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HEALTH SCREENS AND ANEMIA – EVALUATING HEALTH CARE INTERVENTIONS IN NORTHERN INDIAN SCHOOLCHILDREN

Presenting Author(s): Luke Armstrong and Becky Hartley

Armstrong, L., A. Babuk, M. Benusic, B. Brar, R. Hartley, N. Von Alkier, S. Westberg and V. Kapoor

Faculty of Medicine, University of British Columbia, B.C., Canada

Purpose of study: To evaluate the impact of an integrated approach to anemia reduction in a remote Himalayan valley school in Northern India.

Background: Spiti Valley is an isolated region in the Indian Himalayas with poor access to sustainable healthcare. Since 2007, medical students from UBC have travelled to Munsel-ling school in Spiti Valley. The UBC teams have implemented water sanitation, provided health education, aided in diversifying agricultural crops, performed health screens, and dispensed relevant medications. Anemia is a prevalent issue in this region of Northern India; thus, as part of the health screens, hemoglobin (Hb) levels are checked.

Methods: In order to assess more than 400 students, five stations were set up in the school's health clinic. Height and weight were recorded. Basic cardiovascular, respiratory, dermatology, and head and neck exams were performed. A HemoCue monitor was used to sample hemoglobin levels and values used to define anemia were taken from the WHO minimal Hb levels, and calibrated for altitude.

Results: Preliminary data from 2011 suggests that anemia levels have decreased by 5%, from 89.5% to 84% over one year. The Hb levels ranged from 17.7 to 6.9g/dL. The average Hb level was 13.35g/dL, compared to 12.89g/dL in 2010. Other prevalent medical issues discovered included head lice (76%), dental carries (73%) and worms (12%).

Conclusion: High levels of anemia were discovered in the children when our project began in 2007. Through iron supplementation, water sanitation, health education and nutritional support, the goal of our project was to implement a sustainable system to decrease the prevalence of anemia at Munsel-ling school. Each year we have seen a decline in children diagnosed with anemia. From 2007 to 2009 anemia levels decreased by 17% (88.4 to 71.3%). However, in 2009, iron was not distributed due to a conflicting schedule, and the following year the anemia prevalence increased to its original level (close to 90%). In 2010 iron tablets were again distributed to the children and in 2011 the anemia prevalence decreased 5%. Anemia, however, still remains widespread in this population and more work needs to be done to address the issue.

Corresponding author: lukearmstrong3@gmail.com

INVESTIGATION OF GLYCOSIDASE CATALYTIC MACHINERY: CLONING, EXPRESSION, PURIFICATION, AND CHARACTERIZATION OF A GH36 ALHA-GALACTOSIDASE FROM BACTEROIDES THETAIOTAMICRON

Presenting Author(s): Anees Bahji

Bahji, A.

Department of Molecular Biology and Biochemistry, Simon Fraser University, B.C., Canada.

The α-galactosidases are enzymes that cleave terminal α-glycosidic bonds. Because of this function, these enzymes are necessary for the proper metabolism of glycolipids, glycoproteins, and other glycoconjugates in Achaea, eukaryotes, and prokaryotes. In eukaryotes, the α-galactosidases reside in the acidic environment of the lysosome. From a health perspective, these enzymes have become important targets for drug design. It has been shown that inhibitors of α-galactosidases at sub-inhibitory concentrations can act as chaperones to help refold mutated α-galactosidases, and have potential for use as a molecular therapeutic strategy for genetic metabolic diseases, such as the lysosomal storage disorder Fabry's disease, which results from a deficiency of lysosomal α-galactosidase A. Unfortunately, little is understood about how irreversible inhibitors bind to and inactivate the α-galactosidases of glycosyl hydrolase family 36 (GH36), but it is believed that if these interactions could be elucidated through the avenue of X-ray crystallography, or other structural biochemical techniques like NMR or mass spectrometry, it could lead to the rational design of potent, selective inhibitors of α-galactosidases that would be of great benefit for both therapeutic and non-therapeutic purposes. In this study, we have expressed a recombinant GH36 α-galactosidase from the bacterium *Bacteroides thetaiotamicron* (BT) using an *E. coli* system, and performed a series of purifications, and kinetic analyses in an attempt to produce an active enzyme for inhibitor studies. In addition, inhibition profiles have been obtained for four different synthetic, α-galactosidase inhibitors, and the expression conditions have been optimized for the purpose of a generating a pure, concentrated sample that can be used for X-ray crystallography, NMR, or mass spectrometry, to aid in visualizing the interaction between the inhibitor and the GH36 α-galactosidase active site.

Corresponding author: abahji@interchange.ubc.ca

HIGH FLOW LOW MEAN GRADIENT SEVERE AORTIC STENOSIS

Presenting Author(s): Christopher Cheung

Cheung, C., J. Jue and J. Tang

Department of Medicine, Faculty of Medicine, University of British Columbia, B.C., Canada

BACKGROUND: Paradoxical low gradient severe aortic stenosis (AS) with preserved ejection fraction has been a recently described entity. This has been ascribed to low flow and a lower stroke volume (SV) in these patients due to increased afterload from the valvular and vascular impedance. The presence of low gradient severe AS with high flow has not been previously described.
OBJECTIVE: To document the echocardiographic characteristics of patients with severe AS, high flow and low mean gradient (MG) from our echocardiographic database.
METHODS: Patients with severe native valvular AS (aortic valve area (AVA) < 1 cm^2) and a stroke volume index > 50 ml/m^2 were identified. Previously flow of $\leq$ 35 ml/m^2 was used to demarcate low from normal flow. Patients were then divided into those with a high MG (>40 mmHg) and low MG (<40). We excluded any patients with mitral stenosis or prosthesis and more than moderate aortic, mitral or tricuspid regurgitation.
RESULTS: 88 patients were identified, all with an EF $\geq$ 50%. Low MG severe AS patients had smaller BSA, larger AVA, smaller LV size, and stroke volume compared to the high MG group.

	High MG ($\geq$ 40 mmHg) n=40	Low MG (< 40 mmHg) n=48	p
Age	70 $\pm$ 14	77 $\pm$ 14	0.02
BSA (m^2)	1.67 $\pm$ 0.15	1.55 $\pm$ 0.16	<0.001
Mean gradient (mmHg)	59 $\pm$ 16	31 $\pm$ 5	<0.001
AVA (cm^2) AVA indexed (cm^2/m^2)	0.79 $\pm$ 0.11 0.47 $\pm$ 0.06	0.90 $\pm$ 0.09 0.58 $\pm$ 0.08	<0.001 <0.001
Stroke Volume (mL) SV indexed (mL/m^2)	91 $\pm$ 9 55 $\pm$ 4	82 $\pm$ 9 53 $\pm$ 2	<0.001 <0.001
LV diastolic dimension (mm)	46.4 $\pm$ 6.8	42.8 $\pm$ 5.9	<0.01
IV Septum (mm) Posterior wall (mm)	12.3 $\pm$ 1.7 12.0 $\pm$ 1.6	11.0 $\pm$ 1.8 10.5 $\pm$ 1.7	<0.001 <0.001
Relative wall thickness	0.52 $\pm$ 0.09	0.50 $\pm$ 0.10	ns
LV mass (LVM, g) LVM indexed (g/m^2)	216 $\pm$ 70 129 $\pm$ 40	158 $\pm$ 44 102 $\pm$ 24	<0.001 <0.001

CONCLUSIONS: 55% of our high flow (SV index > 50 ml/m^2) severe AS (AVA < 1.0 cm^2) patients had a low MG (<40 mmHg). These patients had a relatively smaller LV and stroke volume compared to the high MG group and thus share similar characteristics to the previously described paradoxical low flow low gradient severe AS population.

Corresponding author: cccheung@interchange.ubc.ca

IMPLEMENTATION AND EVALUATION OF A COMMUNITY BASED TOBACCO CESSATION COUNSELING PROGRAM IN THE EMERGENCY DEPARTMENT: A FEASIBILITY STUDY

Presenting Author(s): Ian Wong

Cheung, K.W. (1), J. Brubacher (1), I.W.H.Wong (4), R. Abu-Laban (1) and M. Schulzer (2,3)

(1) Department of Emergency Medicine, University of British Columbia, B.C., Canada
(2) Department of Statistics, University of British Columbia, B.C., Canada
(3) Center for Clinical Epidemiology and Evaluation, University of British Columbia, B.C., Canada
(4) Faculty of Science, University of British Columbia, B.C., Canada

Objective: Tobacco smoke is the leading cause of preventable deaths in Canada. Previous studies have showed that telephone quit lines increase smoking quit rates. However, the emergency department population has never been studied. In this study, we looked at the feasibility of referring emergency department smoking patients to our provincial telephone quit line, QuitNow Services.

Methods: This was a randomized controlled trial conducted at the Vancouver General Hospital (VGH) Emergency Department (ED) from June to August 2011. Stable patients $\geq$19 years of age presenting to the ED who used a tobacco product within the last 30 days were eligible for the study. Patients randomized into the standard of care arm received no further smoking cessation intervention, and patients randomized into the intervention arm were referred to QuitNow Services. Demographic and smoking data was collected from each patient on arrival to the ED and patients were followed up at 1, 3 and 6 months.

Results: During the study period, 53 patients were enrolled. Twenty-six patients were in the standard of care arm, and 27 were in the intervention arm. The mean age was 35, with 38 males and 15 females. On average, patients were moderate smokers, smoking 10-19 cigarettes/ day, and had smoked for 11-15 years. Although moderate smokers, most patients thought smoking was harmful to their health and "intend to quit and take action within 6 months". Despite the intent, the average smoker rated their confidence to quit at 4.5 out of 10 at 1 week, and 6.0 out of 10 at 6 months. Only 6 individuals were using any form of smoking cessation medication at presentation. We are currently conducting 6 month follow-ups to determine if there are differences in quit rates between the two arms. Results will be available for presentation at the research forum.

Corresponding author: iwh33@hotmail.com

ENGAGING THE NEXT GENERATION IN THE 2015 MILLENNIUM DEVELOPMENT GOALS

Presenting Author(s): Alia Dharamsi

Dharamsi, A. and M. Kriese

Faculty of Medicine, University of British Columbia, B.C., Canada

Description:

The We Are 2015 initiative is a series of interactive modules created to use dialogue, interactive simulations, visual arts and mixed-media to engage students aged 13-20 in discussions on the global health topics to which the MDGs are seeking solutions. The first preliminary module, "MDG #4- Hope for Children," addresses child mortality and through this and future modules, a foundation is built for future student development by increasing understanding of not only the health topics addressed by the MDGs (malaria, diarrhea, malnutrition, maternal health), but also the complexities of international development issues, and the humanitarian/social applications of health and medicine. Key aspects of the module include its highly interactive format, as well as its realistic representation of current MDG parameters. To increase the impact of the module each student serves as the "ambassador" to a country particularly affected by the MDGs—for the duration of the seminar students represent and make decisions on behalf of their country in discussions. Students imagine (with the help of images) what it is like to live and survive in "their country". This module is especially unique in that it is comprised entirely of photographs and images—encouraging students to feel, see, and discuss as opposed to read, analyze and compute.

Recommendations

With the initial success of the first module on child health, further modules can and should be developed to address the other seven MDGs: particularly gender equity and HIV/AIDS. Students surprised presenters with the amount of critical thought, awareness and emotional engagement in discussion, and revision of the module to allow for more time to discuss ideas and feelings would be appropriate, and well-received. The expectation is that with early exposure to these issues, students will look to find ways to apply their current and future education to develop innovative solutions to global inequities. In general more education time should be applied to global health topics in the classroom, as it provides tangible real-world applications to otherwise abstract high school curriculum, and engages students in global issues at an age where they are particularly impressionable, open to new ideas, and optimistic about the world.

Corresponding author: alia.dharamsi@gmail.com

PARENTS' WILLINGNESS TO CONSIDER HAVING THEIR CHILD RECEIVE CARE BY PHYSICIAN ASSISTANTS IN A PEDIATRIC EMERGENCY DEPARTMENT

Presenting Author(s): Anthony Bryson

Doan, Q. (1), A. Bryson (1), S. Sheps (2), H. Wong (2), J. Singer (2), D. Johnson (3) and N. Kissoon (1)

(1) Department of Pediatrics - Child and Family Research Institute and B.C. Children's hospital, University of British Columbia, B.C., Canada
(2) School of Population and Public Health, University of British Columbia, B.C., Canada
(3) Department of Pediatrics - Alberta Children's Hospital, University of Calgary, A.B., Canada

Objective: To determine willingness of parents of children visiting a Pediatric emergency Department to have a Physician Assistant (PA) assess and treat their child, and how much waiting time reduction would be sufficient for them to choose to receive treatment by a PA rather than wait for the physician.

Method: Following information about PAs' training and scope of practice, we surveyed caregivers bringing children for non-emergent care, asking if they would be willing to consider having their child assessed and treated by a PA on that visit: yes (definitely, maybe) or no (never). If they answered yes, we asked what is the minimum amount of waiting time reduction they wish to see before choosing to receive treatment by PAs rather than wait for the doctor.

Result: We approached 320 eligible subjects, 273 (85.3%) consented to participate. 140 (51.3%) respondents answered that they would definitely, 107 (39.2%) answered maybe and 26 (9.2%) were unwilling to have their child receive treatment by PAs. Respondents would choose to have their child seen by a PA instead of waiting for the physician if that resulted in a mean waiting time reduction of 67 minutes (95% CI: 61, 72). While respondents' perception of the child's condition severity was associated with unwillingness to receive treatment by a PA, age of the patients, presenting complaints and actual waiting time were not.

Conclusion: A majority of parents of children visiting a tertiary care PED for non-emergent issues are willing to consider having their child treated by PAs.

Corresponding author: abryson1988@gmail.com

ALCOHOL'S INFLUENCE ON THE SEVERITY OF INJURIES SUSTAINED BY DRIVERS INVOLVED IN MOTOR VEHICLE COLLISIONS

Presenting Author(s): Karan D'Souza and Benjamin Tuyp

D'Souza, K.J. (1)* and B.J. Tuyp (2)*

*These authors contributed equally to this work

(1) Faculty of Science, Department of Integrated Science, University of British Columbia, B.C., Canada

(2) Faculty of Medicine, University of British Columbia, B.C., Canada

Motor vehicle crashes (MVCs) are a substantial contributor to morbidity and mortality, yielding approximately 73,000 casualties and 363 fatalities in 2009 alone in British Columbia.[1] Alcohol impairment, a potent and well-studied contributor to such collisions, was cited as a factor in 39.2% of Canada's MVC-related fatalities in 2008.[2] Alcohol intoxication has also been demonstrated to augment injury severity and medical costs for drivers presenting to the emergency department (ED).[3]

In this study we will present a preliminary descriptive analysis of the effects of blood alcohol levels on injury severity of injured drivers admitted to the Emergency Department of Vancouver General Hospital. We used data from an ongoing multi-centre study on injured drivers presenting to an emergency department in British Columbia with injuries necessitating blood work as part of clinical investigation.

Blood Alcohol Concentration (BAC) at emergency department admission, collision information and hospital admission details were obtained via chart review. 327 individuals (67.6% male) aged 17 to 91, who met inclusion criteria during the study period. 305 (93.3%) were tested for Blood Alcohol Concentration (BAC), 83 (27.2%) of which were positive. Admission to general medical wards or special units, length of stay, administration of head CT scan, and presenting mental status were utilized as indicators of injury severity. The impact of alcohol upon these markers will be evaluated. This study will also provide some evidence of the impact of alcohol on healthcare utilization by injured drivers.

Corresponding author: dsouza.karan@gmail.com

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ULTRA-FAST TWO-PHOTON MICROSCOPE BASED ON ACOUSTO-OPTIC DEFLECTOR FOR IMAGING OF SYNAPTIC AND NEURONAL MORPHOLOGY IN BRAIN OF IN VIVO XENOPUS TADPOLES FOR STUDY OF EARLY BRAIN DEVELOPMENT.

Presenting Author(s): Philip Edgcumbe

Edgcumbe, P. (1,2), K. Podgorski (1) and K. Haas (1)

(1) Department of Cellular and Physiological Sciences, University of British Columbia, B.C., Canada
(2) Engineering Physics Program, University of British Columbia, B.C., Canada

Many neurological disorders, including autism, epilepsy and schizophrenia are associated with abnormal early brain development. During early brain development neurons grow elaborate dendritic and axonal arbors that form precise inter-neuronal synaptic connections and functional neural circuits. To study early brain development we have custom-built a random access ultra-fast two-photon microscope based on acousto-optic deflectors that generate x-y images of 300x300 pixel resolution with diffraction limited resolution of 600x600nm per pixel. A piezoelectric focusing element controls the position of the objective along the optical axis (z-direction) and allows for whole neuronimaging at a rate of 100hz.

One application for the newly-built ultra-fast two photon microscope is the study of schizophrenia in the in vivo model system of the Xenopus tadpole. To do this we will simultaneously image the synaptic and morphological plasticity in vivo in single tectal neurons of Xenopus tadpoles. This allows us to study how schizophrenia affects synaptic plasticity, the correlation between synaptic firing and the relationship between synaptic plasticity and morphological plasticity. It is important to understand if seizures that occur during development affect essential processes associated with neural circuit formation.

We have created a novel visual stimulation imaging chamber for the Xenopus Laevus tadpole. The calcium-sensitive fluorescent indicator Oregon green 488 BAPTA-1 was bulk loaded into neurons within the tadpole brain and light stimuli were presented to the tadpoles and the response of the tadpoles neuronal network was recorded. Visual stimulation elicited a significant neuronal network response in the optic tectum of the Xenopus tadpole with an increase in Oregon green 488 BAPTA intensity of up to 10% in regions of interest. Preliminary visual stimulation results, discussion of future research and design of ultra-fast two-photon microscope are presented.

Corresponding author: edgcumbe@interchange.ubc.ca

COMPLIANCE WITH CAEP ASTHMA CLINICAL PRACTICE GUIDELINES AT A TERTIARY CARE EMERGENCY DEPARTMENT

Presenting Author(s): David Harriman

Filiatrault L (1,2), D.I. Harriman (3), R.B. Abu-Laban (1,2,4), J.M. FitzGerald (2,4,5), A.M. Chahal (1,2) and R.D. McKnight (1,2)

(1) Department of Emergency Medicine, University of British Columbia, B.C., Canada
(2) Vancouver General Hospital, Vancouver Coastal Health, B.C., Canada
(3) Faculty of Medicine, University of British Columbia, B.C., Canada
(4) Centre for Clinical Epidemiology and Evaluation Vancouver Coastal Health, B.C., Canada
(5) (5) Division of Respiratory Medicine, Faculty of Medicine, University of British Columbia, B.C., Canada

Introduction: Although evidence-based clinical practice guidelines (CPGs) exist, emergency department (ED) asthma management remains highly variable. Our objective was to compare asthma management at a tertiary care ED with that advised by the Canadian Association of Emergency Physicians (CAEP) asthma CPG and current best practise.

Methods: This medical record study enrolled patients between the ages of 19-60 with a prior diagnosis of asthma, who were seen for an acute asthma exacerbation at the Vancouver General Hospital ED in 2008. Standard methodology guidelines for medical record review were followed, including explicitly defined criteria and determination of inter-rater reliability. Primary outcomes were the proportion of cases with the following: objective assessment of severity using peak expiratory flow (PEF), use of systemic corticosteroids (SCS) in the ED and at discharge, prescription for any inhaled corticosteroids (ICS) and documentation of outpatient follow-up.

Results: A total of 204 patient encounters were enrolled. Kappa values for inter-rater assessment ranged from 0.93 to 1.00. Compliance with primary outcomes was as follows: measurement of PEF 90% (95%CI 85%-94%); use of SCS in the ED 64% (95%CI 57%-71%); prescription of SCS at discharge 59% (95%CI 51%-67%); prescription of any ICS at discharge 51% (95%CI 41%-61%); documentation of outpatient follow-up 78% (95%CI 71%-84%).

Conclusions: This study indicates an improvement in ED asthma care compared to prior published studies; however, discordance still exists between asthma management at a tertiary care ED and the CAEP asthma CPG and current best practice. Further research is warranted to understand the reasons for this finding.

Corresponding author: harriman@interchange.ubc.ca

VIRTUAL PROBLEM BASED LEARNING (PBL) - A NEEDS ASSESSMENT EXAMINING TRADITIONAL VERSUS VIRTUAL PROBLEM-BASED LEARNING

Presenting Author(s): Amandeep Ghuman and Rachel Lim

Ghuman, A.* (4), R. Lim* (4), D. Chan (5), W. Gourlay (3), B. Fitzgerald (2), J. Masterson (1), A. MacNeily (1) and J. Mickelson (1)

*These authors contributed equally to this work
(1) Department of Urologic Sciences, B.C. Children's Hospital, B.C., Canada
(2) Department of Pediatrics, B.C. Children's Hospital, B.C., Canada
(3) Department of Urologic Sciences, St. Paul's Hospital, B.C., Canada
(4) University of British Columbia, B.C., Canada
(5) (5) St. George's University, London, United Kingdom

Purpose of Study: The University of British Columbia has an increased need for flexibility in undergraduate medicine. Flexibility in curriculum can be created using virtual learning. This is a needs assessment of traditional problem-based learning (PBL) and the interest in virtual learning as part of the PBL experience.
Methods: This is a qualitative and quantitative study utilizing focus groups and an electronic survey of first and second year medical students at UBC. The data from the focus groups was analyzed using constant comparative analysis to identify themes and codes. These themes were then used to determine questions for the electronic survey. Quantitative survey data was analyzed using a Chi-square test.
Results: Two focus groups of 1st and 2nd year students were undertaken to identify themes associated with traditional versus virtual PBL learning. The dominant theme from 1st and 2nd year focus groups was concern over the loss of life skills acquired during face-to-face PBL. The second most prevalent theme identified was the benefit of flexibility and convenience associated with virtual PBL learning. 73% of 1st year and 17% of 2nd year students responded to the electronic survey. 59% of 1st year and 43% of 2nd years felt that face-to-face interaction of PBL was “critically“ or “strongly important” ($p<0.005$). 29% of 1st year and 61% of 2nd year students wanted a hybrid of both virtual and traditional PBL ($p<0.005$). 17% of 1st year students and 36% of 2nd year students felt that the addition of virtual PBL would be most beneficial during the 2nd undergraduate year ($p<0.005$). 66% of 1st year students did not want virtual PBL as part of their undergraduate curriculum.
Conclusion: 1st year students were more strongly guarded than 2nd year students about using virtual PBL. Both groups felt it could be complementary in 2nd year. Respondents felt that a “hybrid” of a virtual and face-to-face experience later in 2nd year training would allow students to benefit from flexibility and convenience provided by virtual learning.

Corresponding author: aghuman@interchange.ubc.ca

A PILOT STUDY OF THE EFFECTS OF MAGNESIUM SUPPLEMENTS ON FATIGUE IN MS PATIENTS

Presenting Author(s): James Gill

Gill, J., M. van den Elzen and G. Vorobeychik

Department of Neurology, Burnaby General Hospital, B.C., Canada

Fatigue is a common symptom experienced by patients with multiple sclerosis. The current pharmacologic fatigue management therapies include regimens with disputed efficacy. Levels of magnesium have been shown to be lower in CNS tissues of MS patients which may be the basis of its correlation with fatigue. The proposed research will attempt to determine the effect of magnesium oxide (250 mg twice a day) supplementation on fatigue in MS patients in a randomized, double blind, sham controlled study. The effect will be measured through subjective means using the Modified Fatigue Impact Scale (MFIS) before and after the treatment. Vitamin C has shown no efficacy in fatigue in MS patients making it an ideal sham treatment, which consisted of 500 mg of vitamin C twice a day. The primary endpoint of the study was a mean decrease in total raw score of the MFIS. Preliminary results indicate magnesium's efficacy in decreasing fatigue. The intervention group had decreases in the physical, cognitive, and psychosocial subscales, and overall fatigue scores. The sham treatment patient had no decreases in these scales. The results show an effectiveness of magnesium supplementation in decreasing fatigue. Magnesium can easily be recommended to MS patients as it is inexpensive, holds little capacity or serious adverse events, but further research needs to be conducted to gain statistically significant data to support its use as a first line MS fatigue treatment.

Corresponding author: jimmyjgill@gmail.com

REGULATION OF METALLOPROTEINASE EXPRESION AFTER TRAUMATIC BRAIN INJURY

Presenting Author(s): Parampal Grewal

Grewal, P., M. Tsang, S. Zhang, L. Kojic, W. Jia and M. Cynader

Department of Surgery, Faculty of Medicine, University of British Columbia, B.C., Canada

Background
Traumatic brain injury (TBI) initiates a deleterious cascade of cellular and molecular events resulting in ischemia of the brain, death of neurons and behavioral deficits. Two major systems involved in this process are matrix metalloproteinases (MMPs) and "A Disintegrin And Metalloproteinases" (ADAMs). These proteinases are implicated in intracellular signaling, cellular proliferation and survival, migration, differentiation, synaptogenesis, axonal growth and myelination.

Methods
Closed and open head TBI were induced in mice. Brain samples were fixed at various time points up to 24 hours. Immunohistochemistry was performed to identify expression of the MMPs. Cell densities were compared between different regions at different time points. Quantitative study and statistics were done to analyze topography of the immunopositive cells.

Results
In the closed head TBI the ventral cortex, dorsal cortex, thalamus and hippocampus were compared as diffuse changes were found across the brain. In the open head TBI a visible brain injury site was found, hence the injury core was compared to the surrounding areas and the contralateral brain regions.
In the closed head TBI cell density of MMP-2, MMP-9, ADAM-10 and ADAM-17 have increased with a peak of expression at 1 hour, followed by a decrease towards the baseline level by 24 hours. This effect was strongest in dorsal cortex but was also present in the thalamus and the ventral cortex. Cell density in the hippocampus remained relatively constant.
In the open head TBI cell density remained relatively constant for ADAM-10 and ADAM-17 in all regions. However, cell density for MMP-2 increased with time in all regions. MMP-9 demonstrated the same trend as MMP-2.

Conclusions
Together, these results suggest that closed and open head traumatic brain injury can induce distinct patterns of metalloproteinase expression in the brain early after injury. Increased expression of metalloproteinases following TBI may be exploited to selectively inhibit the detrimental responses in the brain, while facilitating neural repair and functional brain recovery after injury.

Corresponding author: parampal@interchange.ubc.ca

TEMPLATE-DIRECTED MISFOLDING OF SUPEROXIDE DISMUTASE 1

Presenting Author(s): Will Guest

Guest, W. (1), L. Grad (1), E. Pokrishevsky (1), M. O'Neill (1), A. Yanai (1), E. Gibbs (1), S. Plotkin (2) and N. Cashman (1)

(1) Brain Research Centre, University of British Columbia, B.C., Canada
(2) Department of Physics and Astronomy, University of British Columbia, B.C., Canada

Motor neuron cell death in amyotrophic lateral sclerosis (ALS) progresses in a spatiotemporal manner reminiscent of prion disease. Here we study the effects of intracellular obligately misfolded superoxide dismutase 1 (SOD1) mutant proteins on natively structured wild-type SOD1. Expression of the enzymatically inactive, natural familial ALS SOD1 mutations G127X and G85R in human mesenchymal and neural cell lines can induce misfolding of wildtype natively-structured SOD1, as indicated by: 1) immunoreactivity with SOD1 misfolding-specific mAbs; 2) marked protease sensitivity indicating structural loosening; 3) non-native disulfide-linked oligomer & multimer formation; and 4) increased generation of reactive oxygen species.

Expression of G127X and G85R in mouse cell lines did not induce misfolding of murine wtSOD1, and a species restriction element for human wtSOD1 conversion was mapped to a region of sequence divergence in loop II and β-strand 3 of the SOD1 β-barrel (residues 24-36). These observations unambiguously demonstrate that misfolded SOD1 can induce misfolding of natively structured wtSOD1 in a physiological intracellular milieu. The misfolding reaction is sensitive to SOD1 sequence and/or structure, and is accompanied by generation of toxic oxygen free radicals.

Corresponding author: wguest@interchange.ubc.ca

APPLICATION OF A REAL-TIME RAMAN SCANNING APPARATUS FOR IN VIVO SKIN LESION DIFFERENTIATION AND SKIN CANCER DIAGNOSIS

Presenting Author(s): Lawrence (Marius Laurentiu) Haiducu

Haiducu, M.L. (1), J. Zhao (2) and S. Kalia (2)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) Department of Dermatology and Skin Science, University of British Columbia, B.C., Canada

Skin cancer remains the most common cancer diagnosis in Canada and annual incidence rates have been on the rise. The current gold standard for skin cancer diagnosis is a biopsy with subsequent histological analysis. This technique, however, is invasive, time consuming, expensive, and can lead to medical complications. Given the accessibility of skin tissue, various optical tools may provide a more favourable diagnosis modality. Raman scattering, in particular, has been used extensively in medicine for cellular structure analysis, drug formula characterizations, and non-invasive pharmacokinetic profiling. Previous generation Raman spectrometers have required tissue isolation from the host. Through our improvements in Raman scattered wave capturing techniques and minimization of fluorescence interference, we have permitted an *in vivo* approach to our automated Raman scanning apparatus. The real-time acquisitions may be modified within a pre-determined scanning area of the skin through user input of scanning time, motor velocity, and array dimension parameters. Significant shifts in Raman scattering, if due to underlying alterations of normal skin molecular structure, can be used to aid the clinician in lesion differentiation or to distinguish lesion borders and improve the precision of excision attempts. The rapid spectrometer acquisition times of the device (as low as 0.5 seconds) have been found to lead to ideal patient comfort and compliance. Early investigations have revealed significant and consistent shifts in Raman scattering at well-demarcated lesion borders. Correlation of spectral data to lesion extent and diagnosis upon histological analysis will allow for optimal characterization of spectral patterns.

Corresponding author: haiducu@interchange.ubc.ca

IMPACTING HEALTH HABITS THROUGH PERSONALIZED EDUCATION: THE CASE OF EXCESSIVE UV EXPOSURE AMONG TEENAGERS

Presenting Author(s): Lawrence (Marius Laurentiu) Haiducu

Haiducu, M.L. (1) and D.I. McLean (2)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) Department of Dermatology and Skin Science, University of British Columbia, B.C., Canada

In an era of widespread public education campaigns, Canadians may easily become overwhelmed with diverse, and perhaps conflicting, health recommendations. Among the dermatologic community, concerns over excessive ultraviolet (UV) radiation exposure and rising skin cancer incidence rates have resulted in diverse efforts to curb such trends, including enhancing online teaching resources and public skin cancer screening opportunities, as well as urging policy changes regarding topics of sunscreen labelling and tanning bed accessibility. Such strategies, though possessing opportunities for widespread public influence, are burdened by a relative lack of message personalization.

As a group, teenagers will have acquired over 50% of their lifetime sun exposure by the age of 18. Launched as a province-wide sun safety and skin cancer education campaign, SkinSafe targets this high school population by allowing for student-to-student engagement on topics such as skin physiology; skin damage, wrinkling and burning; skin cancer pathogenesis and appearance; skin self examination; tanning bed dangers; and prevention strategies. Baseline investigations into the knowledge, attitudes, and behaviours of the SkinSafe participants have found that the degree of skin cancer knowledge and family history of skin cancer are both independently and significantly associated with the adoption of sun safe strategies, including wearing sun protective clothing ($p<0.001$), frequency of sunscreen application ($p=0.003$), shade seeking ($p<0.001$), and skin self examination frequency ($p=0.02$). Both skin cancer knowledge and family history of skin cancer are also negatively correlated to daily summer time spent outdoors between 10am and 4pm ($p<0.001$), sun tanning frequency ($p=0.005$), and frequency of tanning bed usage ($p<0.001$). Nearly 70% of students using tanning beds more often than once a month believe that such devices are completely safe and no significant differences in perceived level of future skin cancer risk were found in comparison to students not engaging in such activities ($p=0.51$). No significant relationship was found between online heath information seeking behaviour and skin cancer knowledge ($p=0.169$), with 79% of SkinSafe participants agreeing that they have encountered too many recommendations to know which ones to follow. Such findings reinforce the value of, and need for, the SkinSafe presentation approach.

Corresponding author: haiducu@interchange.ubc.ca

EXERCISE BEHAVIOUR AND COUNSELING ATTITUDES OF 4TH YEAR STUDENTS AT UBC

Presenting Author(s): Kaila Holtz

Holtz, K.A.(1), K.J. Kokotilo (1), B.E. Fitzgerald (1) and E. Frank

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) School of Population and Public Health, University of British Columbia, B.C., Canada

BACKGROUND: U.S. data shows medical students exercise more than the average age-matched population and that a relationship exists between levels of physical activity (PA) and perceived relevance of exercise counseling to clinical practice. While it has been previously shown that Canadian medical students feel unprepared to appropriately counsel patients to exercise, there is no data specific to the habits and attitudes of UBC students. Our study is the first to describe the level of PA and attitudes of 4th year students preparing to enter residency.
HYPOTHESIS: We hypothesized UBC students exercise more than their age-matched peers and that exercise behaviour would significantly related to lifestyle counseling attitudes.
METHODS: N=486 students over four years (2007 - 2010) completed a survey designed to evaluate student PA levels using a Godin exercise questionnaire and health related attitudes and behaviours. A 62% response rate over the four years was achieved.
RESULTS: 64% of students met the Canadian Society of Exercise Physiologists (CSEP) PA recommendations. Attitudes toward healthy living were related to PA levels but counseling practices were not. Students engaged in more strenuous PA per week were more likely to perceive exercise counseling as being highly relevant to future clinical practice (p=0.018). 69% of students perceived exercise counseling to be highly relevant to clinical practice and 86% felt their training in this area was less than extensive.
CONCLUSIONS: UBC medical students engage in more strenuous PA than average age-matched Canadians and PA levels were related to perceived relevance to clinical practice and credibility of physicians as exercise counselors. Targeting both time spent by students participating in strenuous PA and academic training in the area of exercise counseling may be important first steps in preparing future physicians to prescribe exercise effectively.

Corresponding author: kholtz@interchange.ubc.ca

IMPACT OF ASIAN ETHNICITY ON COLORECTAL CANCER SCREENING; A POPULATION-BASED ANALYSIS OF CALIFORNIA

Presenting Author(s): Babak Homayoon

Homayoon, B. (1), N.C. Shahidi (1) and W.Y. Cheung (1,2)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) Division of Medical Oncology, B.C. Cancer Agency, B.C., Canada

Objectives: Although research shows that African Americans and Hispanics frequently receive less colorectal cancer screening (CRCS) than whites, few studies have focused on CRCS among Asians. The aims of this study were to compare CRCS between Asians and whites and to evaluate for clinical predictors of CRCS. Methods: From the 2007 California Health Interview Survey, we identified all Asian and white respondents who were eligible for
CRCS. Logistic regression was performed to evaluate for differences in CRCS. We used stratified and interaction analyses to examine whether associations between race and CRCS were modified by insurance status, birthplace, or language skills, while controlling for other confounders. Results: Baseline characteristics were similar between Asians and whites. Only 58% of Asians and 66% of whites reported undergoing upto-date CRCS ($P < 0.01$). In multivariate analyses, visiting a physician more than 5 times produced the highest odds of being up-to-date with
screening. When compared with whites, Asians had decreased odds of being up-to-date with screening. Stratified analyses showed that this disparity existed mainly in the insured, but not in the uninsured, and it was not modified by place of birth or English language proficiency. Conclusions: Despite its ability to reduce mortality, CRCS is suboptimal in our US population-based cohort of Asians when compared with whites. A contributing factor to this problem for the Chinese and Koreans may be a lack of awareness regarding CRCS, whereas the source of the problem in the Vietnamese seems to be related to healthcare access.

Corresponding author: homayoon@interchange.ubc.ca

ANTENNAPEDIA MEDIATED TRANSDUCTION OF THE TRANSCRIPTION FACTOR CHF1/HEY2 DEMONSTRATES A VIRAL VECTOR-LESS METHOD OF TRANSDUCING FIBROBLASTS IN THE CONTEXT OF CARDIOMYOCYTE TRANSDIFFERENTIATION

Presenting Author(s): Jeffrey Hu

Hu, J., W.M. Chien and M.T. Chin

Division of Cardiology, University of Washington School of Medicine, W.A., USA

Heart disease, a leading cause of morbidity and mortality, typically occurs as a result of pathological hypertrophy mediated by cardiomyocyte dysfunction and apoptosis. The limited regenerative capacity of cardiomyocytes poses an enormous challenge in the treatment of heart disease. Previous study showed mouse fibroblasts infected with retroviruses containing the three transcriptional factors, Gata4, Mef2c, and Tbx5, were able to transdifferentiate cardiomyocyte-like cells. However, the combination of a low reprogramming efficiency and the viral DNA integration into chromosomes limits its use *in vivo*. The cardiovascular-specific hairy-related basic helix-loop-helix (bHLH) transcription factor CHF1/Hey2 (CHF1) promotes ventricular myocardial maturation, as well as physiological instead of pathological hypertrophy through regulation of Gata4 and Tbx5. To determine the effect of CHF1 on reprogramming of fibroblasts into mature cardiomyocyte-like cells, we constructed and purified a CHF1-Antennapedia (CHF1-Antp) fusion protein to facilitate transduction of CHF1 into fibroblasts. Fluorescence microscopy confirmed transduction of CHF1-Antp into fibroblasts *in vitro*. These findings demonstrate a viral vector-less method of transducing transcription factors into fibroblasts that can be applied to an *in vivo* model of heart disease treatment.

Corresponding author: jeffhu@interchange.ubc.ca

RARE OBESITY DISORDERS: METABOLIC PHENOTYPING AND EXOME SEQUENCING IN THE SEARCH FOR NOVEL GENES

Presenting Author(s): Namrata Jhamb

Jhamb, N. (1), S. Gyawali (4), L. Musa (1,2), R. Attariwala (3), S. Lear (4) and W.T. Gibson (1,2)

(1) Department of Medical Genetics, Faculty of Medicine, University of British Columbia, B.C., Canada
(2) Diabetes Research Program, Child and Family Research Institute, B.C., Canada
(3) AIM Medical Imaging, B.C., Canada
(4) Department of Kinesiology, Simon Fraser University, B.C., Canada

Purpose: Major genetic risk factors for obesity (BMI > 30 kg/m2 or >95th%ile for age and sex) are more likely to be found among rare patients with severe early onset obesity or lipodystrophy than among individuals in the general population. Genome-wide association studies have not yet found major genetic risk factors for obesity. The study of patients with rare obesity disorders and lipodystrophy has identified numerous major obesity genes. Understanding of the metabolic consequences of these obesity genes requires both comprehensive genotyping and phenotyping.

Methods: **C**linical history and physical exam are conducted, including measurements of Body Mass Index and waist-hip ratio. An observed test-meal after a 12-hour fast is carried out to provide a weighted measurement of the patient's food intake. Data from the test-meal is integrated with measurement of physical activity via portable accelerometry. Subsequently, cutting-edge research methods are used to measure contributory endophenotypes. Dual X-ray absorptiometry (DXA) scans are conducted to measure total lean tissue mass and fat mass. Resting Energy Expenditure is measured as an estimate of the patient's basal metabolic rate. Whole-body MRI scans are used to isolate images of visceral fat and subcutaneous fat, the ratio of which is calculated. Genome-wide assessment is done by whole-exome sequencing in select families.

Results: To date, 200 subjects have been studied, out of which 75 have either syndromic obesity, lipodystrophy, or monogenic diabetes. Controls are either age, height, weight, and ethnicity-matched to the patients or are unaffected parents of the patients. Currently, DXA scans have been conducted with 25 subjects, Resting Energy Expenditure with 25 subjects, observed test meals with 11 subjects, MRI with 12 subjects, accelerometry with 5 subjects, and whole-exome sequencing with 12 subjects. In addition to subjects already assessed, a further 75 subjects have been identified who are eligible to participate in the study.

Conclusion: Measurements of caloric intake, body composition, and energy expenditure combined with whole exome sequencing create comprehensive assessments for a select population with highly heritable obesity and lipodystrophy syndromes. These details will add to the literature on syndrome description and will increase understanding of pathways that contribute to common obesity.

Corresponding author: namrataj@interchange.ubc.ca

BETWEEN-RATER RELIABILITY OF HISTORICAL VARIABLES USED IN A ROUTINE EMERGENCY DEPARTMENT PATIENT EVALUATION

Presenting Author(s): Andrei Karpov

Karpov, A. (1), E. Yu (1) , C. Mok (1) and Corinne Hohl (1,2)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) Department of Emergency Medicine, Faculty of Medicine, University of British Columbia, B.C., Canada

Introduction: In the Emergency Department (ED), historical information is commonly collected in duplicate by multiple care providers.

Objective: to assess the inter-rater reliability between physicians and nurses in collecting a set of common historical variables.

Methods: This prospective observational study enrolled a systematic sample of patients presenting to an urban academic ED. After enrolment, physicians and nurses independently and blinded to each other's evaluations rated a set of historical variables previously selected because of their association with the ED diagnosis of an adverse drug event (ADE). The inter-rater reliability was calculated using kappa scores (κ) and intra-class correlation coefficients (ICC) and their associated 95% confidence intervals (CIs).

Results: Nurses and physicians evaluated 51 patients with an average age of 57.8 years, of which 26(51%) were female. Their inter-rater agreement was excellent for a history of atrial fibrillation (κ=1, 95%CI 1-1), diabetes (κ=0.86, 95%CI 0.68-1), and the use opioids or benzodiazepines (κ=0.85, 95%CI 0.70-1). Agreement was substantial for use of insulin or oral hypoglycaemic agents (κ=0.74, 95%CI 0.45-1), antihypertensives or diuretics, (κ=0.72, 95%CI 0.51-0.93), anticoagulants or antiplatelet agents (κ=0.65, 95%CI 0.20-1), and a history of congestive heart failure (κ=0.66, 95%CI 0.032-1). Agreement was moderate for a change in medications within 28 days (κ=0.60, 95%CI 0.37-0.82), use of aspirin or salicylates (κ=0.59, 95%CI 0.30-0.89), a history of renal failure (κ=0.48, 95%CI -0.12-1) and a previous ADE diagnosis (κ= 0.43, 95%CI 0.05-0.81). Agreement was only fair for determining whether a patient used recreational or street drugs (κ=0.29, 95%CI -0.21-0.78). There was substantial agreement for determining the number of medications that the patient was taking (ICC=0.70).

Conclusion: There is significant variability in the inter-rater reliability between common historical features often collected in the ED. Variables with high inter-rater reliability may not need to be collected in duplicate for clinical care purposes, and can be considered candidate predictor variables for clinical decision rule development.

Corresponding author: akarpov@interchange.ubc.ca

NEURO-ANATOMIC CORRELATES OF THE FEATURE SALIENCY HIERARCHY IN FACE PROCESSING: AN FMRI ADAPTATION STUDY

Presenting Author(s): Joshua Lai

Lai, Joshua (1), R. Pancaroglu (2), I. Oruc (2), J. Barton (2.3), J. Davies-Thompson (2)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) Deptment of Opthalmology and Visual Sciences, Faculty of Medicine, University of British Columbia, B.C., Canada
(3) Division of Neurology, Faculty of Medicine, University of British Columbia, B.C., Canada

Background: Behavioural studies have shown that faces have a "feature-saliency hierarchy", with some features more important than others for recognition.

Objective: We used fMR-adaptation to ask whether face parts contribute differently to the neural signal in face-responsive cerebral regions.

Method: 18 subjects first performed a same/different behavioural experiment to characterize their perception of different face parts. Next they underwent an fMRI-adaptation study, in which limited portions of the faces were repeated or changed between alternating stimuli.

Results: On fMRI, there was a release of adaptation in the right fusiform face area (FFA) with changes to the top face-half or the eyes. A parametric analysis showed that the neural responses in the right FFA were correlated with both the perceptual experience of the subject, as well as with the physical differences between images, as measured by an ideal observer. Responses in the right occipital face area (OFA) were correlated only with physical image properties. Correlations were not found in homologous left hemispheric regions or the posterior superior temporal sulci (pSTS).

Conclusion: The feature-saliency hierarchy in human face perception is reflected by activity in the right FFA, supporting a key role of this structure in face processing.

Corresponding author: jjlai14@interchange.ubc.ca

A RETROSPECTIVE EVALUATION OF CANADIAN MEDICAL STUDENTS PARTICIPATING IN INTERNATIONAL MEDICAL EXCHANGES

Presenting Author(s): Alison Lee

Lee, A.

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) Canadian Federation of Medical Students, Ottawa, Canada

Objective: There is increasing interest in medical students to participate in international electives. The International Federation of Medical Students' Association (IFMSA), an independently run medical student organization representing over 88 national medical student associations including the Canadian Federation of Medical Students (CFMS), has an exchange program that 1st and 2nd year Canadian medical students can participate in over the summer. Canadian medical students have participated in IFMSA clinical exchanges since 1994.

This study was undertaken to assess the interest and demand for IFMSA clinical exchanges across the 13 CFMS member schools over the past 2 years. The number of exchange applications received at each school is based on many factors including student interest, publicity of IFMSA exchanges, and total number of eligible students.

Methods: In 2010, an electronic application form was created allowing for easy access and central collection of applications, as well as effective storage and analysis of this data. A retrospective quantitative analysis of the number of exchange applications and the number of exchange spots allocated to each school was undertaken.

Results: The number of exchange spots allocated to each school is based on: the number of incoming international students that a school can take and the number of applications received from each school. The applicants from each school are chosen randomly.

A total of 256 1st and 2nd year medical students across Canada applied for 31 clinical exchanges in 2010-2011, resulting in 12.1% of applicants chosen for exchange. From 2011-2012, there were a total of 404 applicants for 45 exchanges, resulting in 11.1% of successful applicants. All schools showed an increase in the number of applications except for University of Calgary and McMaster University.

Conclusion: There is a high interest and demand for international clinical electives in Canadian medical schools. The IFMSA exchanges give 1st and 2nd year students an opportunity to partake in electives abroad during the summer. Over 2 years, the number of applicants has increased except in schools with a 3-year medical program. In the future, the exchange program should expand to accommodate the increasing interest in participation of international elective programs.

Corresponding author: alisonymlee@gmail.com

LEARNING ONCOLOGY FROM AN INTEGRATED INTERDISCIPLINARY PERSPECTIVE

Presenting Author(s): Alison Lee

Lee, A. (1), L. Lai (1), S. Hamilton (2) and P.A. Ingledew (3)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) BC Cancer Agency, Vancouver Center, B.C. Canada
(3) BC Cancer Agency, Fraser Valley Center, B.C., Canada

Objective: A deficit in oncology education exists for medical students in North America. Exposure to oncology in undergraduate medical programs occurs sporadically in a discipline-specific manner, limiting students from experiencing the unique interdisciplinary nature of oncology. Emerging evidence suggests that integrated clerkships, where students work with health care professionals with respect to disease management, improve learning outcomes. The goal of this project is to develop an integrated interdisciplinary oncology elective supplemented by online modules and virtual patients (VP).

Methods: To develop an integrated interdisciplinary elective, the Kern approach to curriculum development was employed. A needs assessment of third year medical students was conducted. The survey polled interest levels for an integrated oncology clerkship and elicited preference for the mode of educational material delivery. In 2008, following survey analysis, development of the elective was underway. To supplement clinical experiences, online modules complimented by branching-logic VP cases have been written and published. VP cases have been created using Vue, Open Labyrinth and Articulate. Software tools have been evaluated for the ability to extract and analyze data from the online modules for education research.

Results: The needs assessment showed a high interest in an integrated oncology clerkship supplemented by online learning. 50% (41/82) of students surveyed had not interacted with cancer patients during clerkship and 62% (51/82) felt their ability to discuss oncology issues with patients was poor or fair. 80% (64/82) felt that online modules would enhance learning. The modules for lung, prostate, breast and colorectal cancer along with associated supplemental VP cases have been written, reviewed, and published online. Jasper iReports has been used to analyze use of the website. The integrated elective will be piloted in 2011.

Conclusion: The gaps in oncology education are addressed by the needs-based development of an integrated oncology clerkship that is complimented with an online module component. Supplemental VP cases offer a unique learning opportunity where students practice clinical reasoning and experience the consequences of their decisions in a safe environment. Additional research will be done to determine the educational benefits of an integrated elective.

Corresponding author: alisonymlee@gmail.com

ABSORPTION AND DISTRIBUTION OF AMPHOTERICIN B FOLLOWING ORAL ADMINISTRATION IN NOVEL LIPID-BASED FORMULATIONS

Presenting Author(s): Molly Lin

Lin, M. (1), P. Gershkovich (2), O. Sivak (2), K.M. Wasan (2)

(1) Department of Medicine, University of British Columbia, B.C., Canada
(2) Faculty of Pharmaceutical Sciences, University of British Columbia, B.C., Canada

Amphotericin B (AmpB) is a drug used to treat systemic fungal and parasitic infections in humans. Due to low solubility in intestinal medium and poor permeability across the intestinal wall, current AmpB formulations are not absorbed into the bloodstream when given orally. Therapy is limited to intravenous administration, resulting in high costs of treatment and limiting the use of AmpB in developing nations. In this study, we investigate the absorption and distribution of a new lipid-based formulation of AmpB following oral administration. Our results showed significant intestinal absorption of AmpB following oral administration in a novel lipid-based formulation in rats.

Corresponding author: molly.m.lin@gmail.com

A CASE STUDY EVALUATION OF A STUDENT DRIVEN GLOBAL HEALTH PROJECT: GHI HONDURAS

Presenting Author(s): Nancy Chang Liu

Liu, N.C. (1), K. Duthie (2), S. Dharamsi (1,3), M. Whitfield (1)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) McGill University, Faculty of Nursing , Q.C., Canada
(3) Global Health Network, Liu Institute for Global Issues

Background
Since 2006, a group of healthcare students from the Global Health Initiative (GHI) at the University of British Columbia have been working each summer in two rural communities in Honduras. The goals of the projects were to understanding the health needs of the community and implement infrastructure changes and health promotion workshops to address those needs. The project ended in July 2011 and a qualitative evaluation was undertaken to assess the impact of the project on the community members and student volunteers.
Methods
20 key informants from the communities and the NGO were interviewed to gain insight on their impression of the benefits and negative impacts the students have had on their communities. Community members were also asked if they have made any changes to improve their health and the health of their community as a result of the project. 7 past students participants were also interviewed to analyze how participating in a global health project has effected their education and personal development. Students described how various challenges and experiences influenced their career/educational decisions and their understanding of the CanMEDS health advocate role.
Results
Findings suggest that the communities did benefit from the project. Examples include teacher observations of better hygiene and dental care practices at schools, greater understanding of women's health issue by community health workers and infrastructure work such as constructing community health centers, latrines, roofs, floors and a community hall. However, unintentional negative influences have also been identified in relation to perceived unmet promises, lack of research feeding back to the community and poor allocation of resources. Students gained insight into working in resource poor settings and steps to developing a collaborative partnership. Students gained valuable skills in team-work, leadership, research, cross-cultural communication, and the ability to adapt to a wide variety of obstacles. The experience both dampened and flourished students' interest in global health work.
Conclusions
International service learning projects can benefit both students and receiving communities but a lack of sufficient communication may lead to issues of dependency and unmet promises that may hinder the effectiveness and sustainability of a project.

Corresponding author: nancy.ch.liu@gmail.com

AMYLOID-BETA CAUSES OVER-EXPRESSION OF INFLAMMATORY CYTOKINES IN THE RETINAL PIGMENT EPITHELIUM AND RETINA IN VIVO

Presenting Author(s): R Tom Liu

Liu, R.T., J. Cui, S. Cao, J. Gao and J. Matsubara

Department of Ophthalmology and Visual Sciences, University of British Columbia, B.C., Canada

Purpose: Amyloid-beta (Aβ) is present in retinal drusen in patients with age-related macular degeneration (AMD), but its role in AMD pathogenesis is unclear. Our earlier study of Aβ stimulation caused dramatic upregulation of inflammatory cytokines and immune response genes in human retinal pigment epithelium (RPE) *in vitro*. This study investigates the effects of Aβ on immune response gene expression in RPE and neuroretina in an *in vivo* rat model.

Methods: Twenty, 5 month old male Long-Evans rats received an intravitreal injection of 7µg Aβ1-40 in one eye and vehicle (PBS) in the fellow eye. Animals were sacrificed at day 1, 4, 14, and 49 post injection and the RPE-choroid and neuroretina were isolated from enucleated eyes (n=3). Remaining enucleated eyes were fixed for section (n=2). Gene expression of a select group of genes (based on *in vitro* work) in RPE-choroid and neuroretina were quantified by reverse-transcription PCR. Protein expression in tissue, microglial activation and retinal thickness was evaluated by immunohistochemistry.

Results: Aβ caused significantly increased transcription of pro-inflammatory cytokines interleukin 1-beta (IL-1β), IL-6, tissue necrosis factor-alpha (TNF-α) in the RPE-choroid on day 4 post injection (fold change compared to control: 5.06±0.74, 7.45±2.04, 5.56±0.76 respectively. Mean±SE. $p<0.05$). inducible nitric oxide synthase (iNOS) and XIAP-associated factor 1 (XAF1) were also upregulated in RPE-choroid on day 4 (5.26±0.74 fold, 4.37±0.64 fold respectively). Vascular endothelial growth factor (VEGF) expression was not significantly elevated. In contrast neuroretina only showed increased transcription of TNF-α on day 14 (3.83±0.75 fold). All gene transcription returned to control levels by day 49 post injection. Immunohistochemistry revealed significantly increased staining for the cytokines in Aβ injected eyes on day 4 and 14. Microglial activation was seen on day 1 only. There was no elevated staining of XAF1 protein or p53 in tissue or any evidence of retinal thinning. Angiogenesis was not observed.

Conclusions: Our results confirmed that inflammatory genes are over-expressed by RPE-choroid and neuroretina upon stimulation by drusen component Aβ 1-40. These results are consistent with earlier reports that AMD progression is associated with chronic, local inflammatory events in the outer retina, and point towards the causal role of drusen components in AMD pathogenesis.

Corresponding author: rztom.liu@gmail.com

POLYUNSATURATED FATTY ACIDS AND AMINO ACID METABOLISM

Presenting Author(s): Vivian Liu

Liu, V. (1), E.M. Novak (1), T.S. Wu (1), R.A. Dyer (1), J. King (1), M.A. George (1) and S.M. Innis (1,2)

(1) Nutrition & Metabolism Research Program, Child & Family Research Institute, B.C., Canada
(2) Department of Pediatrics, Faculty of Medicine, University of British Columbia, B.C., Canada

The n-6 and n-3 polyunsaturated fatty acids (PUFAs) are essential dietary nutrients, meaning that they must be provided by the diet. PUFAs have numerous functions, among which is the regulation of gene expression for enzymes that regulate glucose and lipid metabolism, specifically fatty acid, triglyceride, and cholesterol. In particular, diets rich in the n-3 PUFAs eicosapentaenoic acid (20:5n-3) and docosahexaenoic acid (22:6n-3), of which the major dietary source is fish, are associated with increased fatty acid oxidation, decreased fatty acid synthesis and plasma triglycerides, and increased glucose oxidation. The purported mechanism involves binding to transcription factors, such as PPARs and SREBPs, which in turn control gene expression of regulatory enzymes. We propose that n-3 PUFAs are unlikely candidates for gene regulation, as intakes vary by meal and day, and episodic changes in gene expression in response to short-term changes in intake are metabolically wasteful. Adrenic acid (22:4n-6) is synthesized endogenously from dietary linoleic acid (18:2n-6) and shows a characteristic increase in response to n-3 fatty acids inadequacy. Data from our lab also has also shown that tissue 22:4n-6 is more closely correlated with changes in expression of key enzymes of glucose, fatty acid, and unexpectedly, amino acid metabolism, than 20:5n-3 or 22:6n-3.

The objective of this study is to determine whether 22:4n-6, when compared to n-3 and other n-6 PUFAs, regulates gene and protein expression relevant to glucose and fatty acid metabolism in Hep G2 cells. To achieve this, Hep G2 cells are incubated with delipidated–albumin, to which 22:6n-3, 20:5n-3, 20:4n-6, 22:4n-6, 18:2n-6, 18:3n-3, 18:1n-9 or 16:0 are bound. Time-course and concentration studies are used to determine effects on cell fatty acids using GLC-FID, and characterize conditions to enable 22:4n-6 endogenous synthesis in n-3 fatty acid deficient cells. Real time-PCR and Western Immunoblotting will be used to assess gene and protein abundance of target enzymes. Stearoyl CoA desaturase (SCD) synthesizes monounsaturated from saturated fatty acids, and is decreased by n-6 and n-3 PUFAs. Results available for presentation include cell response to different fatty acids, and SCD-1 protein abundance as a marker of cell culture conditions.

Corresponding author: vivliu@interchange.ubc.ca

PHARMACEUTICAL SALES REPRESENTATIVES AND PATIENT SAFETY

Presenting Author(s): Theresa Lo

Lo, T. (1) and B. Mintzes (2)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) Therapeutics Initiative, Department of Anesthesiology, Pharmacology & Therapeutics, Faculty of Medicine, University of British Columbia, B.C., Canada

Introduction: Physician prescribing practices are influenced by their interactions with pharmaceutical sales representatives (PSRs). Government agencies regulate these interactions, and routinely issue safety advisories on approved drugs based on new research evidence or post-marketing data.

Methods: During January 2008 to May 2009, 1692 questionnaires were collected from 255 family physicians, from Vancouver, Montreal, Sacramento, and Toulouse, related to information presented to them during PSR visits. The responses were compared to safety advisories published within the same period to see whether the new information about contraindications (CIs) and serious adverse events (SAEs) in these advisories was disclosed to physicians.

Results: 30 drugs from the database were mentioned in safety advisories within the designated time period. 6 of these drugs had SAEs published in more than one region, and in 31 promotions for these drugs SAEs were mentioned 32% of the time. 3 drugs had CIs published in more than one region, and in 14 promotions for these CIs were mentioned 29% of the time. When the safety advisory was published in one region only, CIs and SAEs were mentioned only 4% of the time for 24 drugs.

Conclusion: Safety information is more likely to be mentioned when multiple regions have issued safety advisories, but the majority of pharmaceutical sales representatives do not discuss potential CIs and SAEs.

Corresponding author: hml1@interchange.ubc.ca

EVALUATING SCOPES OF PRACTICE RESEARCH SUMMARY

Presenting Author(s): Charmaine Yu Yan Ma, Lindsay McRae and Kristin DeGirolamo

Ma, C.Y.Y., L. McRae and K. DeGirolamo

Faculty of Medicine, University of British Columbia, B.C., Canada

Background: Interdisciplinary healthcare education is the newest direction of many healthcare programs, and is slowly being introduced into medical practice as people realize the benefits of a multidisciplinary team.[1,2] There is no data available that quantifies how much the various disciplines know about each other. A working knowledge of the various healthcare scopes of practice will greatly improve interdisciplinary teamwork.

Methods: In order to assess the current knowledge of various professionals regarding their own scopes of practice as well as that of their multi-disciplinary partners, we designed a survey for pharmacists, nurses and physicians. We created a GoogleDoc survey that we emailed to practicing professionals in the various disciplines and received 97 responses. The questions in the survey covered different core components of each profession's scopes of practice and also asked participants to rate the depth of their own perceived knowledge.

Results: The results for the survey demonstrated 3 important points for consideration: firstly, over half of the participants believed inter-professional education was 'very important' (50% RPh, 62% MD, 55% RN); secondly, participants believed they were either 'somewhat unprepared' (43% RPh, 19% MD, 29% RN) or 'somewhat prepared' (42% RPh, 33%MD, 36% RN) for effective inter-professional practice through their healthcare training program; lastly, every profession performed worse on questions regarding their own scope of practice than they predicted.

Approximately half of participants (RPh, MD, RN) believed that they were 'extremely knowledgeable' about their own scope of practice while their actual scores on profession-specific questions ranged from 50.5-72.3%. The majority of participants (RPh, MD, RN) claimed that they were 'somewhat knowledgeable' about other scopes of practice while their actual scores on questions regarding other scopes of practice averaged 60.5%.

Conclusions: These results demonstrate the continued presence of major gaps in knowledge between professions and also within one's own profession. Although the issue at hand is significantly more complex than our study demonstrates, our survey has highlighted the need for improvements in education programs for both prospective graduates as well as practicing professionals. We hope that our study will inspire enthusiasm that will help lead to changes in education and practice.

Corresponding author: kdegir@gmail.com

DEMOGRAPHIC CHARACTERISTICS AND PRIOR CONTRACEPTION EXPERIENCE AMONG WOMEN ENROLLED IN A TRIAL OF IMMEDIATE VS. DELAYED INSERTION OF INTRAUTERINE CONTRACEPTION AFTER SECOND TRIMESTER ABORTION

Presenting Author(s): Ali Majdzadeh

Majdzadeh, A. (1,2), and W.V. Norman (3,4)

(1) Faculty of Science, University of British Columbia, B.C., Canada
(2) Department of Physics and Astronomy, University of British Columbia, B.C., Canada
(3) Department of Family Practice, Faculty of Medicine, University of British Columbia, B.C., Canada
(4) Women's Health Research Institute, B.C, Canada

Background:
Women seeking second-trimester abortion are disproportionately from marginalized populations and are at high risk for recurrent unintended pregnancy as 38% have had at least one previous abortion. The most effective contraception is forgettable, requiring no user attention for at least three years. The intrauterine contraception (IUC) is effective, but is inserted 4-6 weeks post-abortion to minimize risk of expulsion. Although the expulsion rate is thought to be nominally greater than for immediate insertion, as few as 26% of women return for delayed insertion.

A randomized controlled trial (RCT) has been implemented recruiting 716 women randomized to insertion immediately or 4 weeks post-abortion and who choose their preferred IUC between either Levonorgestrel-releasing Intrauterine Contraception (LNG-IUC) or FlexiT380+ Intrauterine Contraception (CuT380-IUC). The RCT is implemented to assess whether intrauterine contraception placed immediately after a second trimester abortion will result in fewer pregnancies than current recommended practice of intended placement at 4 weeks post-abortion.

Objective:
This poster examines the intake characteristics of women enrolled in the groups receiving a LNG-IUC in this RCT.

Methods and Design:
All clinics providing second trimester abortions in B.C. have been strategically included in this study and actively recruited participants. Consenting women are enrolled in the RCT and choose their preferred IUC. Through provincial government health databases, Contraception Satisfaction Questionnaires filled out by participants during enrollment, and clinical records, participants will be followed and the study outcomes will be determined. Primary outcome measure is pregnancy rate at one year.

Results:
Participants described barriers and difficulties in achieving adequate contraception. Women in the study population tended to have a low level of socio-economic status and educational background, and although nearly all had used prior contraception, most were not using a highly effective method at the time of the current conception. Among women using highly effective methods, such as oral contraceptives, most reported difficulties in achieving consistent use. The advantage of the IUC is that it requires no user attention for up to 5 years. IUC users expressed the highest levels of satisfaction with their contraceptives.

Corresponding author: aliali@live.com

SPONTANEOUS CORTICAL ACTIVITY SYNCHRONIZES NEURAL CIRCUITS PRIOR TO THEIR FUNCTIONAL MATURATION

Presenting Author(s): David McVea

McVea, D.A., M.H. Mohajerani and T.H. Murphy

Department of Psychiatry, University of British Columbia, B.C., Canada

Remarkably, the brain and nervous system are active before they are functional. One role of this activity is promoting neural circuit development. Much as the adult brain improves its performance on a task via repetition, the developing brain benefits from repeated activation of related neural systems. While this process is relatively well understood in localized sensory or motor systems, understanding it in large cortical networks requires high-resolution recordings of activity from large regions of the intact brain.

We accomplished this using voltage-sensitive dye imaging to study activity in the developing rodent cortex *in vivo.* We sought to explore the hypothesis that cortical activity in early life synchronizes neural systems that will be functionally connected in adulthood.

In one set of experiments, we stimulated the skin of the hindlimbs of 4-6 day old rat pups (n=10). We found that, unlike in adult rats, there was activity only on the contralateral somatosensory cortex following this stimulation. However, when we examined brain activity without stimulation, we found that somatosensory cortices on opposite hemispheres of the brain were active together. This correlated activity arose from small spontaneous movements of the limbs and tail; this simultaneous external stimulation gave rise to simultaneous activation of the sensory cortices.

In a second set of experiments, we deflected the whisker of rat pups ranging in age from 5-12 days old (n=25). In the adult rodent, the deflection of the whisker causes an activation of the sensory cortex followed by the motor cortex. The delayed activation of the motor cortex was not present in the five or six day old pups, but was clearly established in twelve day old pups. However, the motor and sensory cortices were *spontaneously* active together, even in young animals in which whisker deflection only activated the sensory cortex.

In summary, these results show two examples of neural circuits in which the spontaneous brain activity reflects a level of maturity not yet present in their functional connectivity. Together, they suggest an important role for spontaneous cortical activity in forming and shaping long-range neural connections during development.

Corresponding author: dmcvea@interchange.ubc.ca

EFFECT OF INSULIN ON SOMATODENDRITIC DOPAMINE CONCENTRATIONS IN THE VENTRAL TEGMENTAL AREA

Presenting Author(s): Dmitry Mebel

Mebel, D.M. and S.L. Borgland

Department of Anesthesiology, Pharmacology and Therapeutics, University of British Columbia, B.C., Canada

Previous research has implicated mesolimbic dopamine (DA) signaling in the incentive, reinforcing, and motivational aspects of food intake. Insulin receptors are expressed on dopaminergic neurons of the ventral tegmental area (VTA) and there is substantial evidence suggesting that insulin may act in the VTA to suppress feeding. However, the neural mechanisms underlying insulin effects in the VTA remain unknown. We sought to determine the effect of insulin on evoked DA concentrations in the VTA.

Somatodendritic DA concentration was monitored in real time in mouse midbrain slices using fast-scan cyclic voltammetry. DA was evoked using an electrical stimulation applied with a bipolar stimulating electrode.

Insulin dose-dependently reduced DA concentration in the VTA. This action required activation of insulin receptor tyrosine kinase and mTOR signaling. Insulin depression of somatodendritic DA was not affected in low external Ca^{2+}. Further, insulin-mediated reduction of somatodendritic DA occurred only at higher frequencies of stimulation. These data suggest that insulin is not likely to affect release of DA. However, GBR 12909, a selective DA transporter (DAT) blocker, abolished insulin-mediated suppression of somatodendritic DA, suggesting that insulin enhances reuptake of DA. In addition, insulin did not alter somatodendritic DA in DAT knock out (KO) mice. In contrast, insulin depressed DA concentration in norepinephrine transporter KO mice to a similar extent as wild-types. In VTA slices pre-treated with cycloheximide, a protein synthesis inhibitor, insulin suppressed DA concentration to a similar extent as control. These data suggest that insulin does not increase de novo DAT synthesis, but may increase the number or function of DAT to attenuate DA concentration.

Taken together, these results indicate that insulin depresses somatodendritic DA concentrations in the VTA via mTOR signaling and increased reuptake of DA through DAT. Insulin-mediated decrease in DA may suppress motivation to seek additional food once satiety is reached. Therefore, disruption of insulin signaling might have significant implications in certain cases of overeating and obesity.

Corresponding author: mebel@interchange.ubc.ca

BREASTFEEDING IS AN EFFECT MODIFIER OF THE ASSOCIATION BETWEEN CAESARIAN SECTION DELIVERY AND ASTHMA IN CHILDHOOD

Presenting Author(s): Gareth Mercer

Mercer, G.

MD/PhD Program & School of Population and Public Health, University of British Columbia, B.C., Canada.

Background: Although it is currently accepted that delivery by caesarian section is associated with a moderately increased odds of childhood asthma, the magnitudes of odds ratios reported in previous studies have been inconsistent. Effect modification by breastfeeding could account for some of this inconsistency.
Methods: This study uses data from a population-based longitudinal cohort of 7577 Canadian children followed-up between 1994 and 2009 to investigate whether having been breast-fed could be an effect modifier of the association between delivery by caesarian section and asthma. Stratified logistic regression is used to estimate odds ratios for being diagnosed with asthma by age six, and after age six comparing caesarian section delivery to vaginal delivery among strata of breastfed and not breastfed children.
Results: Among children who were breast-fed, caesarian section is associated with no increased odds of asthma by age six (Odds Ratio (OR): 0.98, 95% CI: 0.81-1.18), but significantly increased odds after age six (OR: 1.47, 95% CI: 1.05-2.06). Whereas, among children who were not breastfed, caesarian section is associated with significantly decreased odds of asthma by age six (OR: 0.64, 95% CI: 0.43-0.94) and no significant increased odds of asthma after age six (OR: 1.20, 95% CI: 0.64-2.25).
Conclusions: Breastfeeding could modify the effect of caesarian section on odds of asthma through effects on the composition of infant intestinal microflora and development of normal immune system tolerance. Future studies of the association between caesarian section and childhood allergic disease should include assessments for effect modification by breastfeeding.

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Corresponding author: gmercer@interchange.ubc.ca

PERSPECTIVES OF INTRAVENOUS DRUG USERS ON THE HARMS CAUSED BY INSTALLING BLUE LIGHTS IN PUBLIC WASHROOMS

Presenting Author(s): Tracy Tan and Shannon Grant

Mercer, G. (1,2), T. Tan (1), R. Horan (1), S. Grant (1), A. Crabtree (1,2) and J. Buxton (3)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) School of Population and Public Health, Faculty of Medicine, University of British Columbia, B.C., Canada
(3) B.C. Harm Reduction Strategies and Services, B.C. Centre for Disease Control, B.C., Canada

Blue lights are installed in washrooms to discourage public use of intravenous (IV) drugs, yet there are no published studies of the effectiveness and safety of blue lights**.** To address this issue, we engaged IV drug users from Vancouver and Abbotsford, British Columbia on what they perceive to be the benefits and harms of blue lights in public washrooms. A cohort of 18 current and former injection drug users was recruited through drug user community advocacy groups. Participants' perceptions of the impacts of blue lights in washrooms were gathered using interviews, which were then transcribed and analysed according to the method of interpretive description. The majority of drug users interviewed found injecting under blue lights to be difficult and would avoid bathrooms fitted with them. Yet, many described a preference for avoiding injecting in public washrooms, regardless of the presence of a blue light. In situations during which they would violate this preference, namely when in the midst of withdrawal symptoms or when injecting outside was their only alternative, many would inject under blue light. Drug users identified four categories of harms from blue lights: 1) they make it difficult to access veins while injecting making injecting more dangerous and harmful; 2) they make users more likely to miss their veins when injecting, forcing users to seek their next dose of drug earlier than anticipated; 3) by hindering users' ability to inject, they force users to find other more unsafe and unhygienic places to inject; 4) they make it easier for users to get caught and persecuted while using drugs. Despite these harms, many participants were in favour of blue lights in washrooms, which was tied to a belief that their injecting in washrooms would be harmful to others, and that their own health and safety were less important than preventing public harm. Installation of blue lights in public washrooms has harmful effects which are borne disproportionately by those injection drug users who are already most at risk of poor health. Yet, due to internalized oppression, drug users may be unlikely to initiate efforts to remove these harmful installations.

Corresponding author: ttan@interchange.ubc.ca

`DEALING' WITH COMPLEXITY: CONSTRUCTION AND ANALYSIS OF A CARD BASED COMMUNICATION TOOL FOR OBESE PATIENTS

Presenting Author(s): Thomas Merth

Merth, T.D.N., C.L. Matteson and D.T. Finegood

Department of Biomedical Physiology and Kinesiology, Simon Fraser University, British Columbia, Canada

Clinical communication and decision support tools have been used to aid in treating diseases such as diabetes and cancer but not obesity. This project will create and test a card based communication tool for use between patients and practitioners that addresses an individual's challenges in making healthy lifestyle changes.

Initially, cards were developed from the diverse variables on the Foresight Obesity System Map. Tools which assess eating and exercise self-efficacy, binge eating disorder, flexible cognitive restraint, disinhibition, and hunger were utilized to create additional cards. Participants completed semi-structured interviews and a focus group where they sorted through the deck, selected statements which described them, and discussed the activity. Interpretive description methodology was used to analyze data on participants' selection of cards and willingness to use the tool with a healthcare professional.

A total of 64 cards were created. Participants felt the cards did not provide any new information about obesity, but were helpful in organizing and prioritizing existing knowledge. Many participants found the exercise to be a positive experience as some of the card statements reminded them of positive behaviour changes they had made. Most felt that a discussion around the cards they chose would make for a more meaningful conversation with a healthcare provider. Finally, some participants worried that their family physician might not have time to engage in a discussion around obesity.

The cards helped individuals sort through the complexity of their condition, identify their most important variables, and identify potential changes they felt capable of making. Future work will evaluate the use of the tool by both patients and healthcare practitioners.

Corresponding author: tmerth@interchange.ubc.ca

THE VANCOUVER INTERNATIONAL MARATHON: AN ORGANIZED, ON-SITE MEDICAL RESPONSE AND SIX YEARS OF DATA (2006 – 2011)

Presenting Author(s): Justin Mui

Lund, A. (1), S.A. Turris (2), J. Mui (3), P. Wang (4), K. Lewis (1) and S.J. Gutman (1)

(1) Department of Emergency Medicine, University of British Columbia, B.C., Canada.
(2) School of Nursing, University of British Columbia, University of Victoria, B.C., Canada.
(3) Department of Medicine, Faculty of Medicine, University of British Columbia, B.C., Canada
(4) Faculty of Science, University of British Columbia, B.C., Canada

Mass participation events involve thousands of simultaneous participants and pose an increased risk of injury compared to similar populations in informal and non-crowd associated conditions. This study describes an organized, on-site medical response for marathon spectators and participants and report illness/injury rates as well as ambulance transfer rates at the Vancouver International Marathon. In total, 80,234 runners participated in the VIM from 2006-2011. Over the six-year period, 2986 patient encounters were documented on-site and categorized according to chief complaint. Musculoskeletal injuries were the most common medical complaint in five out of the six years, followed by dermatological injuries and medical dispensary requests. Ambulance transfer rates and medical transfer rates varied between 0.07 to 0.50 and 0.08 to 0.93 (rate per 1000 participants), respectively. Thorough pre-race education in conjunction with a coordinated on-site medical team may reduce the incidence of illness and injury for participants at a long distance running event. The provision of comprehensive, multi-disciplinary, on-site care may also reduce the burden on local community services such as emergency departments.

Corresponding author: justinmui0517@interchange.ubc.ca

THE INFLUENCE OF A NOVEL ARM AND LEG CYCLING REHABILITATION INTERVENTION ON POST-STROKE CLINICAL OUTCOMES: A PILOT STUDY

Presenting Author(s): Kulveer Parhar

Parhar, K.S. (1), T. Klarner (2,3) and P.E. Zehr (1,2,3)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) School of Exercise Science, Physical and Health Education, University of Victoria, BC, Canada
(3) Rehabilitation Neuroscience Laboratory, University of Victoria, B.C., Canada

Introduction: Stroke is the third leading cause of death and the leading cause of disability in Canada. With 50,000 strokes occurring each year and 300,000 Canadians living with its effects, stroke continues to place a heavy burden on the patient, their support network, and the healthcare system. By interrupting blood flow to the brain, a stroke causes neuronal damage affecting a number of brain areas resulting in motor, sensory, language, and cognitive deficits. Rehabilitation following stroke can help patients achieve the most optimal function and long-term independence. Motor training interventions take advantage of the central nervous system's plasticity ultimately leading to neuromuscular adaptations. Direct walking training poses a challenge for most stroke patients; however, rhythmic arm and leg cycling has been shown to engage some of the same motor pathways as walking and serves as a safe and feasible alternative.
Purpose: To determine whether an indirect training paradigm involving arm and leg cycling leads to positive modifications in neuronal networks and locomotor capacity following stroke.
Methods:
Participants: Three male, low to moderate functioning stroke patients (ages 47-75).
Intervention: Continuous training on the SCIFIT® arm and leg cycling machine for thirty minutes, three times a week for six weeks.
Measurements: Pre and post assessments of motor function and reflexes. Heart rate, Rating of Perceived Exertion (RPE) and cadence were recorded at five minute intervals throughout each thirty minute training session.
Results: Strength and walking function improved following the training intervention. For all three participants, both ipsilateral and contralateral plantarflexion strength increased. All participants showed an increased range of motion particularly at the ankle joint leading to a more normalized walking pattern. There were improvements in some clinical measures such as the 10m and 6 min walk test. For two participants, stretch reflexes decreased and Tardieu and Ashworth's scores improved.
Conclusion: This pilot study demonstrated that the human neuromuscular system is amenable to an arm and leg cycling training intervention. Spasticity, a limiting factor to optimal motor function, was indirectly shown to decrease through decreased stretch reflexes, increased range of motion of the lower limb joints, and improved clinical scores.

Corresponding author: kulveer@interchange.ubc.ca

CELLULAR RESPONSES TO SPINAL CORD INJURY IN THE DORSAL ROOT GANGLION

Presenting Author(s): Adrian van Stolk

Ramer, L.M. (1,2), A.P. van Stolk (1,5), J.A. Inskip (1,2), M.S. Ramer (1,2), J.D. Steeves (1) and A.V. Krassioukov (1,3,4)

(1) ICORD (International Collaboration on Repair Discoveries), University of British Columbia, B.C., Canada
(2) Department of Zoology, University of British Columbia, B.C., Canada
(3) GF Strong Rehabilitation Centre, B.C., Canada
(4) Department of Medicine, Faculty of Medicine, University of British Columbia, B.C., Canada
(5) Faculty of Medicine, University of British Columbia, B.C., Canada

Introduction: Sensory and autonomic dysfunction following spinal cord injury (SCI) have been attributed in part to aberrant growth of sensory axons within the central nervous system. Comparatively little is known about injury-induced changes in the attached ganglia. These studies characterize neuronal plasticity and glial reactivity in the dorsal root ganglion (DRG) following high-thoracic SCI.

Methods: Adult Wistar rats received a complete transection of the spinal cord at the third thoracic segment (T3), and survived for one, four, or twelve weeks following SCI. Dorsal root ganglia (DRGs) rostral (T1), caudal (T5, T10), and far distal (L1-S1) to SCI were harvested and analyzed immunohistochemically.

Results: Tyrosine hydroxylase (TH)-expressing sympathetic ganglionic axons invaded the rat DRG within one month of SCI. The density of TH-expressing axons in the DRGs rostral (T1) and distal (L4-5) to SCI was significantly increased at one month after SCI. Several phenotypic markers were used to characterize the primary afferent response to SCI. Of all populations examined, only TRPV1+ nociceptors in distal DRGs exhibited hypertrophy following SCI. Nociceptor hypertrophy was accompanied by increases in inflammation, indicated by increased density of ED2-positive macrophages following SCI.

Conclusion: Injury-induced changes in the DRG have the potential to effect neuronal hyper-responsiveness or ectopic activity following SCI. Thus, abnormal sensory activity following SCI may not be due solely to spinal plasticity, but may originate in the peripheral nervous system.

Corresponding author: pvs3000@interchange.ubc.ca

AN ADAPTATION STUDY OF INTERNAL AND EXTERNAL FEATURES IN FACE REPRESENTATIONS

Presenting Author(s): Kali Romano

Romano, K., C. Hills, J. Davies-Thompson and J.S. Barton

Department of Neuro-Ophthalmology, University of British Columbia, B.C., Canada

Background: Previous studies have shown observers rely more on internal than external features when recognising familiar but not unfamiliar faces.

Objective: We used an adaptation paradigm to examine whether this difference in internal and external feature contributions to processing is also reflected in differences in the representations of these two classes of faces in the human visual system.

Methods: Twelve subjects adapted to a) whole faces, b) internal features alone, or c) external features alone for 5sec, and were then asked whether a briefly shown ambiguous whole-face most resembled the first or second person. Ambiguous faces were created by morphing between pairs of faces. One set of blocks used four pairs of celebrities, while the other used four pairs of anonymous faces.

Results: We replicated the finding of face-identity aftereffects with whole face adaptors, with equivalent magnitude for both familiar and unfamiliar faces. For unfamiliar faces, adaptation to internal features alone and to external features alone also generated face aftereffects in whole-face test images, which were similar in magnitude but less than that from whole-face adaptors. However, for familiar faces, identity aftereffects were produced only by whole-face adaptors and not by internal or external features in isolation.

Conclusion: Internal and external features are equivalent in perceptual representations of unfamiliar faces. Familiar faces require the whole-face context for access to their representations, which may reflect another characteristic of holistic mechanisms in face processing.

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Corresponding author: kaliromano@gmail.com

WIRELESS MOTE TECHNOLOGY: APPLICATION, TECHNOLOGY AND FUNCTIONALITY

Presenting Author(s): M. Michiko Maruyama

Schlegel, C. (1), V. Gaudet (2), B. Cockburn (2), D. Truhachev (2) and M. Maruyama (3,4)

(1) Department of Computing Science, University of Alberta, A.B., Canada
(2) Department of Electrical Engineering, University of Alberta, A.B., Canada
(3) Department of Medicine, Faculty of Medicine, University of British Columbia, B.C., Canada
(4) Department of Industrial Design, University of Alberta, A.B., Canada

The High Capacity Digital Communications (HCDC) Group is part of a winning Alberta Heritage Foundation for Medical Research (AHFMR) Team grant in the area of neural prosthetics. The goal of the neuroprosthesis project is "to develop more sophisticated neural prostheses for the treatment of individuals with damage to the nervous system. These include devices that tap into small regions of the spinal cord and brain to activate the groups of nerve cells that regulate walking, touch, pressure, movement, temperature, and pain. Improved neural prostheses will provide personalized medicine to some of the most vulnerable people living with disabilities, restoring function to people with irreparably damaged nervous systems, increasing their independence in daily living and their ability to function in society and the workforce."

The HCDC group will address wireless telemetry with implanted neural stimulators as part of this AHFMR grant. Mobile ad-hoc or mesh networks (MANETs), are self-configuring networks of mobile devices connected by wireless links. Nodes can generate, use, or relay data as required by applications such as monitoring, data communications, surveillance or racking. Such wireless nodes are often called MOTES. These MOTES will eventually be the size of a grain of rice and have self-contained sensing, computation, communication and power.

In all wireless channels the main concern is the power budget from transmitter to receiver, called the link budget. In the link budget we find the transmission loss – usually the largest component – antenna gains, signaling efficiency, implementation losses and the noise power impinging on the receiver. The HCDC Team is working to develop ultra-low power embedded recording systems to integrate into the implantable devices. Apart from inherent limitations on power supplied to miniature transceivers, the information carrying capacity of *ad hoc* networks is severely limited by laws of physics. This requires the design of both extremely power-efficient circuits, as well as highly developed transmission systems -- receivers, signaling methods, and access protocols -- to harness the available capacities. HCDC's specific designs, the random-packet code-division multiple access methodology, is now being ported into FPGA and VLSI test platforms which will verify theoretical claims.

Corresponding author: michiko.maruyama@gmail.com

THE REMODELING OF THE SMALL CONDUCTING AIRWAYS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Presenting Author(s): Nazgol Seyednejad

Seyednejad, N., A. Lam, J.E. McDonough, A. Behzad, F. Chu, J.C. Hogg and D. C. Walker

Faculty of Medicine, University of British Columbia, B.C., Canada

Introduction: Chronic obstructive pulmonary disease (COPD) is defined as an increase in resistance in the small conducting airways and/or an emphysematous destruction of the elastic recoil responsible for driving air from the lungs. Thickening of the small airway walls leading to the progression of COPD is believed to result through remodeling. The epithelial mesenchymal trophic unit (EMTU) is believed to play a role in this remodeling. The EMTU consists of the airway epithelium, basal lamina, subtending fibroblasts, and extracellular matrix (ECM). In this study we used ultrastructural morphometric analysis to determine whether there are significant changes in the epithelial lamnia propria (EMTU) with the progression of COPD.

Methods: The samples of this study were obtained from five controls (smokers with normal lung function), five persons with mild (GOLD-1) and four with moderate (GOLD-2) COPD. 50 mm3 pieces of lung parenchyma were harvested, airways < 2mm diameter were excised and processed for standard transmission electron microscopy (TEM). Images of the airway lamina propria were selected in a standardized random fashion for analysis. From these images quantitative estimates of the ECM abundance (volume fractions of collagen, elastin, cells, space) and collagen fibril diameters (Type-I vs. Type-III) were made. In addition morphometric analysis of the fibroblast reticulum in the lamina propria was performed to detect any changes in its complexity.

Results: The volume fractions of the ECM components within the lamina propria of the small airways does not appear to have begun to significantly change in mild and moderate forms of COPD when compared to control patients. Neither collagen fibril diameters within the lamina propria, nor the degree of fibroblast reticulum interconnection change significantly between controls, mild and moderate forms of COPD.

Conclusions: Previously we have shown that epithelial-fibroblast contacts are significantly reduced in mild and moderate COPD lung conducting small airways (Behzad) when compared to controls. However, there do not appear to be any significant changes evident in the organization of basement membrane fibroblasts or in the organization of cellular and extracellular matrix elements within the lamina propria of small conducting airways.

Corresponding author: nazgols@interchange.ubc.ca

PU.1 AND SPI-B FUNCTION AS TUMOR SUPPRESSORS IN THE DEVELOPMENT OF PRE-B CELL ACUTE LYMPHOBLASTIC LEUKEMIA BY REGULATING TRANSCRIPTION OF B-CELL LINKER PROTEIN

Presenting Author(s): Kristen Sokalski

Sokalski, K.M. (1), K. Hotke (2) and R.P. DeKoter (2)

(1) Department of Medicine, University of British Columbia, B.C., Canada
(2) Department of Microbiology & Immunology, niversity of Western Ontario, O.N., Canada

Transcriptional regulation is critical during hematopoiesis as it ensures proper gene expression in a sequential manner. PU.1 is a transcription factor that belongs to the ETS-transcription factor family and acts redundantly with Spi-B in B-lymphocyte differentiation. When both PU.1 and Spi-B are knocked out in *CD19*$^{cre/+}$*Sfpi1*$^{lox/lox}$*Spib*$^{-/-}$ mice, the mice develop pre-B cell acute lymphoblastic leukemia (pre-B ALL). The purpose of this study was to identify gene(s) that function as tumour suppressors downstream of PU.1 and/or Spi-B. Using reverse transcriptase-quantitative polymerase chain reaction on splenocytes and leukemic cells from a *CD19*$^{cre/+}$*Sfpi1*$^{lox/lox}$*Spib*$^{-/-}$ mouse, B cell linker protein (BLNK) was identified as a candidate tumour suppressor gene as it showed the highest significant reduction in expression. BLNK is an adaptor protein involved in signalling from the B-cell receptor and is a known tumour suppressor in human pre-B ALL. Using bioinformatics, four possible ETS-binding sites were identified in the *Blnk* promoter that are conserved phylogenetically. One ETS-binding site was of particular interest as it showed the highest *matrix similarity value*. A luciferase reporter assay was used to asses *Blnk* promoter activity and it was determined that the *Blnk* promoter displayed directionality. When a point mutation was made to the ETS-binding site of interest, activity from the *Blnk* promoter was decreased by 8-fold. Finally, a retrovirus encoding the wild-type BLNK protein and green fluorescent protein (GFP) as a marker was constructed. Pre-B ALL cells were cultured in interleukin-7 and then infected with the BLNK retrovirus. Following infection, the pre-B ALL cells showed a reduction in proliferation as the relative frequency of GFP positive cells decreased upon serial passage. These findings demonstrate that PU.1 and Spi-B act as tumour suppressors in developing B cells at least in part by activating the transcription of *Blnk*.

Corresponding author: ksokals@interchange.ubc.ca

IS "OLD AGE" A JUSTIFIABLE REASON FOR WITHHOLDING CURATIVE CANCER SURGERY FROM ELDERLY SARCOMA PATIENTS?

Presenting Author(s): Diana Song

Song, D. (1), P. Clarkson (2,3), A. Phillips (2,3) and B. Masri (2,3)

(1) Department of Medicine, University of British Columbia, B.C., Canada
(2) Department of Orthopedics, Faculty of Medicine, University of British Columbia, B.C., Canada
(3) B.C. Cancer Agency, B.C., Canada

Sarcomas affect patients in all age groups but are more common in the elderly. As the population ages, the management of elderly sarcoma patients becomes increasingly challenging. Curative treatment for this type of cancer almost always includes surgical intervention. However, it has been suggested that palliative options be employed in the elderly due to their perceived poor outcomes and difficulty recovering from surgery. Some also believe that surgery itself negatively impact the functional outcomes so significantly in this subpopulation that surgery is not warranted.

Based on previous literature on surgery outcomes in the adult population, there is insufficient evidence to suggest that advanced age is a factor for poor outcomes following surgery. Despite this lack of evidence, treatment decisions are sometimes made based on age. The Vancouver Sarcoma Surgical Tumor Group has not used age as a factor in determining treatment strategy, rather relying on overall health status. We hypothesize that age itself is not an independent predictor of poor outcomes and that elderly patients (>75 years old) will benefit from aggressive surgical treatment with curative intent. Using the orthopaedic oncology clinical database, we identified 181 subjects over the age of 75 years at the time of diagnosis of bone or soft tissue sarcoma seen in a 10 year period. A retrospective chart review was done. The data collected included multiple indicators of physiological and functional outcomes.

Sixty-nine percent of patients over 75 years of age who were seen at the BC Cancer Agency received aggressive cancer surgery with curative intent. Of these patients, 70% had no evidence of cancer on the latest follow up. The majority of the patients who received definitive surgery were living independently at the time of their diagnosis and nearly all of these patients (93%) resumed independent living post-operatively. Elderly patients performed high in all of the areas measuring regain of function post-operatively. The results support our hypothesis that elderly patients receive much benefit from aggressive curative treatment and age alone is not a valid reason for withholding the appropriate surgical intervention.

Corresponding author: sdiana.ubc@gmail.com

INFLUENCE OF SUNSCREENS ON SKIN WATER BARRIER FUNCTION

Presenting Author(s): Bahman Sotoodian

Sotoodian, B. (1) and H.I. Maibach (2)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) Department of Dermatology, University of California Medical School, CA, USA

The crucial role of sunscreen (SS) in providing protection against harmful UVA and UVB radiations has been extensively investigated. However, the sole influence of SS on skin barrier function has not been studied. This experiment studied the influence of four major SS on transepidermal water loss (TEWL). SS with their unique excipients did not cause any statistically significant ($p>0.05$) influence on epidermal barrier function; however, transitory increase in TEWL measurements after applying SS were observed. The skin barrier deterioration as a result of applied SS could have caused the observed phenomena. Further studies with greater selections of SS with unique physicochemical properties would provide more insights into the nature of SS and their direct influence on skin barrier function. Our findings support the widely accepted but not fully investigated notion that SS have minimal affect on skin barrier function.

Corresponding author: bahman.sotoodian@gmail.com

ANALYSIS OF MITOCHONDRIAL DNA MUTATIONS IN PATIENT SAMPLES SUSPECTED OF HAVING MULTIGENERATIONAL MITOCHONDRIAL DISEASE

Presenting Author(s): Andrea Tam

Tam, A. (1), M. Sharma (2), J. Lee (2), B. Sattha (2), H. Côté (2) and A. Mattman (3)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) Department of Pathology and Labratory Medicine, Faculty of Medicine, University of British Columbia, B.C., Canada
(3) B.C. Children's Hospital Department of Pathology, B.C., Canada

Background: Mutations and deletions in the mitochondrial DNA (mtDNA) are major causes of mitochondrial dysfunction. Some mtDNA mutations can develop with age and oxidative stress, other mtDNA defects can be maternally inherited.

In this study, we analyzed muscle biopsies from two unrelated patients suspected of having multigenerational mitochondrial disease characterized by fatigue, myopathy and decreased mitochondrial complex IV activity. Routine mtDNA tests failed to identify any defect that could explain their disease. Thus, we investigated the muscle and blood samples for mutations or rearrangements in the mtDNA.

Methods: DNA was extracted from quadriceps muscle samples. The amount of mtDNA relative to nuclear DNA (mtDNA/nDNA ratio) was determined by quantitative PCR. Large rearrangements were qualitatively analyzed by long PCR on the mtDNA followed by agarose gel electrophoresis. Finally, point mutations or small rearrangements on the mtDNA were studied by sequencing the long PCR products. The same experiments were carried out on the blood samples.

Results: The first sample studied (pt1) showed no mtDNA alteration. However, the second sample (pt2) had low mtDNA/nDNA ratio (1505) compared to pt1 (3198) or to controls (mean ± SD; 3088 ± 1543). The long PCR from pt2 showed a ~4 kb mtDNA deletion affecting a small percentage (~10%) of the mtDNA. Also, a potentially clinically relevant insertion at position nt194 within the non-coding regulatory D loop region was present in 35-40% of the mtDNA extracted from muscle of pt2. Preliminary analysis of blood samples from pt2 and one sibling showed no signs of this mutation.

Conclusion: The insertion seen in pt2's muscle derived- mtDNA is very close to the origin of replication and may affect mtDNA replication and/or transcription. This finding is consistent with the low levels of mtDNA found in pt2's muscle biopsy. Surprisingly, the mtDNA insertion was not found in pt2's blood. However, it is common to detect mitochondrial DNA mutations only in the skeletal muscle. Current work includes determining the rate of heteroplasmy of the nt194 insertion. The identification and characterization of a disease causing mutation would clarify the diagnosis and thus be of benefit to the families.

Corresponding author: andreawingkwantam@gmail.com

REDUCED INCIDENCE OF EARLY INVASIVE FUNGAL INFECTIONS IN ALLOGENIC TRANSPLANT PATIENTS FOLLOWING MICAFUNGIN PROPHYLAXIS

Presenting Author(s): Derek To

To, D.C. (1), D. Warkentin (2), R. Broady (3) and M. Power (3)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) CSU Pharmaceutical Sciences, Vancouver Coastal Health, B.C., Canada
(3) Leukemia/Bone Marrow Transplant Program, B.C. Cancer Agency, B.C., Canada

Introduction: Invasive fungal infection (IFI) is a significant cause of morbidity in allogeneic stem cell transplant (HSCT) patients. The incidence of IFI in our HSCT patients using low dose amphotercin B (LDAB) (10mg/m2) during the neutropenic phase is 20%. This study was performed to determine whether an alteration in prophylaxis was effective in reducing the incidence of IFI. We also aimed to identify risk factors for IFI.
Methods: We performed a retrospective analysis of the 67 patients undergoing HSCT between January 2010 and June 2011 and compared the incidence and risk factors for IFI (EORTC criteria) to our historical controls (n=69). Patients with a prior history of IFI were excluded. Inpatients undergoing myeloablative or unrelated donor non-myeloablative transplantation received micafungin 100mg daily. Prophylaxis began on day +1 and was continued until absolute neutrophil count >0.5 X 10^9/L.
Results: There was a slight decrease in the incidence of IFI (10/67;15%), with 5% proven/probable and 10% possible IFI. The median time to diagnosis of IFI was 78 days. One patient developed an IFI during the first 30 days post HSCT (10%), three patients between days 30 and 100 (30%) and six patients developed an IFI after day 100 (60%). 50% (5/10) of patients who developed an IFI have died compared to 9% of the patients in the no IFI group (5/57). Mortality due to IFI was 30% in the IFI group. A significant risk factor for developing an IFI was steroid refractory graft versus host disease (GVHD) with an incidence of 56% (5/9) compared to 7% in patients with GVHD who did not require second line therapy($p<0.01$).
Conclusion: We show a reduction in early IFI in those receiving micafungin prophylaxis possibly due to a reduction in the rate of early (< day +30) IFIs. Late IFI remains a problem and patients with steroid refractory GVHD have a higher risk of developing an IFI. The significant mortality due to IFI in HSCT patients dictates that a prophylactic approach should be adopted for high risk patients.

Corresponding author: derekto@interchange.ubc.ca

WORKING PAPER: DISSOCIATION OF SUBJECTIVE AND OBJECTIVE HEALTH STATUS IN THE CHINESE POPULATION

Presenting Author(s): Sian Tsuei

Tsuei, S.H.T. (1) and A. Sen (2)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) Department of Economics, University of Waterloo, O.N., Canada

Background: Obesity is becoming a more recognized global health problem. In developed nations, higher socioeconomic status (SES) has been shown as a positive determinant of health, and as the general Chinese population becomes more overweight, pressure mounts to explore if the Chinese have an accurate perception of their own health status and if health education is a suitable intervention for addressing the increasing obesity prevalence.
Method: Four waves of the Chinese Health and Nutrition Survey (CHNS) are pooled into two groups—2004 with 2006 and 1997 with 2000. Two multilinear regressions were performed using Stata. The first regression uses the perceived health status and the objective health status—such as being overweight, diabetic, or hypertensive—as the dependent variables. The independent variable included the SES—defined as a combination of education and income—and supplementary independent variables such as gender, age, insurance coverage, year of the survey and urban livelihood. The second regression uses the SES as the dependent variable. The different health lifestyle knowledge and health habits are set as the main independent variables with the same supplementary variables.
Results: The first regression showed that the SES and being male are positively correlated with *perceived* health status, but also correlated with higher likelihood of being overweight, diabetic, or hypertensive. Contrary to previous theories, in the Chinese population, higher SES is also generally positively correlated with better health lifestyle knowledge, and negatively correlated with daily consumption of alcohol and cigarette consumption.
Conclusions: The negative correlation between higher SES and health may be due to increased opportunity cost of time, such that the higher the SES an individual has, the less likely the individual will be healthy. We also advance that individuals may perceive their health status based on acquiring status valued by society, which may not accurately represent their objective health status. We find no evidence to support the idea that individuals with higher SES consume more sin goods such as alcohol and tobacco. Additional research needs to address underlying mechanisms for the increasing obesity prevalence in Chinese.

Corresponding author: sian.tsuei@gmail.com

PROTON BLOCK OF THE PORE UNDERLIES THE LOSS OF HERG CHANNEL CONDUCTANCE DURING ACIDOSIS

Presenting Author(s): Aaron Van Slyke

Van Slyke, A.C., Y.M. Cheng, M. Pouya, C.R. Allard, C. Hull, P. Shi andT.W. Claydon

Department of Biomedical Physiology and Kinesiology, Simon Fraser University, B.C., Canada.

The human ether-a-go-go related gene (hERG) encodes the cardiac potassium channel underlying the delayed rectifier current, I_{Kr}, in the heart. Previous reports have demonstrated that extracellular acidosis inhibits hERG channel maximal conductance, yet the site and mechanism of action is unclear. In other voltage-gated potassium channels, proton inhibition is due to titration of histidine residues and a subsequent stabilization of inactivated states. Here, we have demonstrated that histidines are not the pH sensor in hERG channels. Instead, the reduction in maximal conductance observed at low pH_o is due to proton block of the pore. Several observations support this. First, proton inhibition was voltage dependent, with protons experiencing approximately 20% of the electric field ($\delta = 0.18$, as predicted by the Woodhull model). Second, proton block was relieved by potassium occupancy of the pore in the presence of external sodium, with a Kd of 0.96 mM. Third, acidic pH_o reduced the apparent single channel current amplitude by approximately 35% ($p = 0.001$). Finally, introduction of negative charges within the conducting pathway alter proton binding. Taken together, these data strongly suggest that extracellular protons inhibit hERG maximal conductance by directly blocking the outer pore.

Corresponding author: vanslyke@interchange.ubc.ca

MULTIPLE PATHOLOGIES ARE COMMON IN ALZHEIMER PATIENTS IN CLINICAL TRIALS

Presenting Author(s): Bing Wei Wang

Wang, B.W. (1), E. Lu (1), I.R.A. Mackenzie (2), M. Assaly (1), C. Jacova (1), P.E. Lee (1), B.L. Beattie (1) and G.Y.R. Hsiung (1)

(1) Department of Medicine (Neurology), University of British Columbia, B.C., Canada
(2) Department of Pathology and Laboratory Medicine, Faculty of Medicine, University of British Columbia, B.C., Canada

OBJECTIVE: To determine the frequency of multiple pathology [Alzheimer Disease (AD) plus Vascular Dementia and/or Dementia with Lewy Bodies] in patients enrolled in clinical trials of AD therapy, and to compare the cognitive and functional assessments between patients with pure AD and AD with multiple pathology.
METHODS: We conducted a retrospective analysis of patients with clinical diagnosis of AD who were enrolled in AD therapy clinical trials and subsequently received an autopsy for confirmation of their diagnosis from 2000 to 2009. Performance on cognitive screening tests, namely Modified Mini Mental State (3MS) exam, Mini Mental State Exam (MMSE) and Functional Rating Scale (FRS) were compared between patients with pure AD and multiple pathology.
RESULTS: Autopsy reports were available for 16/47 (34%) of deceased patients. Of these 16 patients, 5 (31%) had pure AD pathology, 10 (63%) had AD with other pathology, and 1 (6%) had non-AD pathology. Compared to patients with pure AD, patients with AD mixed with other pathology had poorer baseline FRS in problem-solving ($p<0.01$) and community affairs ($p<0.02$).
CONCLUSION: While the strict enrollment criteria for clinical trials identified the presence of AD pathology in the majority of cases (15/16), multiple pathology was more common than pure AD in our series of autopsied patients. Premortem biomarkers that can distinguish between pure AD and AD with multiple pathology will be beneficial in future clinical trials and dementia patient management.

Corresponding author: bweiwang@gmail.com

THE UTILIZATION AND IMPACT OF CORE BIOPSY DIAGNOSIS ON OUTCOMES FOR PATIENTS WITH BREAST CANCER

Presenting Author(s): Kristy Cho

Wilson, C.M. (1,2), S.K. Tyldesley (2) and K.K. Cho (3)

(1) Department of Medical Imaging, B.C. Cancer Agency, B.C., Canada
(2) Department of Radiation Oncology, B.C. Cancer Agency, B.C., Canada
(3) Department of Medicine, Faculty of Medicine, University of British Columbia, B.C., Canada

Purpose: To determine: 1) the proportion of women in British Columbia who have an image guided preoperative diagnosis of breast cancer; 2) whether women who have a preoperative radiologic diagnosis of breast cancer have less breast surgeries as part of their initial therapy; 3) whether local relapse is lower in women who have had a pre-operative diagnosis of breast cancer; 4) whether there is regional variation in the use of preoperative image guided diagnosis of breast cancer in BC.
Methods: All women diagnosed with breast cancer in 2006 were reviewed. The women are divided into two groups - those who have had a tissue diagnosis via image guided core biopsy prior to surgery and those who have had fine wire localization on the day of surgery, without a preoperative tissue diagnosis. Women with cancer metastasis, previous cancer within 6 months of diagnosis and locally advanced disease were excluded.
Results: 3130 patients and 8424 breast procedures from 2006 were recorded initially. After taking in account of the exclusion criteria, 2634 patients remain included in the study. The project is currently a work in progress.
Conclusions: This analysis will provide population based information on the prevalence of preoperative image guided diagnosis of breast cancer and its impact on outcomes.

Corresponding author: kristych@interchange.ubc.ca

TREATMENT PROTOCOL AND OUTCOMES FOR FRONTAL SINUS POSTERIOR WALL FRACTURES: A REVIEW OF INPATIENTS 1999-2009 AT VANCOUVER GENERAL HOSPITAL

Presenting Author(s): Nathan Wong

Wong, N.C. (1) and K. Bush (2)

(1) Department of Medicine, University of British Columbia, B.C., Canada
(2) Department of Surgery, Faculty of Medicine, University of British Columbia, B.C., Canada

Background: Appropriate management of frontal sinus posterior wall fractures remains controversial due to lack of statistical data and difficulty with measuring long-term outcomes. Nasofrontal outflow tract (NFOT) involvement and obstruction have been previously described as important indicators for surgical management. In this retrospective study, we review the incidence, etiology, and treatment patterns of patients with frontal sinus posterior wall fractures.
Methods: A retrospective review of patients with frontal sinus posterior wall fractures admitted between 1999 and 2009 at Vancouver General Hospital was conducted. Using hospital database, frontal sinus posterior wall fractures were identified in 96 patients. Hospital records and preoperative CT scans were reviewed. Radiographic evidence of NFOT involvement included: NFOT obstruction, frontal sinus floor fracture and/or anterior ethmoid cell fracture.
Results: The average age of patients was 41 and 85.4% were males. The most common mechanism of injury was falls followed by motor vehicle accidents. 65 patients were managed conservatively and 31 underwent surgery. There were 14 major complications with CSF leaks (50%) being most common.

NFOT involvement was found in 93.8% of patients. In patients without NFOT involvement, all were treated conservatively and there were no complications.

Of patients with NFOT involvement, 33.3 % had NFOT obstruction (1 of the 3 criteria for NFOT involvement). The complication rate of patients with NFOT obstruction (26.7%) was 2 times greater than without obstruction (10.0%). In patients without obstruction, there were similar complication rates between patients managed conservatively (9.8%) and operatively (11.1%). Similarly, in patients with NFOT obstruction, there were similar complication rates between patients managed conservatively (25%) and operatively (27.2%).
Conclusions: Patients without NFOT involvement may be safely managed conservatively. Since NFOT obstruction had a higher complication rate, these patients should be monitored more closely for complications. However, with or without obstruction, there were similar complication rates between patients managed conservatively and operatively. According to our findings, CT findings of NFOT obstruction should not play a significant role in the management of frontal sinus posterior wall fractures and a larger subset of patients should be managed conservatively.

Corresponding author: n8cwong@gmail.com

EXPRESSION OF SURFACTANT PROTEINS A AND D IN THE AIRWAY EPITHELIUM AND THE ROLE OF CONJUGATED LINOLEIC ACID IN MODULATING RESPIRATORY SYNCYTIAL VIRUS INFECTION

Presenting Author(s): Janet Xu

Xu, J. (1), G.K. Singhera (1) and D.R. Dorscheid (1,2)

(1) James Hogg Research Centre, Institute for Heart + Lung Health, St. Paul's Hospital, University of British Columbia, B.C., Canada
(2) Department of Medicine, Faculty of Medicine, University of British Columbia, B.C., Canada

Background: Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract infections and has been linked to the etiology of asthma. Surfactant proteins A and D (SP-A and SP-D) are pattern recognition molecules which regulate innate immune cell function and participate in host defense. SP-A and SP-D are involved in the clearance of RSV from the airways. Conjugated linoleic acid (CLA) is a free fatty acid which has been associated with diverse biological properties. Our lab previously demonstrated that CLA treatment reduces hyper-reactivity in asthmatic airways and viral-induced inflammation in cultured airway epithelial cells.
Hypothesis: We hypothesize that SP-A and SP-D are expressed differently in the airway epithelium of asthmatic and non-asthmatics and CLA pretreatment prior to RSV infection would affect the expression of SP-A and SP-D.
Methods: Sections from human airways and differentiated air-liquid interface (ALI) cell cultures grown from primary airway epithelial cells (AEC) were used. SP-A and SP-D expression were characterized in the asthmatic and non-asthmatic airway sections by immunohistochemistry. Quantification was performed using color segmentation via ImagePro Plus. Expression of SP-D in response to RSV infection, CLA treatment, or CLA pretreatment followed by RSV infection was examined in ALI cultures of non-asthmatic AEC.
Results: SP-A and SP-D molecules were expressed in human airway sections from asthmatic and non-asthmatic donors. SP-A expression was low and localized mainly to small airways, whereas SP-D was highly expressed and detected in airways of different sizes. SP-A expression in small airways (< 1 mm) was found to be 150% higher ($p=0.018$) in asthmatic airways compared to non-asthmatic airways. SP-D expression was found to be 33% higher ($p=0.004$) in asthmatic airways. In the ALI cultures, RSV infection induced a marked reduction in SP-D expression. However, a 3.8 fold increase ($p= 0.05$) in SP-D expression was observed in cultures pre-treated with CLA prior to RSV infection as compared to RSV infection alone.
Conclusion: Surfactant proteins may be involved in modulating innate immune responses in the airway epithelium. The higher SP-D levels detected in the asthmatic airway may reflect an increased susceptibility to viral infections or dysfunctional SP-D expression or function.

Corresponding author: janet.xu@hli.ubc.ca

HYPERCALCEMIA AFTER KIDNEY TRANSPLANTATION AS PREDICTOR FOR PATIENT AND GRAFT OUTCOMES

Presenting Author(s): Howard Yan

Yan, H. (1), E.H. Cole (2), C. Rose (3), J. Dong (3) and J.S. Gill (3)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) Division of Nephrology, Department of Medicine, Faculty of Medicine, University of Toronto, ON, Canada
(3) Division of Nephrology, Department of Medicine, Faculty of Medicine, University of British Columbia, B.C., Canada

Demand for kidney transplantation greatly exceeds the supply of transplantable organs. Patients with end-stage kidney disease typically wait 5-8 years on dialysis for transplants, and develop chronic uremic complications that can limit the health benefits of transplantation, including tertiary hyperparathyroidism and hypercalcemia. However, little is known about the natural history of these latter complications. This study aimed to determine the incidence, risk factors and consequences of hypercalcemia in kidney transplant patients.

We conducted a retrospective study of n=1352 adult kidney-only transplant recipients in Toronto General Hospital and St. Paul's Hospital, Vancouver between January 2000 and August 2007. Research datasets were constructed from electronic data banks from both hospitals that contain all laboratory investigation results used to support patient management and key clinical outcomes including allograft and patient survival.

In the first post-transplant year, a striking 40% of patients developed at least one episode of hypercalcemia (defined as serum calcium ≥2.6 mmol/l), and 12% of patients had mean serum calcium ≥2.6 mmol/l (post-transplant hypercalcemia). Post-transplant hypercalcemia resolved in 25%, 36%, and 54% of patients by 2, 3, 5 years post-transplant, respectively, with n=21 patients requiring surgical parathyroidectomy.

In a multivariate logistic regression model, the follow factors were associated with development of post-transplant hypercalcemia: older age; high pre-transplant serum calcium (OR 5.77 (3.17-10.49) for >2.6 compared to ≤2.6 mmol/l); elevated pre-transplant parathyroid hormone (iPTH) (OR 4.11 (1.69-10.00), 11.18 (4.60-27.18) for iPTH 10.6-53, >53, respectively, compared to <10.6 pmol/l); and pre-transplant dialysis duration >5 years.

In Cox multivariate regression analysis, increased allograft failure was not associated with post-transplant hypercalcemia, but was associated with elevated pre-transplant iPTH (HR 1.80 (1.05-3.61) for iPTH >53 compared to <10.6 pmol/l). Post-transplant iPTH values are not obtained in routine clinical practice and were not available for analysis.

We conclude that hypercalcemia is a common post-transplant complication that can be predicted by pre-transplant clinical and laboratory data. Derangements of bone mineral metabolism are associated with an increased risk of allograft failure and are not directly dependent on development of hypercalcemia. Prevention and treatment of hyperparathyroidism may be an important strategy to improve transplant outcomes and further studies are warranted.

Corresponding author: akhaian@gmail.com

DOES OPTIC NERVE SHEATH DIAMETER ON MRI DECREASE WITH CLINICALLY IMPROVED PEDIATRIC HYDROCEPHALUS?

Presenting Author(s): Michael Yang

Yang, M.M., A. Singhal and D.D. Cochrane

Department of Surgery, University of British Columbia and B.C. Children's Hospital, B.C., Canada

Introduction: Serial change in ventricular size is recognized as an imperfect indicator of ongoing hydrocephalus in children. Potentially, other radiographic features may be useful in determining the success of hydrocephalus interventions. In this study, optic nerve sheath diameter (ONSD), optic nerve tortuosity and optic disk bulging were assessed as indicators of hydrocephalus control in children who underwent endoscopic third ventriculostomy (ETV) or posterior fossa tumor resection.

Methods: Thirty-seven children underwent ETV or tumor resection for treatment of hydrocephalus. T2-weighted axial magnetic resonance (MR) images of the orbit were obtained and the ONSD was measured posterior to the optic globe, pre- and post-intervention. Evidence of optic disk bulging and optic nerve tortuosity were also assessed. Ventricular size was estimated using the frontal and occipital horn ratio (FOR).

Results: There was significant reduction in the ONSD post ETV (n=19) and after tumor resection (n=18). Average pre-operative ONSD was 6.42mm versus 5.73mm post-operatively ($p<0.0001$). There was also a 90% ($p<0.0001$) and 61% ($p=0.005$) reduction in optic disk bulging and tortuosity, respectively. The magnitude of ONSD reduction was similar in both groups. Conversely, the FOR normalized in the tumor resection group but not the ETV group. After intervention, all patients showed improvement in signs and symptoms of hydrocephalus.

Conclusion: In our study population, ONSD decreased in response to measures to reduce hydrocephalus. Optic disk bulging and optic nerve tortuosity also appear to resolve. Serial reduction in ONSD, optic disk bulging and optic nerve tortuosity may be indicators of improved hydrocephalus following pediatric neurosurgical interventions.

Corresponding author: yangmh@interchange.ubc.ca

THE NEGATIVE PREDICTIVE VALUE OF SONOGRAPHICALLY-GUIDED 14-GAUGE CORE NEEDLE BIOPSY OF BREAST MASSES

Presenting Author(s): Charlie Zhang

Zhang, C. (1), D. Lewis (2), P. Nasute (2), L.J. Warren (2,3) and P.B. Gordon (2,3)

(1) Faculty of Medicine, University of British Columbia, B.C., Canada
(2) Vancouver Breast Center, B.C., Canada
(3) Department of Radiology, University of British Columbia, B.C., Canada

Background and Purpose
Percutaneous image-guided core needle biopsy (CNB) is currently the standard of care for the initial diagnosis of suspicious breast lesions. It is less invasive, less time-consuming and less expensive than surgical excision, and causes minimal to no scarring. We aim to determine the negative predictive value (NPV) of sonographically-guided 14-gauge CNB of breast masses, with detailed analysis of any false negative cases.

Materials and Methods
All patients who have had benign pathologic findings on sonographically-guided 14-gauge CNB of breast lesions from March 2005 through April 2011 at the Vancouver Breast Center were reviewed. 'Strict' true negative cases were defined as lesions which had benign pathology on core biopsy and had either benign pathology upon surgical excision or at least 2 years of stable imaging and/or clinical follow-up. False negative cases were defined as lesions which had benign pathology on core biopsy but malignant histology upon surgical excision. A benign CNB lesion subsequently confirmed to be malignant was considered an "applied true negative" if it was immediately referred to surgery due to suspicious imaging findings. In other words, the false negative histology did not result in delayed diagnosis. The definition of 'applied' NPV was introduced to acknowledge that in actual practice, the imaging findings are considered along with the histology to inform follow-up recommendations.

Results
Of the 339 breast lesions in 319 patients, 117 were confirmed to be benign via surgical excision, and 220 were stable on ≥ 2 years of imaging or clinical follow-up (mean follow-up time 33.1 months). The 'strict' NPV of sonographically-guided 14-gauge CNB was determined to be 99.4% (337/339 cases), while the 'applied' NPV was determined to be 100%. There were 2 (0.6%) false negative cases. In both cases of invasive carcinomas, the radiologist determined recognized discordance between imaging and core biopsy pathology, and recommended surgical excision despite the benign CNB pathology.

Conclusions
Sonographically-guided 14-gauge CNB provides a high NPV in assessing breast lesions. Radiologic/pathologic correlation should be performed to avoid delay in the diagnosis of carcinoma.

Corresponding author: charliezhang825@hotmail.com

CLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES OF WOMEN UNABLE OR UNWILLING TO USE A PESSARY FOR THE TREATMENT OF PELVIC ORGAN PROLAPSE

Presenting Author(s): Tina (Wanting) Zhang

Zhang, W.T. (1), G.W. Cundiff (1,2) and R. Geoffrion (1,2)

(1) Department of Medicine, University of British Columbia, B.C., Canada
(2) Department of Obstetrics and Gynaecology, Faculty of Medicine, University of British Columbia, B.C., Canada

BACKGROUND: Pelvic organ prolapse (POP) is a disabling and chronic condition that affects women of all ages. Pelvic organs can protrude outside the body through the vagina due to weakness in the pelvic floor. POP affects patients both physically and psychologically. Most women with POP suffer from at least one other pelvic floor disorder, such as incontinence. Its negative impact on body image can result in social isolation.

One of the main conservative treatment options for POP is the use of a pessary, a supportive silicone ring that is worn inside the vagina to relieve prolapse symptoms. Fitting a pessary involves a trained professional and is a trial and error process. Previous research has shown that prior prolapse surgery and prior hysterectomy are possible risk factors for an unsuccessful fit. However, consistent predictors of failure to fit a pessary have still not been identified.

METHODS: A retrospective chart review was performed for 116 women who presented for pessary treatment of symptomatic POP between 2008 and 2011. Women who declined or had unsuccessful pessary fittings were compared to women who were successfully fitted. Success in this study is defined as a successful clinical fitting with continued use for at least 1 month. Clinical characteristics were compared between the two groups, including demographics, physical examination parameters, and questionnaire scores of symptoms and quality of life.

RESULTS: 28% of women had unsuccessful pessary fittings. Stepwise regression analysis using AIC suggests a prediction model of increasing odds of failure with the following parameters: patients aged 65 or less, versus more than 65 (OR=4.34), those who had no previous pelvic surgery (OR=2.17), current or past smokers (OR=3.62), or a higher score on a Colorectal-Anal Impact Questionnaire CRADI-8 (OR=1.02 per point increase). On univariate analysis, those who had a baby greater than 8 pounds were also more likely to be failures (40.4% versus 19.6%).

CONCLUSIONS: Our study identified predictors of unsuccessful pessary fitting which may guide patient counseling for the management of POP.

Corresponding author: twz@interchange.ubc.ca