

Medical Student Research Day award winning abstracts

Congratulations to all who participated in the inaugural combined undergraduate research day on Wednesday, February 7, 2007. Forty-seven students from medicine and health professions presented their research findings to the judges, who had a very challenging task of reviewing the presentations. By all accounts, the event was a success and the Research Committee is anxiously awaiting next years' research day.

Thank you to our sponsors: Faculty of Health Professions, Dalhousie Medical Alumni Association, Capital District Health Authority, IWK Health Centre, Dalhousie Medical Research Foundation, Faculty of Medicine

\$150 cash prizes were awarded to:

Winner of the Platform Presentation

ROLE OF ANGIOTENSIN II IN MYOCARDIAL INFLAMMATION

Mike DaRosa, Jean-Francois Legare

Departments of Immunology and Microbiology, Pathology and Surgery

Introduction: Myocardial infarction (MI) typically results in both ischemic and inflammatory injury to the myocardium, subsequent tissue degradation, and a progression to heart failure. Mononuclear cell infiltration has been shown to be important in the inflammatory reaction seen post-MI, but, the mechanism of this infiltration is far from clear. Angiotensin II (Ang II), a vasoactive hormone, has recently been implicated in myocardial injury, with elevated levels appearing for several weeks following MI. Recent studies have shown that Ang II alone can induce the transcription of numerous pro-inflammatory mediators suggesting that Ang II may be involved in the post-MI migration of mononuclear leukocytes into the myocardium. In the present pilot experiment, we hope to show that Ang II invokes mononuclear cell infiltration and may in the future provide a means of studying the infiltration, fibrosis, and the development of heart failure that follows MI, independent of the confounding effects of ischemia. **Methods:** Male Lewis rats were randomly assigned to receive an infusion of Ang II (n=2) or saline (n=2) via subcutaneous osmotic minipump (0.7mg Ang II/kg/day). After 7 days, all animals were sacrificed and the hearts weighed for evaluation of cardiac hypertrophy before being formalin fixed. Myocardial infiltration was examined using H&E and immunohistochemistry for the mononuclear leukocyte marker ED-1. Collagen deposition was evaluated using Masson's Trichrome stain, and myocardial cell injury was quantified with a Troponin I assay. **Results:** After 7 days of treatment, heart weights corrected for body weight in control animals were 3.43 ± 0.27 mg/g versus 4.17 ± 0.03 in the Ang II group ($p = 0.06$), suggesting potential cardiac hypertrophy in the Ang II infused animals. In control hearts, H&E staining revealed few leukocytes and a normal mor-

phology, while Ang II hearts showed regions of perivascular and interstitial infiltration, edema, and thinning of the cardiac myocytes. Almost no ED-1 positive cells were seen in the control animals, while Ang II animals revealed significant ED-1 positive infiltration in perivascular regions and select regions of both the right and left ventricle. Masson's Trichrome staining revealed normal collagen levels in control animals versus significant regions of perivascular and interstitial collagen deposition in Ang II animals corresponding to the areas of mononuclear cell infiltration. Troponin I levels were below the detectable limit of 0.156 ng/ml in one of the Ang II animals and in both control animals, while the second Ang II animal had a slightly elevated troponin I level of 0.368 ng/ml. **Conclusions:** This pilot study confirms that Ang II invokes a clear inflammatory response in rat hearts, a result made evident by several supporting observations: mononuclear cell infiltration; increased collagen deposition; and myocardial cell damage. Each of these processes has been proven to participate in the progression from MI to heart failure. Given this, and the fact that Ang II levels are elevated following MI, Ang II-induced inflammation may be beneficial to the study of mononuclear cell migration into the myocardium, independent of the effects of ischemia. Future work is needed to uncover the mechanisms involved in myocardial leukocyte infiltration, the kinetics of this infiltration, and the functional damage inflicted.

Poster Presentation Winners

AGE AND OVERUSE RUNNING EFFECTS ON COLLAGEN CROSSLINKING PATTERNS IN ACHILLES TENDONS USING HYDROTHERMAL TESTING

Paul Gomez, Mark Glazebrook
Department of Surgery

Non-insertional disorders of the Achilles tendon cause pain, disability, catastrophic rupture, and are increasing in frequency. The pathobiology of Achilles tendon disease is poorly understood. This paper seeks to improve the understanding

of Achilles tendon disease by using Hydrothermal Isometric Tension (HIT) testing to determine the effect of ageing and overuse running on the collagen cross linking profile of rat Achilles tendons. During ageing the rat Achilles tendons were shown to undergo alterations in collagen crosslinking profile that included a greater proportion of reducible intrahelical crosslinking. This was similar to changes observed when an over-exercise running regime is imposed. It is suggested that the changes observed with ageing and over-exercise may be the result of a remodeling process.

COMPARISON OF THE AIRWAY TOOL WITH THE DIRECT LARYNGOSCOPE IN EASY AND DIFFICULT SIMULATED AIRWAY SIMULATIONS

Jackie Kerr, George Kovacs

Department of Emergency Medicine

Purpose: To compare the Airway Tool (AWT), a new intubation device, with direct laryngoscopy (DL) in easy and difficult airway simulations with respect to time to intubate (TTI), success, and laryngeal view obtained. An additional outcome was to assess participants' opinions of the AWT. **Methods:** 102 subjects participated in this study. Following the collection of demographic information subjects completed a brief training session reviewing techniques for DL and an introduction to the AWT. Subjects were given the opportunity to practice each technique five times in a mannequin. Practice intubations in a randomized order consisting of: DL in the easy airway, DL in the difficult airway, AWT in the easy airway, and AWT in the difficult airway. TTI, laryngeal view, confidence in correct tube placement, and success were recorded. Failure was defined as an esophageal intubation or as an attempt lasting more than 60 seconds. Subjects were given a second attempt if they failed the first attempt. Subjects then completed a survey assessing their subjective views on various aspects of using the AWT. **Results:** The DL/easy airway was the fastest (17.48 ± 6.34) and most successful scenario, followed by the AWT/easy airway (23.95 ± 8.97), and finally the DL/difficult airway (32.74 ± 12.78). There was no difference in TTI for the normal and difficult AWT scenarios. All other TTI were found to be significantly different. The AWT and DL in the easy airway experienced equal success (99.02% and 97.06%, respectively). However, the AWT in the difficult airway was more successful than the DL in that scenario (88.23% and 52.94%, respectively). Similar percentage of glottic opening (POGO) scores were achieved with the DL/easy, AWT/easy and AWT/difficult scenarios. The DL/difficult had a substantially poorer view than the other three scenarios. Subjects rated the AWT as very good in all categories surveyed (e.g. handling and balance, ease of tube passage, field of view). The second intubation attempts demonstrated similar results. **Conclusions:** Despite considerably less training and practice with the AWT, it afforded similar fields of view and success rates as the DL in the easy

simulated airway. The AWT took more TTI than DL in the easy airway but less time than the DL in the difficult airway. The AWT provided subjects with better glottic opening views and a higher rate of success than the DL in the difficult airway.

THE EFFECTS OF BETA-BLOCKADE IN DIASTOLIC HEART FAILURE PATIENTS: INTERROGATION OF THE CANADIAN CONGESTIVE HEART FAILURE CLINICS NETWORK DATABASE

Nathan Lamond, Jonathan Howlett

Department of Medicine

Diastolic heart failure is the disease in which patients have symptoms and clinical findings of heart failure, yet show a normal or near-normal left ventricular ejection fraction (LVEF). Despite a large proportion of diastolic HF, little evidenced based treatment strategies exist to date. The purpose of this study was to determine the effect of beta blocker prescription on morbidity and mortality in a population of unselected diastolic HF patients. For this purpose we interrogated the Canadian Congestive Heart Failure Clinics Network database. Patients were included in this review if they had a recent documented LVEF > 40% at index appointment in this clinic and at least one year of follow up available. The database was then interrogated for beta blocker prescription along with mortality, hospitalizations, patient gender, LVEF, and duration of follow up. There were 105 patients with LVEF > 40% at index appointments during the study period and complete 1-year data available. The Beta Blocker and No Beta Blocker groups did not differ significantly by gender, measured LVEF, or duration of follow up. The mortality rates in the Beta Blocker group and the No Beta Blocker group were 24.7% and 29.2%, respectively. This difference was not significant. Due to a lack of stored hospitalization data in the CCHFNCN database before January 1, 2003, hospitalization data was excluded from this review completely. These data showed that 77.1% of diastolic HF patients indexed at this clinic received beta blocker prescriptions, despite the lack of evidence for this therapy. In order to further explore the usefulness of beta blockade in this patient population and complete our own objectives, we will be repeating this study using data from the ICONS database.

NEONATAL OUTCOMES ASSOCIATED WITH MATERNAL ANTIDEPRESSANT USE IN A POPULATION COHORT OF NOVA SCOTIAN PREGNANCIES BETWEEN 1994 AND 2003

Chris Nash, Colleen O'Connell and Alexandra Howlett

Department of Pediatrics

Background: Depression has a high prevalence among woman of child bearing age, often requiring medication. Prenatal exposure to antidepressants is associated with

poor adaptation, neonatal withdrawal syndrome, congenital malformations and respiratory difficulties. **Objective:** To investigate a correlation between maternal antidepressant use and negative neonatal outcomes using a population-based maternal-newborn database. **Design/Methods:** Data was collected on all infants born at the IWK Health Centre from 1994 to 2003 using the Nova Scotia Altee Perinatal Database (NSAPD), a validated, population-based database containing prospectively gathered standardized information on all pregnancies and infants born in the province of Nova Scotia. Women with documented antidepressant use during pregnancy were identified from the NSAPD. Patient charts were subsequently examined to gain further information surrounding their antidepressant use. Comparison of selected maternal and newborn factors associated with antidepressant use was examined by univariate analysis. **Results:** Of the 57,870 infants included in this study, 739 (1.26%) were exposed to at least one antidepressant during gestation. Antidepressant exposure was associated with an increased risk for infant convulsions of unknown etiology ($p=0.02$); however, cardiac malformations were not associated ($p=0.255$). However, the subgroup with SSRI exposure had a higher incidence of cardiac anomalies ($p=0.0359$), drug-induced convulsions ($p=0.0077$) and convulsions of unknown etiology ($p=0.0001$). Tricyclic antidepressant (TCA) exposure was not associated with cardiac anomalies or CNS convulsions. No association with persistent pulmonary hypertension of the newborn (PPHN) and any antidepressant agent was found ($p=0.57$). **Conclusions:** In this study, cardiac anomalies were associated with prenatal SSRI but not TCA exposure. Prenatal exposure may increase risk for neonatal drug withdrawal symptoms as suggested by the increased occurrence of convulsions with unknown etiology.

THE VAXED PROJECT: A CANADA-WIDE CURRICULUM REVIEW AND ASSESSMENT OF IMMUNIZATION KNOWLEDGE AND ATTITUDES AMONG TRAINEES IN UNDERGRADUATE HEALTH PROFESSIONAL PROGRAMS

Lorine Pelly, Beth Halperin, Darlene Baxendale, Donna Pierrynowski-Gallant, Susan Bowles, Noni MacDonald, Robert Strang, Karen Mann, Shelly McNeil
Department of Medicine

Introduction: Knowledge and attitudes of healthcare providers (HCP) have significant impact on frequency with which vaccines are offered and accepted but many HCP are ill equipped to make informed recommendations about vaccine merits and risks. We performed a comprehensive assessment of trainee needs regarding immunization, to be used to develop a multi-faceted, evaluable, interprofessional educational intervention. **Methods:** (i) A 5-part questionnaire was sent to all Canadian nursing, medical and pharmacy schools to assess immunization-related curriculum

content; information was elaborated by phone interview; (ii) A 77-item web-based, validated questionnaire was emailed to final-year students in medicine, nursing, and pharmacy at Dalhousie Univ. and St. FX Univ. School of Nursing to assess knowledge, attitudes, and behaviors reflecting current immunization curriculum. **Results:** The curriculum review yielded responses from 18%, 48%, and 56% of medical, nursing, and pharmacy schools, respectively. Time spent on immunization content varied substantially between and within disciplines from <1 to >50 hrs. Most schools reported some content regarding vaccine preventable diseases, immunization practice and clinical skills but there was considerable variability and fewer schools had learning objectives or formal testing in these areas. Gaps in knowledge of vaccine indications/contraindications and safety were identified in all programs (mean correct = 13.5/21); 33.4% of trainees were unsure if there is a relationship between pertussis vaccine and sudden infant death syndrome and 22.3% were unsure whether current evidence supports a link between vaccines and chronic diseases. 74% of respondents don't feel comfortable discussing vaccine side effects with parents/patients and only 21% felt they received adequate teaching regarding immunization during training. **Conclusions:** Important gaps were identified in knowledge of graduating nursing, medical, and pharmacy trainees regarding vaccine indications/contraindications, adverse events and safety. The national curriculum review revealed wide variability in immunization curriculum content and evaluation. The results suggest that all HCP trainees could benefit from development of core objectives for immunization providers and comprehensive, interprofessional education strategies to achieve these objectives during training.

THE HANDLING OF MORPHINE IN PATIENTS WITH SEVERE CNS TRAUMA/INFLAMMATION

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Departments of Pharmacology, Medicine and Anesthesia

Intracranial hemorrhage and closed head trauma in humans induce an acute lasting inflammatory response within the central nervous system (CNS). Morphine is commonly employed for analgesia in patients who have suffered head injury and may lead to neuroagitation observed in head injury patients. This neuroagitation is thought to be caused by the predominant metabolite of morphine, M3G. M3G is a substrate of the blood brain barrier (BBB) drug transporter, P-glycoprotein (pgp), which limits morphine and metabolite access to the CNS by reverse brain-to-blood transport. Pgp has been shown to be reduced in concentration and function during inflammatory responses involving the CNS. Our working hypothesis was that a morphine metabolite which is a CNS irritant (M3G) permeates the brain in increased amounts because Pgp in the BBB is diminished during the

central inflammatory response. To determine if the disposition of M3G into the brain varies with head injury, we studied 20 patients over a one-year period who were admitted to an intensive care unit (ICU) for intracranial hemorrhage or closed head injury and fitted with a ventricular cerebrospinal fluid (CSF) catheter and an intravenous (IV) catheter for therapeutic reasons. Patients received intermittent boli or an IV infusion of morphine. Blood samples (2 mL) were obtained on entry to ICU and subsequently at 12, 24, 36, 48, 72 and 96 hours from the indwelling IV catheter. At these time points a 5 mL of CSF was collected from the ventricular CSF catheter. We identified 20 patients aged 51.5+15.6 over a one-year period. Of these 20 patients, 43.8% were male and most (56.3%) suffered a subarachnoid hemorrhage. They were on multiple medications, none of which were found to interfere with the pharmacokinetics of morphine or M3G. Only a single patient representation of the effect of severe head injury on morphine disposition is presented in this summary as statistical procedures on the entire data set are complex and not yet complete. The full analysis will be conducted and a manuscript will be written and submitted for publication within the next 6 months. Preliminary data shows a profound inflammatory response in the CNS, with the inflammatory marker IL-6 contained in cerebrospinal fluid at concentrations greater than 20,000 pg/mL. M3G penetrated the BBB and was present at peak concentrations greater than 20 ng/mL. M3G stayed elevated in CSF even after the concentration had declined in the serum. The implications of these results require further analysis and interpretation



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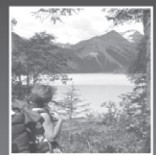
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