

Medical Student Research Day award winning abstracts

A wide variety of research is conducted by medical students and other undergraduate health science students at Dalhousie. Much of this research is presented each year at Dalhousie's Undergraduate Health Science Student Research Day. The abstracts included here were selected for awards from the more than forty that were presented.

\$200 cash prizes were awarded to:

Winner of the Platform Presentation

MODULATION OF DENDRITIC CELL FUNCTION BY ACTIVATED PROTEIN C

Kathleen A. Matheson¹, Konrad Kronenberger¹, Derek Minney¹, Michael Bezuhly¹, Kenneth A. West,^{1,2} and Robert S. Liwski¹

Departments of Pathology¹ and Medicine², Dalhousie University

Activated protein C (aPC) is a natural anti-coagulant that also possesses potent anti-inflammatory properties. Recombinant aPC has been shown to be effective in treatment of severe sepsis. The receptor for aPC, the endothelial cell protein C receptor (EPCR) was originally identified on vascular endothelium. Recently EPCR expression has been demonstrated on various inflammatory cells such as monocytes, neutrophils and eosinophils. Interestingly, EPCR mediated signaling in these cells downregulates their ability to produce inflammatory cytokines and to migrate to sites of inflammation. Dendritic cells (DC) are the most potent professional antigen presenting cells and are critical for the activation of T cells and initiation of immune responses against transplanted organs. In this study we investigated whether EPCR is expressed by DC and whether signaling through this receptor modulates DC function. Using RT-PCR, immunofluorescence microscopy and flow cytometry we demonstrate that both bone marrow-derived and splenic DC express EPCR. Furthermore, we show that EPCR expression by DC is increased in response to maturation signals such as LPS. Treatment of DC with aPC increases IL-12 production but has no effect on the expression of class II MHC or costimulatory molecules such as CD86 and CD40. Importantly, aPC markedly reduces the ability of DC to activate naïve CD4+ T cells, leading to reduced T cell proliferation. This study demonstrates that DC express EPCR and that treatment with aPC modulates DC function. The results are consistent with general anti-inflammatory properties of aPC. Further studies in this system could suggest a novel therapeutic use of aPC for prevention of allograft rejection.

Poster Presentation Winners

PRE-SURGICAL LOCALIZATION OF FRONTAL LANGUAGE AREAS WITH fMRI: A PRELIMINARY INVESTIGATION

Sarah Ironside¹, Gail Eskes¹, David Clarke²

Departments of Psychiatry¹ and Surgery², Dalhousie University

Purpose: To determine the inter- and intra-participant reliability of fMRI activation in the inferior frontal gyrus (Broca's area) during an orthographic verbal fluency task. The study was conducted in the context of task validation in healthy controls of a presurgical functional brain mapping protocol for patients with brain tumors.

Methods: BOLD activation was measured in five university-aged volunteers (mean age 23.8), participating in a verbal fluency task while being scanned in a 1.5T MRI scanner. A block design was used with 21s alternating rest and activation blocks. Performance was measured with a response pad. All participants underwent repeat scanning one week later. A ROI approach was applied to the evaluation of verbal fluency task reliability.

Results: The verbal fluency task was found to reliably produce BOLD activation in the left inferior frontal gyrus in all subjects at both time points. Over all subjects (corrected to $p=0.05$), 75.6% of the voxels active within the ROI were also active at the second scanning session. We observed high intra-subject reliability with all five subjects (100%) demonstrating significant BOLD activation within the ROI at time 1 and again at time 2. Participants generated significantly more words during the second scanning session with no significant differences in reaction time.

Conclusion: Preliminary results indicate that verbal fluency is a reliable task for localizing frontal language regions with fMRI. The study contributes normative data to the establishment of a preoperative protocol using fMRI to localize areas involved in language and speech production for use with patients with brain tumors who require surgery.

UTILIZATION OF INTRAVENOUS IMMUNOGLOBULIN IN THE ATLANTIC PROVINCES

Nathan WD Lamond¹, Chris Caudle², Erica Burton², Adam Webber¹, and David R Anderson¹

Department of Medicine¹, Dalhousie University, Nova Scotia Blood Coordinating Program², Queen Elizabeth II Health Sciences Centre

Introduction: In Canada, yearly use of IVIg doubled between 1998 and 2006. This represents a large healthcare expenditure and, due to fixed production rates, promotes future IVIg shortages. Recently, Canadian Guidelines were published by Canadian Blood Services and the National Advisory Committee on Blood and Blood Products to guide the clinical use of IVIg. However, there are little data regarding the current use of IVIg in Canada. The aims of this study were to further describe IVIg use in Atlantic Canada, to identify practice variations between the individual Atlantic Provinces, and to identify areas of inappropriate IVIg use by analyzing data from the Atlantic Collaborative IVIg Utilization Registry.

Materials and Methods: Data on IVIg use in Atlantic Canada from 1 April 2004 to 31 March 2007 were collected as part of the Atlantic Collaborative IVIg Utilization Registry. These data included the indication for use, dose, date, amount of IVIg, attending/consulting physician service as well as an anonymous physician identification code, patient date of birth, gender, weight, and a unique anonymized patient identifier. IVIg use was designated as acute/chronic and supported/unsupported based on the duration of and the indication for use, respectively. Only IVIg use from districts responding to the Registry for the entire study period were included in this study. Data were grouped by fiscal year and analyzed in a series of general linear models in order to identify clinical divisions with increasing use, practice differences between provinces, and changes in use over the study period.

Results: During the study period, the Atlantic Collaborative IVIg Utilization Registry reported 456901g of IVIg used for 102 indications. IVIg use (g) was 137549, 145693, and 173659 during 2004, 2005, and 2006, respectively. The most common indications for use were immune thrombocytopenic purpura, primary immunodeficiency, and chronic immune demyelinating polyneuropathy. These indications were also increasing at the fastest rate over the study period. Similarly, the neurological, immunological, and haematological disease categories were the largest users of IVIg and also increased at the fastest rates. The proportion of supported IVIg use remained stable throughout the study period at approximately 91%. Finally, 83.3% of IVIg used for the three most common indications was used chronically.

Discussion: This study confirmed that IVIg use in the Atlantic Provinces increased throughout the study period. The established common indications for IVIg use continued

to dominate its utilization and increased faster than less common indications. There was a high proportion of supported IVIg use based on indication in Atlantic Canada. Due to a large proportion of chronic use, which has little support in the literature, future research into evidence-based dosing parameters is required. Finally, these results suggest that effective utilization policy must target supported as well as unsupported indications.

CORRECTING COMPENSATORY MISARTICULATIONS WITH CORRECTIVE BABBLING®: A PARENT BASED APPROACH

Jennifer Parker

Health Professions, Dalhousie University

Individuals with velopharyngeal dysfunction secondary to cleft palate or other palatal anomalies typically exhibit compensatory articulation errors. These errors are a result of difficulty producing consonants requiring a lot of intraoral pressure, such as stops, fricatives and affricates. The misarticulations are initially developed in order to counterbalance inability to attain velopharyngeal closure. After surgery to repair the palate, compensatory misarticulations remain because they are learned behaviours, integrated in the child's phonetic repertoire. Corrective Babbling® is a phonetic approach designed to remediate speech sound errors in children post-palatal surgery. The therapy attempts to recreate the babbling stage of speech development that normally occurs between birth and the first year of life (Jobe, 2006). Using a single-subject replicated design, this study investigated Corrective Babbling® to see if it was beneficial for five children who have residual speech errors after palate surgery; and examined progress made within a four month period.

LONG QT SYNDROME IN A FOUNDER POPULATION IN NORTHERN BRITISH COLUMBIA

Zoe Dyer, Laura Arbour

Department of Medical Genetics, University of British Columbia

Introduction: Long QT syndrome (LQTS) is a potentially fatal inherited disorder characterized by a prolongation of the QT interval on ECG and a propensity for syncope, polymorphic ventricular tachycardia, and sudden death. LQTS is disproportionately prevalent in a Northern British Columbia Community of Gitsxan people (usually rare at 1/7,000). A novel gene mutation (V205M) has been identified in an affected community member and in another affected Gitsxan woman not known to be related to the proband, suggesting a founder affect might be present. The novel mutation was identified in exon 3 of the gene for LQT1, KVLQT1. Patch clamp technique proved pathogenesis.

Methods: Through community based participatory research methods, the two affected probands and 164 relatives were ascertained. Their medical records were reviewed and clinical data was evaluated. The QTc's were measured and recorded by one reviewer. 124 subjects were genotyped and the results were used to compare those with the mutation and those without.

Results: 122 relatives of the probands were genotyped for the presence of the V205M KCNQ1 mutation. 20 individuals were found to have the mutation (22 when you include the probands) and 102 did not have the mutation. Of those with the mutation, 77% were female compared to 56% without (OR 2.2 95% CI 0.9-5.6). Adult females with mutations (n=18) were compared to adult females without mutations (n=40) for the most significant result (471 +/- 6 versus 438 +/- 4 msec, p<0.001). Mutation carriers had significantly higher QTc intervals as compared to the non-carriers (466.8 +/- 28 msec versus 435.2 +/- 26 msec, p<0.0001). Despite the higher QTc mean, 30% of mutation carriers had at least one QTc measurement below 440 msec. Considerable inpatient variability existed for measured QTcs.

Conclusion: A community based approach to the study of LQTS in a northern British Columbia First Nations community has led to the identification of a novel LQTS mutation, V205M KCNQ1. Although there are statistically significant differences between the cases and controls for all comparisons of QTc, this study demonstrates the difficulty in making a diagnosis from any single QTc measurement. Although the life-time clinical implications remain unclear for each individual found to have the mutation, the knowledge of having it will allow directed management of at least avoiding medications that prolong the QT interval and additional monitoring to prevent mortality.

HEPATITIS A AND TRAVEL AMONGST NOVA SCOTIA POST-SECONDARY STUDENTS: EVIDENCE FOR A TARGETED VS. UNIVERSAL IMMUNIZATION STRATEGY

Katherine Matheson¹, Scott Halperin¹, Shelly McNeil² Departments of Pediatrics¹, and Medicine, Division of Infectious Disease², Dalhousie University

Background: Current Canadian guidelines recommend hepatitis A virus (HAV) vaccination for groups at high risk of contracting the infection, such as travelers to HAV-endemic areas. However, the Centers for Disease Control and Prevention the United States advocates a universal approach to HAV vaccination that calls for the immunization of all children.

Objectives: Our objective was to determine whether the Canadian recommendation for HAV vaccination for high-risk groups such as travelers is being followed within the post-secondary student population. We planned to use these data

to help determine whether or not a universal immunization strategy for HAV rather than the current targeted approach is justified.

Methods: We designed and distributed by mass email an electronic survey to assess the knowledge, attitudes, beliefs and behaviours of a convenience sample of four groups of post-secondary students (community college students, university undergraduate students, graduate students and medical students). The survey was constructed to elicit HAV risk factors, HAV knowledge and immunization history, and known disease status to determine whether the Canadian guidelines for HAV vaccination are being followed. Questions were included to help determine the factors that predisposed to or prevented vaccination when indicated under the current guidelines.

Results: We received 2279 completed surveys (10.6% response rate estimated from school enrolment figures). A total of 1380 (60.6%) participants had traveled to HAV-endemic regions in the past and 1851 (81.2%) respondents were planning to do so within the next 5 years. The mean number of HAV and HAV vaccine questions answered correctly was 9.4 (67%) of 14. Less than half (662; 48.0%) of the students who traveled to HAV-endemic areas reported a history of HAV vaccination. The vast majority (93.9%) of unvaccinated students surveyed indicated a willingness to receive the immunization if it were provided free of charge.

Conclusions: The current Canadian guidelines for HAV vaccination are not being followed within the post-secondary student population. Given the high rates of travel to HAV-endemic regions by post-secondary student population, a universal approach to HAV vaccination may be warranted.

MATERNAL AND PERINATAL MORTALITY AND MORBIDITY WITH SPONTANEOUS ONSET OF LABOUR AND OBSTETRICALLY INDICATED DELIVERY IN WOMEN WITH PRETERM PRELABOUR RUPTURE OF THE MEMBRANES

Jenny JY Lim, Victoria Allen

Department of Obstetrics and Gynecology, Dalhousie University


Background: Options for the management of preterm prelabour rupture of the membrane (PPROM) take into account the risks of prematurity and infections. This study aims to compare maternal and neonatal outcomes between spontaneous labour and indicated delivery for PROM, with delivery occurring < 37 weeks.

Methods: Data was obtained from the Nova Scotia Atlee Perinatal Database (NSAPD). Preterm births complicated by PROM were included in this retrospective, population-based study. The cohort was categorized by type of labour (spontaneous, induction, or no labour) and by mode of delivery (vaginal or caesarean). Outcomes were compared,

stratified by gestational age (GA). Significance was estimated by ANOVA, χ^2 , or Fischer's test, where appropriate.


Results: A total of 2,265 deliveries were identified to be PPRM. Smokers at <34 weeks were more likely to have been induced. The major significant outcomes for deliveries at < 37 weeks were placental abruption and respiratory distress. These outcomes were highest in caesarean deliveries, irrespective of spontaneous labour. Indicated deliveries had the highest proportion of neonatal death and caesarean sections. Comparison of outcomes following indication and spontaneous labour demonstrated an increased risk of placental abruption (RR 2.2, 95% CI 1.14-4.23) at < 34 weeks, and an increased risk of cord prolapse (RR 11.73, 95% CI 1.37-100.19) at 34+0 to 36+6 weeks.

Conclusions: PPRM with delivery < 37 weeks is associated with significant risks of maternal and perinatal infection and neonatal respiratory morbidity, but no difference in the majority of outcomes were observed in patients undergoing indicated vs spontaneous labour.



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