### Richard Knill Competition

**Co-chairs:**
Dr François Donati, Department of Anesthesiology, University of Montreal, Montreal, QC  
Dr Donald Miller, Department of Anesthesia, University of Ottawa, Ottawa, ON

**Monday June 24**
**10:15 – 12:00**  
TELUS 104/105/106

#### 1651722 - Celecoxib for Pediatric T&A: A Double Blinded RCT
**Presenter:** Kimmo Murto, Clinical Research Unit, Children’s Hospital of Eastern Ontario Research Institute, Ottawa, ON  
**Co-authors:** Christine Lamontagne, Johnna MacCormick, Kelly-Ann Ramakko, David Rosen, Colleen Daly, Mary Aglipay, Regis Vaillancourt

#### 1652221 - Proposing Formal Diagnostic Criteria for Post-Epidural PDPH  
**Sponsored by Carf / Commandité par la FCRA**
**Presenter:** Pamela Angle, Department of Anesthesia, Sunnybrook Health Sciences Centre, Toronto, ON  
**Co-authors:** Joanne Douglas, Christine Lay, Marek Gawel, Jean Kronberg, Patricia Morley-Forster, Ronald B George, Dolores McKeen, Roanne Preston, Indu Singh, Stephen Halpern, Shalini Dhir, Jasmine Djordjevic, Mary Jo Ricci, Alex Kiss

#### 1652406 - Inhibition of Acetaminophen Analgesic Action by Ondansetron After Amygdalectomy in Children: The Paratron Randomized Trial.
**Presenter:** Pierre Beaulieu, Anesthesiology & Pharmacology, Faculty of Medicine, Montreal, QC  
**Co-authors:** Lucie Ramirez, Jérome Cros, Patrice Boulogne, Nathalie Nathan-Denizot

#### 1653425 - Carbetocin at Elective Cesarean Delivery: A Randomized Controlled Trial to Determine the Effective Dose, Part 3-Final
**Presenter:** Jose Carvalho, Department of Anesthesia and Pain Management, Mount Sinai Hospital, University of Toronto, Toronto, ON  
**Co-authors:** Mubeen Khan, Iram Ahmed, Mrinalini Balki, Dan Farine, Gareth Seaward

#### 1653520 - Glycosylated Hemoglobin Screening for Elective Surgical Patients
**Presenter:** Yuri Koumpan, Anesthesiology and Perioperative Medicine, Queen's University, Kingston, ON  
**Co-authors:** Elizabeth Vandenkerkhof, Janet M van Vlymen

#### 1653570 - Incidence and Severity of Residual Neuromuscular Blockade in Canada: The Final Results of the Recite Study: A Prospective, Multicenter, Observational Study.
**Presenter:** Louis-Philippe Fortier, Hopital Maisonneuve-Rosemont, Montreal, QC  
**Co-authors:** Dolores McKeen, Kim E Turner, Brian Warriner, Étienne De Médicis, Alan J Chaput, Philip Jones, Robin Curtis, Jean-Francois Pouliot, Andre Galarneau
CELECOXIB FOR PEDIATRIC T&A: A DOUBLE BLINDED RCT

Kimmo Murto, Christine Lamontagne, Johnna MacCormick, Kelly-Ann Ramakko, David Rosen, Colleen Daly, Mary Aglipay, Regis Vaillancourt

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Introduction: Celecoxib is an effective analgesic in adult surgery patients, but no comparable pediatric literature exists. Our objective was to determine the effect of a short course of an oral celecoxib suspension on pain and functional recovery in pediatric adenotonsillectomy (T&A) patients.

Methods: With REB approval 282 children, 2-18yrs, scheduled for elective T±A were randomized in a double blinded fashion to receive preoperative celecoxib 6 mg/kg or placebo. BMI extremes were excluded. Anesthesia was standardized. After surgery patients received either celecoxib 3 mg/kg or placebo twice daily for 5 doses. Analgesics (acetaminophen and morphine) were administered as needed. Daily age appropriate diaries were completed by parents and children (≥5yrs) to document recovery for postoperative days (PODs) 0-7. The primary outcome was a once daily score recording the “worst pain over previous 24 hours” for PODs 0-2. Total analgesic use was monitored. Celecoxib-related side effects were recorded and functional recovery in terms of QOL and fatigue were measured at POD 7 and compared to baseline. Hospital contact for bleeding and need for intervention were recorded. Parent satisfaction was measured. The genotype of the CYP2C9 liver enzyme responsible for celecoxib metabolism was determined. Repeated measures ANOVA and t-tests were used as indicated for comparisons.

Results: The intention-to-treat analysis included 272 (135 celecoxib, 137 placebo) children of which 204 (106 celecoxib, 98 placebo) returned the diaries and 183 (96 celecoxib, 87 placebo) were suitable for pain analyses. Demographics including distribution of CYP2C9 genotypes were similar. Celecoxib significantly reduced “worst pain” on PODs 0 and 1, but not 2 (Fig. 1). Similarly, it reduced pain with swallowing for PODs 0 (44±3 vs 53±3, p=0.04) and 1 (45±3 vs 57±3, p=0.01) only and pain at rest in the evening of POD 0 (44±3 vs 54±3, p=0.02). Total PODs 0-2 acetaminophen consumption (mg/kg ± SD) was significantly lower in the celecoxib group (78±57 vs 96±59, p=0.04) and morphine consumption trended lower (0.56±0.47 vs 0.70±0.56, p=0.06). There was no difference in the incidence of celecoxib-related side effects, level of functional recovery or satisfaction. There was minimal difference in tonsil bleeds requiring a hospital visit (6 celecoxib, 5 placebo) or surgery (3 celecoxib, 2 placebo).

Discussion: In children, a short course of an oral celecoxib suspension after T&A reduced early static and dynamic pain and analgesic consumption. However, it had no effect on functional recovery. Celecoxib appears to be beneficial for T&A in children.
Introduction: Advances in the management of postdural puncture headache (PDPH) after epidurals cannot take place without use of meaningful diagnostic criteria for outcome measurement in clinical trials. We compared performance of new clinical diagnostic criteria, developed by the Primary Investigator, vs International Headache Society (IHS) criteria (Ref1) for diagnosis of post-epidural PDPH within the Canadian PDPH Trial.

Methods: Following REB approval and written informed consent, this multicenter RCT randomized laboring women to receive a large (≥18g) vs small (19g) Tuohy-type needle for epidural placement. The primary outcome was PDPH within the first 14 days of procedure based on formal Study Criteria. The diagnosis was made by a blinded external expert adjudicating body which also examined cases for PDPH based on IHS criteria (Table 1). First pass agreement between adjudicators was assessed (kappa) followed by a consensus diagnosis if required. A second external independent headache specialist/neurologist (Umpire Reference Test/gold standard), examined all 184 previously adjudicated cases, blinded to needle and previous diagnoses, over the full course of study/clinical followup (> =13 weeks, maximum 1 year) for a diagnosis of symptoms consistent with CSF leakage.

Results: 1080 women were recruited. Study criteria demonstrated improved interrater reliability (first pass) between adjudicators for PDPH diagnosis (Kappa 0.93, 95% CI 0.85, 1.0) vs IHS Criteria (kappa 0.70, 95% CI 0.49, 0.92) with PDPH diagnosed in 25/184 cases based on Study Criteria vs 16/184 using IHS criteria. Thirty-one/184 of these same cases were diagnosed with CSF leakage based on longterm followup (Umpire Reference Test). Study Criteria also demonstrated improved diagnostic performance compared with IHS Criteria: Sensitivity 71% (vs 36%), Specificity 98% (vs 97%), NPV 94% (vs 88%), PPV 88% (69%), LR+ 36 (12,142) (vs LR 10.9 (3.9, 34)), IHS criteria included air headaches (3) as false positives and missed clinically important PDPH detected by the Study Criteria. Two women, diagnosed with CSF leakage symptoms, were missed by Study Criteria despite the increased diagnostic window of 14 days. One woman diagnosed with chronic headache had symptoms up to one year; another had symptoms for 6 months.

Discussion: Study Criteria improved diagnosis of CSF leakage symptoms (ie clinically important PDPH) post-epidural when compared with IHS criteria, suggesting that these criteria should be adopted for use in clinical practice and research. Improved surveillance for PDPH post-epidural placement as well as development of objective diagnostic tools to further refine PDPH diagnosis are required.

References: 1. international Classification of Headache Disorders, 2nd edition, Cephalagia, 24, supplement 1, 2004

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<tr>
<th>Formal Study Criteria</th>
<th>IHS Criteria (ICHD-II)</th>
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<td>1. Postural headache or neckache that occurs or worsens within 15 minutes of sitting/standing and improves within 15 minutes of lying down.</td>
<td>1. Headache that worsens within 15 minutes of sitting/standing and improves within 15 minutes of lying down with at least one of the following criteria (must include criteria 3&amp;4 as well): neck stiffness, tinnitus, photophobia, nausea, hypacusis</td>
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<td>Symptoms may include visual or auditory symptoms, neck stiffness, tinnitus, diplopia, photophobia, nausea/vomiting</td>
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INHIBITION OF ACETAMINOPHEN ANALGESIC ACTION BY ONDANSETRON AFTER AMYGDALECTOMY IN CHILDREN: THE PARATRON RANDOMIZED TRIAL.

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Introduction: The mechanism of action of acetaminophen is still unclear. One hypothesis involves an interaction with the serotonergic system. Furthermore, setrons have antiemetic properties by acting as antagonists at serotonin (5-HT3) receptors. Therefore, co-administration of acetaminophen and a setron could lead to a decrease or a loss of acetaminophen analgesic effects. Indeed, interactions between setrons and acetaminophen have been reported in different animal studies and in human volunteers although its existence has never been demonstrated in the clinic. The aim of this study was to demonstrate that the association acetaminophen/ondansetron is not as effective as acetaminophen/droperidol in the treatment of pain in children following tonsillectomy.

Methods: This study was approved by our institutional ethics committee. Paratron trial was designed as a prospective, randomized, double blind, parallel group trial. Children aged 2-7 years old and scheduled for a tonsillectomy ± adenoidectomy were recruited. All patients received intraoperatively acetaminophen together with ondansetron or droperidol (Figure). At the end of surgery, patients received i.v. morphine. Pain scores using CHEOPS scores, morphine consumption and the incidence of postoperative nausea and vomiting (PONV) were measured during 24 h. The primary outcome was pain scores at 4 h after administration of acetaminophen and ondansetron or droperidol. Secondary objectives were morphine consumption, cumulated incidence of PONV. Comparison of CHEOPS scores and morphine consumption between groups was performed using Student t test or Wilcoxon rank signed test. The level of significance was set at 5%.

Results: From October 2011 to June 2012, 69 patients were included: 35 in the ondansetron group and 34 in the droperidol group. CHEOPS scores were not different at all times during the first 24 h. However, mean morphine consumption (in µg) in recovery was 279.5 ± 271.5 and 97.6 ± 201.5 in the ondansetron and droperidol groups, respectively (p = 0.004). Furthermore, the percentage of patients who received morphine titration was 57.1% and 20.6% in the ondansetron and droperidol groups, respectively (p = 0.008). No significant difference was present for PONV. An interaction between acetaminophen and ondansetron did occur with children receiving 3 times more morphine during pain titration in the recovery room.

Discussion: This is the first time that the interaction between acetaminophen and a setron is reported in a clinical setting. More studies are necessary to evaluate if it is clinically relevant to preclude the simultaneous peroperative administration of both drugs in the future.

Trial assignment to study medications.
Introduction: Carbetocin has been recommended as the preferred uterotonic at elective cesarean delivery (CD) by the Society of Obstetricians and Gynecologists of Canada since 2009 (1). Its main advantage is a longer half-life compared to that of oxytocin (40 min vs. 4-10 min) (2). A systematic review comparing carbetocin 100 mcg with variable doses of oxytocin at CD showed a reduction in the need for additional uterotonic with carbetocin, but no difference in the incidence of postpartum hemorrhage or side effects (3). Two previous dose-finding studies of carbetocin at elective CD, with doses varying from 20 to 120mcg, have shown similar efficacy across all doses (4,5). We aimed to determine the minimum effective dose of carbetocin (ED90) at elective CD.

Methods: Following REB approval, and with written informed consent of all subjects, we conducted a randomized, double-blind, dose-finding study of carbetocin. Inclusion criteria were ASA I/II women undergoing elective CD under spinal anesthesia. Carbetocin was administered intravenously over 1 minute upon delivery of the fetus. The obstetrician assessed the uterine tone at one-minute interval for 5 minutes and then at his/her discretion until the end of surgery and decided on the need for additional uterotonic. The dose of carbetocin for each patient was determined according to a biased coin up-and-down sequential allocation scheme designed to cluster doses close to ED90. The initial dose was 10 mcg, with increments/decrements of 5 mcg. The obstetrician, anesthesiologist, and patient were blinded to the study dose. The primary outcome was the need for additional uterotonic intraoperatively, in which case the treatment was considered a failure. Secondary outcomes included use of additional uterotonic agents within 24 hours of the completion of surgery, estimated blood loss and side effects. Data analysis was done by the Dixon-Mood method for non-parametric data.

Results: Forty patients were recruited. The ED90 of carbetocin was calculated as 14.8 mcg (95% CI 13.7-15.8mcg). Thirty-seven patients did not require additional intraoperative uterotonic. Of the three patients that required additional uterotonic, one had received 15 mcg and two had received 10 mcg of carbetocin. Overall estimated blood loss using a hematocrit variation method was 785.6±402.8 ml. The overall incidence of hypotension was 37.5%.

Discussion: Our study shows that at elective CD, the ED90 of carbetocin is about 15mcg, which is less than one fifth of the currently recommended dose of 100 mcg. The lower incidence of hypotension in our study, as compared to 45-55% previously reported in other studies (4,5) may represent an advantage, however, this trend warrants confirmation in a larger study. Consideration should be given to the use of lower doses of carbetocin at elective CD.

GLYCOSYLATED HEMOGLOBIN SCREENING FOR ELECTIVE SURGICAL PATIENTS

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Introduction: Uncontrolled blood glucose levels in the perioperative period are associated with a higher incidence of surgical site infections, greater utilization of resources, and increased mortality.1,2 These outcomes are modifiable with improved blood glucose control. However, preoperative screening for diabetes in elective surgical patients is not routinely done. The objective of this study was to determine 1) the incidence of elevated glycosylated hemoglobin (HbA1c) in patients with no previous history of diabetes; 2) the adequacy of recent glycemic control among diabetic patients; and 3) the validity of random blood sugar (RBS) and fasting blood sugar (FBS) (using HbA1c as the gold standard) to identify patients with sub-optimal glycemic control.3

Methods: Following local ethics committee approval, 406 patients were enrolled in the study. All patients ≥18 presenting to the pre-surgical screening clinic in preparation for elective surgery were eligible. All participants completed a questionnaire to identify risk factors for diabetes and patients with a history of diabetes completed an additional questionnaire assessing their perceived level of glycemic control. HbA1c and RBS testing were completed in the clinic and FBS was done on the day of surgery. Frequencies and valid percentages were calculated

Results: Of the 406 patients screened, 82% (n=334) had no history of diabetes and 18% (n=72) had a previous diagnosis of diabetes. Among patients with no previous diagnosis of diabetes, 23% (n=77) were considered to have pre-diabetes (HbA1c= 6.0-6.49%) and 3.9% (n=13) had a provisional diagnosis of diabetes (HbA1c ≥6.5%). The majority of diabetic patients, 56% (n=39/70), had sub-optimal glycemic control (HbA1c >7.0%) and 26% (n=18/70) had poor glycemic control (HbA1c ≥8.5%). Of the poorly controlled diabetics, 50% believed that their blood sugars were reasonably or very well controlled. For patients with a provisional diagnosis of diabetes (HbA1c ≥6.5%), only 15% (n=2/13) had an elevated RBS (≥11.1) while 67% (n=8/13) of had an elevated FBS (≥7.0) on the day of surgery. For the sub-optimally controlled diabetics (HbA1c > 7.0%), 42% (n=16/38) had an elevated RBS (≥11.1) while 86% (n=31/36) had an elevated FBS (≥7.0).

Discussion: There are a significant number of elective surgical patients who have previously undiagnosed pre-diabetes or a provisional diagnosis of diabetes. These patients are at considerable risk for unrecognized postoperative hyperglycemia and the associated adverse outcomes. Among patients with a history of diabetes, the majority have sub-optimal glycemic control. Relative to HbA1c, RBS testing has limited value in identifying patients with poor glycemic control in pre-surgical screening. These results suggest that HbA1c may be a more appropriate test for the preoperative assessment of diabetic patients. Future study is needed to determine if HbA1c testing is a cost-effective screening tool for patients with no previous history of diabetes.

1653570 - INCIDENCE AND SEVERITY OF RESIDUAL NEUROMUSCULAR BLOCKADE IN CANADA: THE FINAL RESULTS OF THE RECITE STUDY: A PROSPECTIVE, MULTICENTER, OBSERVATIONAL STUDY

Louis-Philippe Fortier, Dolores McKeen, Kim E. Turner, Brian Warriner, Étienne De Médicis, Alan J. Chaput, Philip Jones, Robin Curtis, Jean-François Pouliot, Andre Galarneau

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4. Vancouver General Hospital, Vancouver, BC, Canada
5. CHUS, Sherbrooke, QC, Canada
6. The Ottawa Hospital, Ottawa, ON, Canada
7. London Health Sciences Centre, London, ON, Canada
8. Red Deer Regional Hospital, Red Deer, AB, Canada
9. Merck Canada, Kirkland, QC, Canada

Introduction: Postoperative residual neuromuscular blockade (rNMB), defined as a train-of-four (TOF) ratio of <0.9, is an established risk factor for critical respiratory events and increased morbidity. At present, little is known about the occurrence of rNMB in Canada. The RECITE (Residual Curarization and its Incidence at Tracheal Extubation) study was a prospective observational study at eight hospitals in Canada investigating the incidence and severity of rNMB. The primary and secondary objectives were to determine the incidence and severity of rNMB (TOF ratio <0.9) just before tracheal extubation and at arrival in the post-anesthesia care unit (PACU).

Methods: Prior to patient enrolment, all documentation regarding the design, objectives, and conduct of the study was reviewed by the Institutional Review Board (IRB) or Independent Ethics Committee (IEC) at each study site. Written informed consent was obtained from all candidates prior to entry in the study. Subjects were enrolled if they were adult patients undergoing open or laparoscopic abdominal surgery expected to last < 4 hours, ASA class 1-3, and scheduled for general anesthesia with at least one dose of a non-depolarizing neuromuscular blocking agent for endotracheal intubation or maintenance of neuromuscular blockade. Neuromuscular function was assessed using acceleromyography with the TOF-Watch® SX. The attending anesthesiologist and other observers were blinded to the TOF ratio results.

Results: A total of 302 subjects were entered. Data were available for 241 patients at tracheal extubation, and 207 patients at PACU arrival. Rocuronium was the NMB agent of choice. Approximately 74% of subjects received neostigmine as the NMB reversal agent. The incidence of rNMB was 56% (95% CI 49.7% to 62.3%) at tracheal extubation, and 44% (95% CI 37.7% to 50.2%) at arrival at the PACU. There were no statistically significant differences in the incidence of rNMB between sites or associated with gender, age, BMI, ASA Class, type of surgery or comorbidities. The proportion of patients with rNMB was higher at tracheal extubation (58.4% vs 49.2%) and at arrival at the PACU (47.7% vs 34.5%) when neostigmine was used as a reversal agent although differences were not statistically significant. The use of subjective peripheral neuromuscular monitoring was associated with a modest reduction in rNMB at extubation and at PACU arrival, but the differences were not statistically significant. Using univariable logistic regression analyses to assess risk factors for rNMB we identified that the dose of rocuronium used was statistically associated with rNMB both at tracheal extubation and at arrival to the PACU.

Discussion: Residual paralysis is common at tracheal extubation and PACU arrival despite subjective neuromuscular monitoring and the use of conventional NMB reversal agents. More effective detection and management of rNMB is needed to reduce its incidence and the risk of postoperative respiratory complications.
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<td>2. Patients may or may not have a recognized dural puncture (after epidural needle placement in the spine)</td>
<td>2. Dural puncture has been performed</td>
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<td>3. Headache and/or neckache persists at least 24 hours and occurs within 14 days of epidural needle placement</td>
<td>3. Headache develops within 5 days of dural puncture</td>
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<td>4. Headache resolves spontaneously within one week of dural puncture or within 48 hours of effective therapy (ie epidural blood patch)</td>
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