – Toronto Western Hospital

Introduction
Neurolytic blocks are an important armamentarium for interventional pain physicians who manage cancer pain. The perineural administration of alcohol or phenol results in protein denaturation and consequently, neurolysis. This produces a long-lasting block with a duration of 3 to 6 months. Although neurolytic blocks for the brachial plexus have been described in multiple review articles and textbooks, they are rarely performed. As such, little is known about the efficacy and adverse effect profile of this commonly described treatment. In this article, we report the outcomes of a patient who underwent a left brachial plexus neurolytic block for the management of upper limb pain arising from a malignant peripheral nerve sheath tumour (MPNST).

Case Description
Our patient is a 56 year old female with a one year history of a MPNST at the left scapula with metastasis to the lung. Her main complaint was that of severe pain in her whole left upper limb and over the posterior aspect of the shoulder. This was accompanied by significant sensitivity to touch and weakness. The pain had been refractory to pharmacological treatment. We first performed a diagnostic supraclavicular plexus block with local anesthetic, which provided her with complete pain relief for 12 hours. As such, we performed neurolysis with alcohol of the supraclavicular plexus, which provided her with a significant but incomplete pain relief that was maintained at the 6 week follow-up.

Discussion
Neurolytic blocks of the brachial plexus can be a useful adjuvant in the management of cancer pain in the upper limb. However, the morbidity of the block limits its widespread use and careful patient selection is necessary to obtain the best possible outcome. Our case report highlights the benefits of a performing a diagnostic block (prior to neurolysis), the safety considerations for performing a neurolytic brachial plexus block and the partial effectiveness of the block due to replacement of the patient’s usual pain by deafferentation pain. It is important to tamper the patients’ expectations about the blocks as the outcomes from an anesthetic block cannot be extrapolated to a neurolytic block.


Elevated Red Cell Distribution Width (RDW) is an Adverse Prognostic Indicator in Elective Noncardiac Surgery: A Retrospective Cohort Study

Justyna Bartosko - Resident
UHN – Toronto General Hospital

Background
Red cell distribution width (RDW) is a routinely reported component of the complete blood count and involves no additional cost to measure. Elevated RDW reflects greater variability in red cell size, and is influenced by numerous physiologic and pathologic processes. Traditionally, the usefulness of the RDW to clinicians has been limited to the differential diagnosis of anemia. However, recent evidence indicates the RDW may have much broader implications, particularly for patient risk stratification and prognostication across a wide range of disease states. In patients with coronary artery disease and heart failure, elevated RDW is strongly associated with mortality. Limited prior data suggest a similar association in surgical patients. We examined the adjusted association between elevated RDW and 30-day hospital mortality and morbidity in a cohort of elective noncardiac surgical patients.

**Methods**
We included adults (≥18 y) undergoing inpatient noncardiac surgery at a multisite tertiary-care hospital network from 2008 to 2015. Institutional research ethics review was obtained. The exposure of interest was the most recent RDW within 60 days before the index surgery. The primary outcome was 30-day in-hospital mortality. The secondary outcomes were postoperative cardiac events (troponin elevation, myocardial infarction, or cardiac arrest) and post-operative renal dysfunction (doubling of serum creatinine from baseline on postoperative days 1-4). Multivariable logistic regression was used to examine the association of RDW (categorized into quartiles) with outcomes while adjusting for age, sex, BMI, comorbidities, surgical procedure, and preoperative hemoglobin.

**Results**
The primary analysis included 27,943 patients. There were 499 (1.8%) deaths, 1026 (3.7%) cardiac events, and 2604 (9.3%) renal events. After risk adjustment, the highest quartile of RDW (>13.0) was associated with an increased odds of death [adjusted odds ratio (aOR) 2.34 (1.60-3.42), p < 0.001]. When compared with the lowest RDW quartile (≤11.6), all higher quartiles had increased risk for cardiac events, with the highest quartile (RDW>13.0) having an aOR of 1.41 (1.10-1.82), p=0.02. The models predicting death (c-statistic 0.82, 95% CI 0.79-0.84) and cardiac events (c-statistic 0.79, 95% CI 0.78-0.81) had good discrimination. Quartiles of RDW were not predictive of renal events.
Table 1. Adjusted Odds Ratios for Events per RDW Quartile. A stepwise increase in mortality and cardiac events is shown, which persisted despite adjustment for standard predictors and hemoglobin.

<table>
<thead>
<tr>
<th>Outcome: In-hospital 30-day mortality</th>
<th>Predictor</th>
<th>OR</th>
<th>95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RDW Quartile</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (≤11.5%)</td>
<td>Reference</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (11.7-12.1%)</td>
<td>1.19</td>
<td>0.78-1.83</td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>3 (12.2-12.9%)</td>
<td>1.52</td>
<td>1.02-2.24</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>4 (≥13.0%)</td>
<td>2.34</td>
<td>1.60-3.42</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome: Cardiac Events</th>
<th>Predictor</th>
<th>OR</th>
<th>95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RDW Quartile</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (≤11.5%)</td>
<td>Reference</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (11.7-12.1%)</td>
<td>1.37</td>
<td>1.06-1.78</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>3 (12.2-12.9%)</td>
<td>1.33</td>
<td>1.04-1.72</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>4 (≥13.0%)</td>
<td>1.41</td>
<td>1.10-1.82</td>
<td>0.01</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome: Renal Events</th>
<th>Predictor</th>
<th>OR</th>
<th>95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RDW Quartile</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (≤11.5%)</td>
<td>Reference</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (11.7-12.1%)</td>
<td>0.87</td>
<td>0.71-1.02</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>3 (12.2-12.9%)</td>
<td>0.95</td>
<td>0.80-1.11</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>4 (≥13.0%)</td>
<td>0.89</td>
<td>0.72-1.06</td>
<td>0.16</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions.
Elevated RDW is associated with clinically important increases in perioperative mortality and cardiac events, independent of concurrent anemia. Further research is needed to validate these findings, and determine how best to incorporate RDW into assessing perioperative risk and targeting patients for risk reduction interventions.

Collaborators: Justyna Bartoszko, Stephanie Ladowski, Gordon A. Tait, W. Scott Beattie, Duminda N. Wijeysundera

C 2+ A Carbon Nanotube Sensor to Develop Precision Therapies for Heart Failure

Manpreet Malhi – Graduate Student
The Hospital for Sick Children

Background
The genetic and environmental factors contributing to heart failure are quite diverse from patient
to patient. Due to this heterogeneity, there is currently a need to develop tools which can predict the most efficacious heart failure treatments for specific patient populations. Here we describe a method of assessing heart function in vitro using a carbon nanotube (CNT) sensor. We can generate cardiomyocytes from patients, each with distinct disease characteristics, and use our CNT sensor to measure parameters such as beat rate, rhythm and contractility. Utilizing this approach, we hope to develop precision therapies for heart failure based on the unique requirements of each patient, or group of patients, affected by this condition.

**Methods**
A microdevice array was prepared by embedding CNT sensors in a polydimethylsiloxane membrane. Human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) are plated onto the microdevice and cultured for several weeks, during which changes in resistance across the CNT sensor are measured in real-time. These resistance changes are a direct measure of cardiac contractility. To validate the clinical relevance of this device, hiPSC-CMs were treated with known inotropes and chronotropes and their functional response was determined.

**Results**
Within five days of culture, hiPSC-CMs from a synchronously beating monolayer on the CNT sensor. We can successfully reproduce the clinical effects of various heart medications in these cardiomyocytes. For example, cells treated with isoproterenol, a positive inotrope and chronotrope, exhibit an increase in beat rate and contractility whereas cells treated with verapamil, a negative inotrope and chronotrope, exhibit a decrease in beat rate and contractility. Omecamtiv, which is exclusively a positive inotrope, increased contractility without affecting beat rate whereas ivabradine, which is exclusively a negative chronotrope, decreased beat rate without affecting contractility.

**Conclusions** We have developed a CNT sensor capable measuring heart function in vitro and reproducing the effects of several clinically used drugs. This platform may be used to analyze patient-derived cardiomyocytes and tailor treatments towards specific populations. Furthermore, we can use our device to screen these patient cells against drug libraries to discover novel medications for heart failure.

**Collaborators:** Li Wang, Wenkun Dou, Haijiao Liu, Yu Sun

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**C 3+ Competency By Design: A Mixed Methods, Ethnographic Study**

**Gianni R. Lorello – Faculty**
UHN – Toronto Western Hospital

**Introduction**
Our health care system is continuously evolving with its ever-changing demands and expectations. Despite this, little parallel change has occurred in the medical education system over the past century, since the Flexner Report in 1910. In 2015, the Royal College of Physicians and Surgeons of Canada launched “Competence By Design” (CBD): a competency-based medical education (CBME) approach to training residents to better meet and respond to patient and societal needs. Although high hopes for CBME exist, there is no data comparing residents undergoing CBME training to those in the traditional time-based model.
Methods
This study was reviewed and accepted by our university research ethics board; informed consent was obtained from all participants. Using mixed methods and ethnographic methodology, we aim to understand the sociocultural and behavioural differences between residents who have completed three months of training in the new CBD model [i.e., starting Foundations Of Discipline (FOD)] compared to traditional anesthesiology residents beginning their post-graduate year (PGY)2 year of training. Secondary measures include: clinical skills [e.g., spinal checklist and global rating scale (GRS)], behaviours, and perceived independence (i.e., time staff left the resident alone). Purposive sampling will be used. Field observations were translated into notes and took place at two academic centres.

Analysis
Qualitative Data: We utilized Wilcott’s three-step approach to analyzing ethnographic data: description, analysis, and interpretation.2 As we developed and redeveloped codes at each stage of our analysis, we documented our decisions to enhance confirmability. We utilized a Framework Method to present the data from the two different cohorts. Quantitative Data: Descriptive statistics (means +/- standard deviations for continuous data and medians with inter-quartile ranges for ordinal data) were calculated for procedural and behavioural performances. The independent Student's t-test was used to assess for any differences in continuous variables; a Mann-Whitney test was used to assess any differences in ordinal data between the two groups.

Results
There were no differences between cohorts' spinal checklist, GRS, behaviours, or perceived independence (p>0.05). However, the qualitative data demonstrates differences that our quantitative metrics could not perceive, of greatest importance, knowledge-patient comfort dissonance and training latent safety threats within the CBD residents; also, time-based residents collaborate with allied healthcare providers rather than working in silos.

Discussion
Minimal evidence for CBD exists, and a randomized control trial comparing CBD residents with time-based residents will never exist. This study demonstrates that CBD residents tend to prioritize patient comfort at the expense of safety as they lack knowledge. Time based residents participate in multidisciplinary discussions for shared mental models. Future studies why CBD residents work in silos and why training latent safety threats exist will be evaluated.

Collaborators: Stephanie Ladowski, Carol-anne Moulton, Lisa Bahrey

C 4* The Risk of Severe Aortic Stenosis in Elective Non-Cardiac Surgery

Jay S. Han - Resident
UHN – Toronto General Hospital

Introduction
The Current American College of Cardiology and American Heart Association guidelines suggest that Severe Aortic Stenosis (SAS) places a patient in a high-risk category for non-cardiac surgery. SAS is defined as an aortic valve area (AVA) < 1.0 cm2, mean gradient of ≥ 40 mmHg and a peak velocity of ≥ 4 m/s. This designation results in cancellation of essential surgery, or referral for aortic valve...
replacement procedures. The AHA/ACC guidelines, with respect to AS where developed from studies limited by their retrospective nature, number of patients and from data almost a decade ago. Advances in anesthetic and surgical care demonstrate a declining perioperative risk in terms of deaths and post operative myocardial infarction (MI). We therefore conducted an analysis of a large patient population database from a single centre. Our primary hypothesis was that SAS was associated with increased mortality and cardiovascular complications.

**Methods**
Data from patients having undergone non-cardiac procedures between June 2007 - December 2014 was retrieved from the perioperative anesthesia database. All elective patients are screened in a preoperative assessment clinic by advanced practice nurses, using validated assessment tools which captures details of cardiac risk factors and all previous cardiac investigations and interventions. A consecutive sample of 42,458 elective non cardiac patients was included in this analysis. With respect to AS the following factors were extracted to determine their effects on the likelihood of the primary outcome of death at 90 days: Aortic valve area (AVA), Mean Gradient (mmHg), Procedural OR times and Revised Cardiac Risk Index (RCRI) Scores. Statistically a multivariable logistic regression analysis with forced entry was performed, mortality at 90 days was the outcome of interest. The included co-variates were AVA < 1.0 cm2, AVA 1.0 cm2 - 1.5 cm2, AVA > 1.5 cm2 - < 3.0 cm2, Mean Gradient ≥ 40 mmHg, RCRI scores and OR procedure times. Sensitivity analyses included 1. Rates of MI 2. A RCRI matched cohort.

**Results**
The sensitivity analysis found no difference in the primary outcome or the rates of MI between patients with AS and without AS in a matched cohort using the RCRI score (RCRI 1, RCRI 2 and RCRI >3). The logistic regression model found no significant association between the following factors and the primary outcome of death at 90 days: AVA < 1.0 cm2, AVA 1.0 cm2 - 1.5 cm2, AVA >1.5 cm2 - < 3.0 cm2, or a Mean Gradient of ≥ 40 mmHg. In contrast, patients with higher RCRI scores, OR 1.9 (95% CI [1.705, 2.132]), or procedures with increasing OR times, OR 1.0 (95% CI [1.00, 1.004]), were more likely to develop the primary outcome.

**Conclusion**
In this single center study of patients undergoing non-cardiac surgery severe aortic stenosis was not associated with an increased risk of death or MI.

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Ketamine Prevents a Persistent Increase in 1-Aminobutyric Acid Type-A Receptor Function In Hippocampal Neurons After General Anesthesia

Winston Wenhuan Li – Graudate Student
Sunnybrook Health Sciences Centre

**Background**
Postoperative delirium and cognitive dysfunction are complex, multifactorial disorders that are associated with poor short- and long-term outcomes and increased healthcare costs (Deiner et al. 2009). The exact etiology of these disorders is unknown; however, general anesthetics are likely contributing factors. Preclinical studies have shown that commonly used general anesthetics trigger an increase in the cell-surface expression of GABAA receptors (GABAAR). The resulting increase in tonic current in neurons, which persists long after the drug has been eliminated, causes cognitive impairment (Zurek et al. 2014). Ketamine, a dissociative, non-GABAergic anesthetic, is reported to
attenuate cognitive deficit in patients after surgery but its effects on tonic current are unknown (Hudetz et al. 2009). Given the clinical evidence supporting the cognition-sparing properties of ketamine, we hypothesize that: 1) ketamine prevents a persistent increase in GABAAR function following treatment with a GABAergic anesthetic drug and 2) ketamine’s action is mediated by the neurotrophic factor BDNF.

Methods
Studies were approved by the local Ethics Committee. Cocultures of hippocampal neurons and cortical astrocytes were prepared from fetal mice and were treated with either etomidate (1 μM), ketamine (10 μM) or etomidate plus ketamine for 1 hour then washed. After 24 hours, tonic current was recorded from hippocampal neurons using patch clamp techniques. GABA (0.5 μM) was applied and a change in holding current during the application of bicuculline (20 μM) was measured. In addition, the role of BDNF was studied by treating some cultures with the TrkB receptor antagonist, ANA12.

Results
Etomidate triggered a persistent increase in the amplitude of the tonic current (Figure 1). Ketamine alone had no effect on tonic current (control: 0.92±0.20 pA/pF vs ketamine 1 mM: 0.78±0.18 pA/pF, p > 0.05). Co-treatment of etomidate with ketamine prevented the etomidate-induced persistent increase in tonic current. ANA12 reduced the effects of ketamine.
Conclusions
A clinically-relevant concentration of ketamine, prevented the etomidate-induced increase in tonic current. This effect may be mediated by the neurotrophic factor BDNF. This study offers a novel mechanism to account for the cognition-sparing properties of ketamine.

Collaborators: Agnes Crnic, Kirusanthy Kaneshwaran, Shahin Khodaei, Dian-Shi Wang, Beverley A. Orser

Mental Illness After Intensive Care: A Population Based Cohort Study

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Sunnybrook Health Sciences Centre

Background
Small studies have reported increased risk for new-onset mental illness in intensive care unit (ICU) survivors. Only one has examined this on a population-level, but was restricted to psychiatrist
diagnoses so may have underestimated diagnosis rates. We sought to determine the incidence of new-onset mental illness across a large population of ICU survivors, including diagnoses by nonspecialist and specialist physicians, and to identify common ICU procedures associated with a higher risk of mental illness.

Methods
This population-based observational study including adult ICU survivors (age ≥ 18) in Ontario, Canada (2005-2015) excluded patients with previously diagnosed mental illness, acute neurological injury (e.g., traumatic brain injury, stroke, intracranial monitors, cardiac arrest), and conditions already known to increase risk of mental illness (e.g., cardiac surgery, pregnancy). The primary outcome was a new diagnosis of mental illness during 1-year of follow-up after discharge, identified using Ontario health administrative datasets. For comparison, we measured outcome rates in patients hospitalized during the same period but not requiring ICU admission. Fine and Grey multivariable models were used to evaluate outcome incidence after adjusting for confounders (age, sex, length of stay, rurality and income quintile), while accounting for the competing risk of death. Results: 1,847,631 patients survived their index hospitalization, of whom 121,125 (6.6%) required an ICU admission. Patients who were admitted to ICU had a higher 1-year crude and adjusted incidence of mental illness than hospitalized (non-ICU) controls (crude rates 17% vs 15%, p<0.001; adjusted HR 1.1, 95%CI 1.1-1.1, p<0.001). Most mental illness diagnoses (90%) were made by non-psychiatrists. Among ICU patients surviving to hospital discharge, several interventions were associated with increased risk of mental illness: mechanical ventilation (HR: 1.2, 95%CI 1.1-1.2, p<0.001), tracheostomy (HR: 1.3, 95%CI 1.2-1.4, p<0.001), percutaneous feeding tube (1.2, 95%CI 1.1-1.3, p<0.001), bronchoscopy (HR 1.2, 95%CI 1.1-1.3, p<0.001), and chest-tube (HR: 1.1, 95%CI 1.1-1.2, p<0.001).

Conclusions
Rates of incident mental illness after hospitalization are high, and ICU admission slightly increases the risk. Several common ICU procedures are associated with increased risk of subsequent mental illness; these patients could be considered for more targeted support following discharge.

Collaborators: Damon Scales, Hannah Wunsch Simone Vigod

Comparison of the North American Caffeine Halothane Contracture Test and The Japanese Calcium-Induced Release Test for Diagnosis of Malignant Hyperthermia Susceptibility

Carlos Alberto Ibarra Moreno – Fellow
UHN – Toronto General Hospital

Background
Malignant hyperthermia (MH) susceptibility is determined by measuring the contracture response of fresh skeletal muscle to caffeine and halothane. In Japan, an alternative diagnostic approach determines the calcium-induced calcium release rates (CICR) from sarcoplasmic reticulum (SR) using skeletal muscle skinned fibers. The advantage of CICR test is the much smaller muscle sample, and feasibility of technique up to 4 days after biopsy. The aim of this study is to assess the agreement between the Japanese CICR test and the North American caffeine-halothane contracture test (CHCT) for diagnosis of MH susceptibility.

Methods
After REB approval and written informed consent, all patients referred to the MH investigation unit for CHCT were deemed eligible. Gracilis muscle was harvested according to the CHCT protocol. Chemically skinned fibers were prepared according to Endo’s method and exposed to a series of solutions in a stepwise manner, as follows: 1) the SR is loaded with calcium in the presence of Mg-ATP; 2) a solution with calcium and no ATP is applied to induce CICR; 3) the calcium left over in the SR is released by a caffeine challenge. Using isometric contraction as an indicator of myoplasmic calcium concentration, CICR was determined by calculating tension/time integral of the caffeine-induced contracture. CICR was considered non-accelerated if within the 95% confidence interval around mean reference values from the Japanese Malignant Hyperthermia Association measured in low-risk subjects, or as accelerated if it was 1.5 standard deviations above the corresponding reference mean at two or more calcium concentrations. Level of agreement between CHCT and CICR tests was quantified using Cohen’s Kappa.

Results
Binary outcomes of CHCT and CICR test are showed in the table. Out of 13 patients, 6 (46.2%) were diagnosed as MHsusceptible by CHCT while 11 (84.6%) were positive on the CICR test. Overall agreement between the tests was 61.5%. Cohen’s Kappa was 0.27, indicating slight agreement.

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Conclusion
Our current CICR cutoff values for MH susceptibility diagnosis may yield a high sensitivity at the price of an unacceptably high likelihood of false positive results. Strategies to increase the CICR test’s accuracy of will be discussed.

Collaborators: Carlos A. Ibarra Moreno; Yasuko Ichihara; Natalia Kraeva; Elena Zvaritch; Hirosato Kikuchi; Sheila Riazi.

Risk Factors for Opioid Induced Respiratory Depression in Surgical Patients: A Systematic Review and Meta-Analysis

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UHN – Toronto General Hospital

Background
Postoperative opioid induced respiratory depression (OIRD) may result in serious morbidity and mortality.1,2 This systematic review and meta-analyses highlights the important risk factors associated with OIRD in the post-operative period. Knowledge of the risk factors of OIRD will help the health care providers to take appropriate precautions, plan risk-mitigation, titrate the dose of opioids and use enhanced monitoring in patients with high risk.

Methods
A systematic literature search was performed on postoperative OIRD in adult patients of the following databases from 1947 to November 2017: PubMed-MEDLINE, MEDLINE in-process, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, PubMed and Clinicaltrials.gov. All adult surgical patients (≥18 years) who were administered opioids during their hospital stay after surgery and had post-operative OIRD (OIRD group) were included. The studies which reported data on the control group (patients who did not develop OIRD) for each risk factor were included in the meta-analysis. Only the published articles in English language were selected. We used a random-effects inverse variance analysis to evaluate the existing evidence of risk factors associated with OIRD. Meta-analysis was conducted using Cochrane Review Manager 5.3.

Results
A total of 8,690 citations were screened, and 12 studies were included. The incidence of post-operative OIRD was 5.0 per 1,000 anesthetics (95% CI: 4.8 - 5.1; Total patients: 841,424; OIRD: 4,194). Eighty-five percent occurred within the first 24 hours after surgery. Increased risk for OIRD were associated with pre-existing cardiac disease (OIRD vs. control: 42.8% vs. 29.6%; OR:1.7;95%CI:1.2-2.5; I²:0%; p<0.002), pulmonary disease (OIRD vs. control: 17.8% vs. 10.3%; OR:2.2; 95%CI:1.3-3.6; I²:0%; p<0.001) and obstructive sleep apnea (OIRD vs. control: 17.9% vs. 16.5%; OR:1.5; 95%CI:1.2-1.8; I²:50%; p=0.0005). The morphine equivalent daily dose of the post-operative opioids was higher in the OIRD than control; 24.7±14 mg vs. 18.9±13.0 mg; MD:2.8; 95%CI:0.4-5.3; I²:98%; p=0.02) (Figure 1). The quality of the study evaluated by Newcastle Ottawa scale scoring system varied from 5 to 9.
**Conclusions**
This systematic review and meta-analysis demonstrated that patients with cardiac disease, pulmonary disease and obstructive sleep apnea are at increased risk for OIRD. Patients with OIRD received higher postoperative morphine equivalent doses.

**References**

**Collaborators:** Kapil Gupta, Mahesh Nagappa, Arun Prasad, Lusine Abrahamyan, Jean Wong, Toby Weingarten, Frances Chung
D2 ♦ Anesthetic Activation of GABA (A) Receptors in Astrocytes Triggers a Persistent Increase in a Tonic Inhibitory Current in Hippocampal Neurons

Arsene Pinguielo – Graduate Student
Sunnybrook Health Sciences Centre

Background
Preclinical studies have shown that several commonly used general anesthetic drugs trigger a sustained increase in a tonic inhibitory GABAergic current in neurons. This inhibitory current impairs memory performance long after the anesthetic drug has been eliminated from the body. Interestingly, anesthetic drugs stimulate astrocytes to release soluble factors that drive the increase in tonic inhibitory current in neurons; however, the underlying mechanisms are unknown. Since GABA(A) receptors are important targets for general anesthetics and astrocytes express these receptors, the goal of this study was to test the hypothesis that anesthetic activation of GABA(A) receptors in astrocytes triggers the persistent increase in tonic inhibitory current in neurons. We also investigated the subunit composition of GABA(A) receptors in astrocytes.

Methods
Studies were approved by the local Ethics Committee. Primary hippocampal neurons and cortical astrocytes were prepared from fetal mice. Astrocyte cultures were treated with etomidate (1 microM) with or without the GABA(A) receptor antagonist bicuculline (20 μM) for 1 hour. Following washout, the cultures were incubated for 2 hours. The conditioned medium was then transferred to hippocampal neuron cultures. 24 hours later the tonic current was recorded in neurons with patch clamp technique. Western blotting was used to examine the subunit composition of GABA(A) receptors in the cultured astrocytes.

Results
Medium from astrocytes treated with etomidate but not etomidate plus bicuculline increased the amplitude of the tonic current. Western blots showed that astrocytes express alpha2 and beta2, but not alpha5 subunits of GABA(A) receptors.

Conclusions
Activation of GABA(A) receptors in astrocytes is necessary for anesthetic-induced persistent increase in tonic inhibitory current in neurons. These receptors likely contain alpha2 and beta2 subunits, and may be therapeutic targets for the prevention and treatment of cognitive deficits after anesthesia and surgery.

Collaborators: Sean C. Haffey, Irene Lecker, Dian-Shi Wang, Beverley A. Orser

D3 ♦ Weeding Out The Problem: The Impact of Preoperative Cannabinoid Use on Pain in The Perioperative Period

Weiyang Christopher Liu - Fellow
UHN – Tornoto Western Hospital

Background
The use of cannabinoids has been increasing due to recreational use of cannabis and medical access via special exemptions.1 While most studies and reviews2,3 have looked at whether cannabinoids
have a role in the management of acute pain, no study has examined the postoperative outcomes of surgical candidates who use cannabinoids preoperatively. We designed a propensity score-matched retrospective cohort study to examine the impact of preoperative cannabinoid use on postoperative pain scores and pain-related outcomes in patients undergoing major orthopedic surgery.

Methods
After Institutional REB approval, we conducted a retrospective study of patients who had major orthopedic surgery at Toronto Western Hospital between April 1 2015 and June 30 2017. Data was obtained from NOPAIn, a locally developed database of our Acute Pain Service. Propensity score matching was used to balance baselines variables including age, gender, type of surgery, history of depression or anxiety and perioperative use of regional anesthesia. The primary outcomes were numerical rating scores (NRS) for pain at rest and on movement, and analgesic consumption in the first 24 hours following surgery. The secondary outcomes were the presence of pruritus, nausea and vomiting, sleep, sedation, delirium, constipation, physical activity impairment, satisfaction and required length of APS follow-up.

Results
A total of 3793 patients were included in the study. Of these, 156 patients were identified as being on cannabinoids in the preoperative period. After propensity score matching, we analyzed 156 patients who were on cannabinoids and 156 patients who were not on cannabinoids. There was no difference in the baseline characteristics of these two groups of patients. Patients who were on preoperative cannabinoids had higher pain NRS [mean (SD)] at rest [4.38 (2.57) vs. 3.66 (2.34), p=0.045] and on movement [6.85(2.96) vs. 5.96(3.13), p=0.045] compared to patients who were not on cannabinoids. (Figure 1) There was however, no differences in opioid consumption on the first postoperative day [185.8 (232.1) mg vs. 155.8 (318.1) mg, p=0.448]. There were also no differences in the incidence of pruritus, nausea, vomiting, patient satisfaction, sedation, delirium and constipation between the two cohorts on the first postoperative day but there was more physical activity impairment in patients not using cannabinoids and more sleep interruption for patients who used cannabinoids.

Conclusions : This retrospective study with propensity-matched cohorts showed that chronic cannabinoid use preoperatively was associated with higher pain scores at rest and movement in
patients undergoing major orthopedic surgery. We propose that the possible explanations for the findings in our study are acute cannabinoid withdrawal or chronic cannabinoid use inducing hyperalgesia.


D4  Morphine Alters Cancer Metabolic Pathways

Doorsa Tarazi – Graduate Student
Hospital for Sick Children

Introduction
Many cancers have been shown to exploit metabolic pathways to promote growth and metastasis. Over 70% of low grade gliomas contain a mutation in isocitrate dehydrogenase 1 (IDH1), an essential metabolic enzyme with roles in cell stress and gene regulation. When mutated, IDH1 produces 2-hydroxyglutarate (2HG), a compound that alters DNA epigenetics (methylation) and thereby gene expression. Nevertheless, the presence of IDH1 mutations have been correlated with improved prognoses in gliomas. Morphine is the primary option for pain management amongst cancer patients, yet its impact on cancer progression remains inconclusive. Through screening, we found that the opiate morphine is a specific inhibitor of IDH1, potentially providing a beneficial effect in aggressive cancers.

Methods
The U87 high grade glioma cell line was treated for 7 days with clinically relevant serum concentrations of morphine or hydromorphone (0.01uM – 50uM). Resultant changes in 120 metabolites were determined by targeted metabolomics. Methylation profiling was performed by an antibody based assay. Oncogenic aggression was quantified using proliferation and migration wound-healing assays.

Results
Detectable changes to 82 metabolites were observed following opioid treatment, most notably morphine resulting in decreased glutamate and increased pentose phosphate pathway metabolism, consistent with cellular oxidative stress. Following morphine treatment, we observed a dose-dependent increase in 2HG levels (58-86% increase), which was consistent with an increase in total DNA methylation (p < 0.05). Morphine reduced cell proliferation and migration, both following a dose-dependent pattern (p < 0.05).

Conclusions
We illustrated that morphine was able to alter DNA methylation and gene regulation through an increase in the oncometabolite 2HG. The metabolic profile following morphine treatment is similar to that of low-grade gliomas that are sensitized to oxidative stress, and have not undergone malignant progression. This may indicate that the interaction between morphine and IDH1 mimics the metabolic and methylation phenotype of IDH1-mutant tumors, consistent with the observed decrease in invasive cancer phenotype (lower proliferation and migration). Our findings contribute
to the understanding of the relationship between disease progression and pain treatment, while highlighting the need for cancer-specific precision pain management.

Collaborators: Dr. Jason T. Maynes and Dr. Yanan Tang

D5 ♦ Using Patient-Reported and Wearable-Technology Date to Assess Outcomes of Spinal Cord Stimulation Trials for Neuropathic Pain Syndromes

Nimish Mittal - Fellow
UHN – Toronto Western Hospital

Background
Spinal cord stimulation (SCS) is used to ameliorate chronic neuropathic pain (NP)1. A trial of SCS is recommended prior to considering implantation of a SCS system. Though chronic NP negatively impacts several pain-related domains including physical activity2 and quality of sleep2, pain scores - a subjective measure - are the most frequent and often the only outcome monitored during SCS trials. Validated questionnaires can be used to track activity and sleep during SCS trials but recall bias limits their reliability3. We hypothesize that objective tracking of these domains using wearable biosensors allows better-informed decisions based on comprehensive assessment of multi-dimensional impact of SCS.

Methods
Pre- and post-SCS trial data has been collected from 20 patients undergoing percutaneous SCS trials (duration of one to two weeks) for persistent refractory NP in the back and lower limbs. Validated questionnaires were used to collect patient-reported data on intensity and character of pain, activity, and sleep. These include numerical rating scores for pain, DN4 questionnaire, Oswestry Disability Index (ODI), Pain Disability Index (PDI), and Pain and Sleep Questionnaire three-item index (PSQ-3). Patients were also provided with wrist-worn accelerometer biosensors (GENEActiv®, Activeinsights, UK), that track physical activity and sleep metrics throughout the trial period as a standard clinical practice. Institutional REB approval has been obtained for reporting this data.

Results
Our preliminary analysis reveals that wearable biosensors yield valuable information about impact of SCS on physical activity and sleep. Similar trends in changes of physical activity and sleep (improvements in patients with analgesic benefit and lack thereof in patients with no benefit) were observed in patient-reported scales and biosensors analysis. Further, analysis indicates the potential utility of correlating trends from validated patient reported questionnaires with those from wearable biosensors (Figure 1) in predicting benefits from SCS implants.
Figure 1. Changes between end-of-trial and baseline activity and Oswestry Disability Index (ODI) scores as measured by the accelerometer (positive changes in activity indicate increase in physical activity and negative changes in ODI scores indicate improvement in physical ability). Green dots indicate successful trails and red dots are failed trials.

Conclusions: Using data obtained from accelerometer-based sensors and validated questionnaires during SCS trials can improve long-term outcomes of SCS through more appropriate patient selection for permanent implants.

References

Collaborators: Anuj Bhatia, Mandeep Singh, Suneil K. Kalia, Mojgan Hodaie, Andrew Lim, Jamal Kara, Filomena Mazzella, Alina Mednikov, Darcia Paul

D6 ♦ Heart Rate Variability can Predict Post-Induction Hypotension in Patients with Cervical Myelopathy

Sujoy Banik – Fellow
UHN – Toronto Western Hospital

Introduction
Maintaining adequate spinal cord perfusion (Mean Arterial Pressure (MAP) >80mmHg) is important in patients undergoing cervical spinal surgery to prevent postoperative neurological impairment. [1, 2] Autonomic dysfunction is common in patients with cervical myelopathy and increases the likelihood of perioperative hypotension.[3] Heart rate variability (HRV) has been used
to detect autonomic dysfunction,[4, 5] The aim of our study was to determine if reduced HRV can predict post-induction hypotension in patients with cervical myelopathy undergoing spine surgery.

**Methods**

After REB approval, 40 patients (18-70yrs) with cervical myelopathy undergoing anterior and/or posterior cervical decompression and fusion were consented for this prospective observational study. Patients at risk for autonomic neuropathy (diabetes), or those with arrhythmia and resting tachycardia (heart rate > 100bpm) were excluded. Resting ECG (5 minutes) was recorded preoperatively with the patient in a relaxed state in supine position. onto a computer using custom software (s5collect). HRV analysis was performed postoperatively using Labchart 8 software. Total power, proportions of very low frequency (VLF), low frequency (LF) and high frequency (HF) spectra and LF/HF ratio were calculated. Intraoperatively, episodes of hypotension (MAP <80 mmHg, lasting > 5minutes) and the number of interventions (Phenyephrine 40mcg, ephedrine 5mg) required to treat the hypotension during the period from induction to surgical incision were recorded. Categorical data was analysed using Fisher’s exact test whilst non-parametric data was analysed using Mann-Whitney U test using SPSS software. A p value <0.05 was considered significant.

**Results**

30 patients (27% female; mean age 54±10.6) were recruited for the study. 80% (24/30) patients developed hypotension post-induction and required a mean of 2.20 interventions to maintain their MAP above 80. There was no statistically significant difference in age (p=0.36), gender (p = 1.00), ASA score (p = 0.30), type of procedure (p = 1.00) or the severity of myelopathy (Japanese Orthopaedic Association Score) (p = 0.14) between those with and without hypotension. Among the indices of decreased HRV, total power <500ms2.Hz-1 was not predictive of post-induction hypotension (p = 0.30). Increasing LF/HF ratio was predictive (p = 0.009) with a LF/HF ratio > 2.5 indicated post-induction hypotension was likely (p = 0.017). Furthermore, there was a correlation between increasing LF/HF ratio and the numbers of interventions need to maintain MAP above 80mmHg (r = 0.28). (Figure 1)

**Conclusions**

Our results suggest that an LF/HF ratio >2.5 can predict which patients with cervical myelopathy will develop hypotension after induction allowing anesthetists to pre-emptively treat such patients thereby avoiding spinal cord hypoperfusion.

**Collaborators:** Dr Sarah Boyle, Dr Pirijo Manninen, Dr Lashmi Venkatraghavan