2014-15

LEADERS IN MEDICINE

UNIVERSITY OF CALGARY
CUMMING SCHOOL OF MEDICINE

Sixth Annual Leaders in Medicine Research Symposium
Award Winners with LIM Directors

This is a report of accomplishments and highlights of the University of Calgary's Leaders in Medicine (LIM) program for the period of May 2014 to April 2015

Prepared for the Dean of Medicine, Faculty of Medicine
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INTRODUCTION

Each year since the first student joined the Leaders in Medicine program in 1996, it has grown and improved, this year is no different. Student input and participation has enhanced mentorship, seminars and events adding to the success of this integrated program, which is designed to encourage clinical-research as a career. With the increased enrollment, student participation in program content has grown, with fresh ideas about visiting speakers and how to improve the program to meet expectations and strengths. Enrolment has grown steadily and stays over 60. This year there are 61 active joint degree students. The Affiliate program is becoming more active with over 70 members.

The LIM joint degree program remains unique in Canada, in that, it includes students who are pursuing their PhD or MSc and their medical degree and also students working on an MA and a MBA. The majority of students' graduate degrees are in the health sciences, but we have now have students in Anthropology, English, and Engineering. By including disciplines outside health sciences, the program's intention, to train and create leaders and pioneers in a variety of facets for our future health care system, is enriched. Award winning students continue to graduate from this innovative program.

Continued funding from, Canadian Institute of Health Research (CIHR), Alberta Innovative Health Solutions (AIHS) and money from our anonymous donor allows the program to grow and succeed. Funds from our generous anonymous donor are used for miscellaneous travel awards, visiting speaker luncheons, the research symposium, MD/PhD tuition awards and, new this year, approximately four $5000 MD/MSc academic awards. CIHR's program award allows LIM to fund stipends and research allowances for several MD/PhD trainees each year while they are in the medical portion of their studies. AIHS continues to generously fund joint degree MD/PhD candidates for up to 6 years, with an award which starts in their graduate program and follows them through medical school.

There is no limit to the number of students admitted into the joint degree program, nor the Affiliate program. The joint degree program admission is measured by the number of people offered admission into the University of Calgary's Undergraduate Medical School, and how many of them are either current graduate students here or who have applied and are accepted into a graduate program. This year's new admissions in the joint degree program totaled 13, with 16 (a record number) of current joint degree candidates starting medical school.

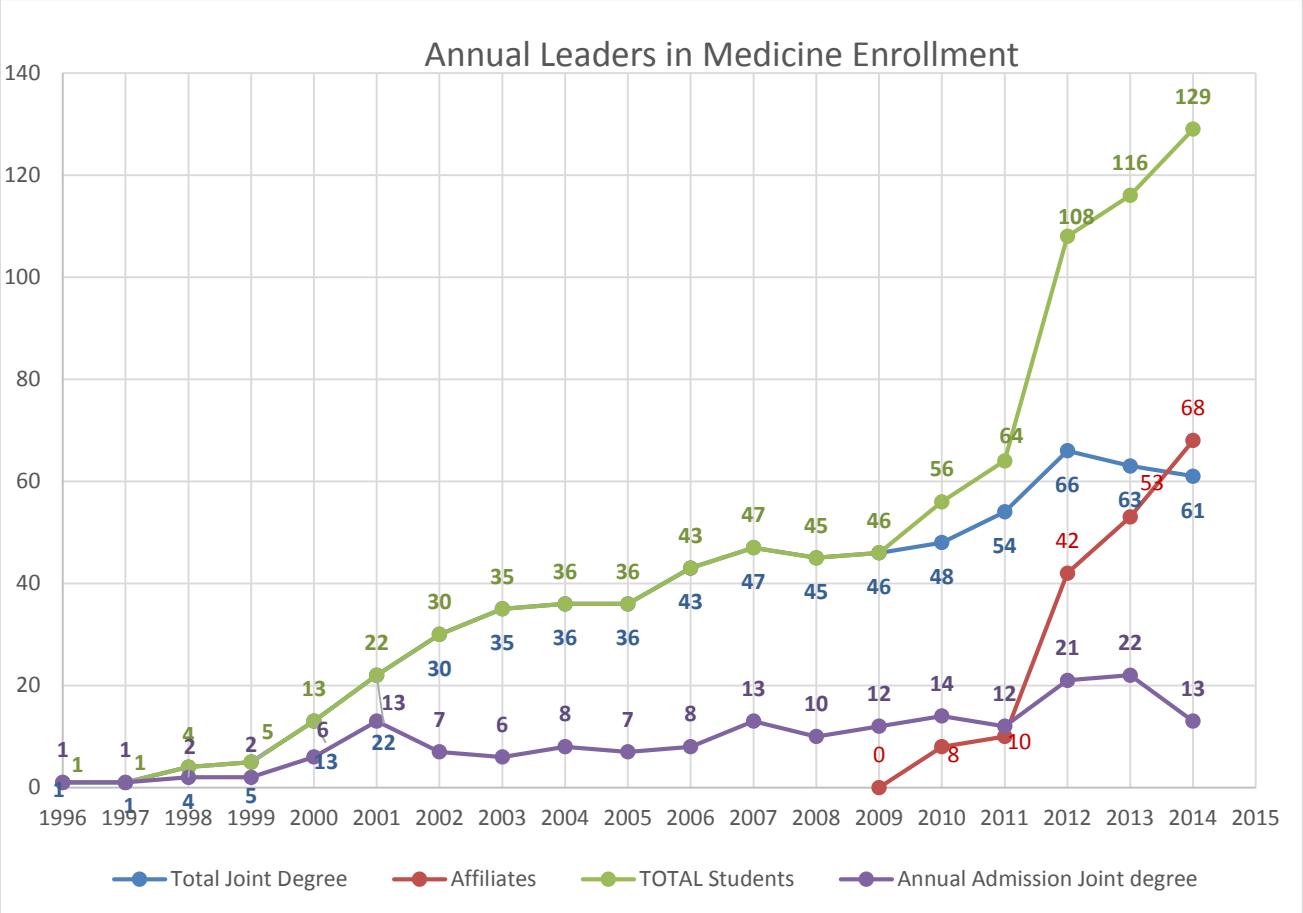
STUDENT ENROLLMENT

Students in the LIM program are from the following graduate programs:

MDBC – Biochemistry & Molecular Biology
MDCH – Community Health Sciences
MDIM – Immunology
MDMI – Microbiology & Infectious Diseases
MDBT – Biomedical Technology
BMEN- Biomedical Engineering
ENG – English
MBA – Master of Business Administration
MDCV – Cardiovascular/Respiratory Sciences
MDGI – Gastrointestinal Science
MDSC – Medical Sciences
MDNS – Neuroscience
KNES – Kinesiology
BISI – Biological Sciences
SOC – Sociology

This year there are 35 PhD, 23 Masters, 1 MBA and 2 MA students for a **total of 61.**

LIM ENROLLMENT CHART



OVERVIEW

The Leaders in Medicine program is designed to offer the opportunity to pursue combined degrees at the University of Calgary. It enables highly motivated students to complete a graduate and medical program degrees concurrently.

The program's objective is to train clinicians for a diverse range of careers – from academic medical research to the design, management, and evaluation of healthcare delivery systems. Medicine has changed dramatically over the last 50 years and is expected to change further every year. MDs are some of the top researchers in the world; they are educators, administrators, politicians, business leaders and innovators in many areas. Our program is designed to educate and provide students with a unique experience so they are better equipped, not only to meet the ever-changing expectation of medicine, but to become leaders in the field of medicine.

One of the hallmarks of the LIM program is flexibility where we try to best adjust MD or graduate training to meet the needs of the students. The LIM program is also very attentive to the changing needs of students and twice yearly LIM members complete a questionnaire on the program and the student government of LIM and staff then meets to try and implement the suggested changes.

PROGRAM ADMINISTRATION

The Administrative infrastructure of the program includes Dr. Paul Beck, Director, Dr. Morley Hollenberg, co-Director, Dr. Bryan Yipp, Associate Director and Michelle Selman, Program Administrator/Advisor. The other departments and faculties involved include Graduate Science Education (GSE), Dr. Tara Beattie, Associate Dean, Undergraduate Medical Education (UME), Dr. Sylvain Coderre, Associate Dean and Faculty of Graduate Studies (FGS), Dr. Julie Deans, Associate Dean.

Cumming School of Medicine's GSE office has always supported the LIM program. Not only by providing one-third to one-half of a program administrator/advisor's (PA) time for daily administration of the program, but also with travel funds. Each of the above faculties or departments has at least one contact person with whom program administrator works to process program applications and ensure appropriate registration. The PA also processes LIM tuition and CIHR awards, student travel and other expenses and is the program contact for questions or concerns. This position is an integral part of successful functioning of the program. The program is also organized and run by an executive committee, elected each year by the students, and by volunteers who help with planning and events. This year they successfully organized the Sixth Annual Research Symposium, monthly Research in Progress (RIP), translational Journal Club meetings and a Visiting Speaker series. The LIM student executive work closely with the program administrator for events budgets and planning of program functions.

LEADERS IN MEDICINE STUDENT COMMITTEE

2014-2015 LIM EXECUTIVE

Chair	Michael **Keough**
Committees:	
Communications	Jason **Bau** and Kristine **Woodward**
Visiting Speaker Series	Kristen **Barton**, Lauren **Capozzi**, Emily **McKay** & Sarah **MacEachern**
LIM Research Seminar	Jodie **Roberts,** Jennifer **Beatty** and Michael **Peplowski**
Research in Progress	Christina **Thornton** and Alex **Frolkis**
Journal Club	James **Cotton**, Craig **Beers** and Taryn **Ludwig**
Social Committee	Ann **Zalucky** and Monica **Faria-Crowder**
2017 Med Class Representative	Monica **Faria-Crowder**

EXECUTIVE COMMITTEE CHAIR REPORT

I had the pleasure of serving as chairperson of the Leaders in Medicine Executive Committee for the academic year of 2014-2015. Attendance at our monthly activities felt fuller than ever, due in part to the increased number of students in the program as well as a general willingness and excitement to participate. This was the first year LIM was recognized on the co-curricular record as a measure of student's involvement in the program, and it resulted in volunteers signing up to present at events months in advance!

This year, Visiting Speaker seminars were particularly impressive, in that the committee arranged 7 speaker events plus the annual pre-clerkship panel. Journal club saw it's first "debate-style" session where 2 students battled on either sides of a controversial medical issue, and Research in Progress's freeform content rules resulted in students showing their creativity with sharing new ideas.

Along with 20 other of my colleagues, I was privileged to attend the Clinical Investigator Trainee Association of Canada (CITAC/CSCI) annual general meeting in Toronto, Ontario. It was clear from the distribution of attendees that University of Calgary Leaders in Medicine students represented the largest group by a significant margin. Apart from learning from plenary sessions and skill-building workshops, our students won awards for poster and oral presentations and had the chance to interact and bond with each other and with clinician-scientist trainees from across the country. Overall, I feel we left the impression that our program is a powerhouse of clinician-scientist training in Canada.

I am excited about what the future holds for the Leaders in Medicine program. A priority is the installation of a unified alumni program. This will be used to track the career paths of our graduates as a measure of our program outcomes, as well as provide a large pool of potential contacts for future residency panel discussions and visiting speakers. This year steps were made to advance this priority. The need to collect data on our graduates will only get greater as the program continues to grow. I look forward to working through this need in the next year of Leaders in Medicine.

Michael Keough, Chair of Executive Committee 2014-15

PROGRAM DIRECTORS' REPORT

***Program Director**, Dr. Paul Beck*

Dr. Paul Beck was recognized for his mentorship work and awarded the University of Calgary, Medical School Alumni of Distinction, for Mentorship. Along with many mentoring awards, he received one of the highest awards given out by the University of Calgary, Faculty of Medicine, the Watanabe Distinguished Achievement Award, for overall excellence. In 2014-15, Dr. Beck was awarded the Canadian Association of Gastroenterology Visiting Professorship and the Canadian Association of Gastroenterology Research Excellence Award which is the highest such award for research in gastroenterology in Canada. He was also awarded the 2015 Killam Professorship as a recognition of overall excellence and service.

***Co-Director**, Dr. Morley Hollenberg*

Dr Hollenberg is the recipient of numerous awards for research and mentorship. He was recently recognized internationally as one of the highest cited people in Science.

Dr. Hollenberg and I are pleased to report that, once again, the LIM Program at University of Calgary continues to grow! Last year we reported a record breaking enrolment, this year the program broke that record with membership of 129 and growing; 61 of whom are joint degree students. Affiliates are previous graduate degrees and/or simply interested in the goals and aims of the LIM program. The number of affiliates grows continually since there is no specific application date required to join, at this time there are 68 active members. Under Dr. Bryan Yipp's, Associate Director, guidance, our Research in Progress Meetings, Translational Journal Clubs and Visiting Speaker Series continue to improve with attendance and participation increasing each year.

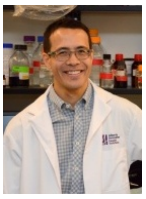
The 6th Annual Research Symposium was the most successful symposium thus far, with highest participation to date and a very successful keynote speaker. Dr. Danuta Skowronski, MD, MHSc, Epidemiology Lead for Influenza and Emerging Respiratory Pathogens, B.C. Centre for Disease Control, gave a stimulating keynote address. Her presentation was well received and her interaction with the students was exceptional. Highlights of the Symposium are give further in this report. This year again, the proceedings and abstracts of LIM Research Symposium were submitted for publication in the CIM Journal.

Leaders in Medicine students continue to excel, with several receiving the coveted MD-PhD Studentships from Alberta Innovates Health Solutions. Our students received over 35 other awards and scholarships during the year, publishing 93 papers with another 53 submitted and/or in press. (Listed further in the report.) They published six (6) book chapters and over 100 abstracts. You will see that again LIM student excelled in residency matching with the vast majority of student getting their first choice of specialty and location.

Our mentorship network is growing with willing mentors. The program is reaching out to LIM alumni to become mentors and we are continuing to work on a student based additional mentorship program to work with new members.

As we receive feedback from our student body, we tweak the program. Students continue to show that student are pleased with enhanced programs and with the Research in Progress and translational Journal Clubs and their ability to request outside and local visiting speakers and have input into who will be Keynote Speaker at the Symposium. As we grow we will continue to enhance the program for the benefit of student who are interested in clinical and research based careers. *Dr. Paul L. Beck*

ASSOCIATE DIRECTOR'S REPORT



***Associate Director**, Dr. Bryan Yipp*

Dr. Yipp, a Leaders in Medicine Alumni, is a Canada Research Chair holder in Biomaterials and Pulmonary Immunology, Inflammation and Host Defence

2014-2015 was a busy and exciting year. There were 10 'research in progress' (RIP) sessions allowing 27 LIM and Affiliate LIM trainees a forum to openly discuss their research interests. The breadth and variety of presentations was remarkable. Presentations included topics such as genetic ethics and public self-genetic testing, primary research in inflammatory meditators, kidney function, neurosciences, as well as interesting patient clinical encounters. Additionally, LIM held 10 translational journal clubs. In contrast to conventional journal clubs, the LIM members presented topical papers for 30 minutes followed by group breakout sessions to explore specific questions related to the science, the applicability to human clinical practice and solutions to translate the findings into humans. Again, the variety of topics was broad, ranging from obesity, microbiota and e-cigarettes to synaptic function and cognitive neurological decline. Finally, LIM was given the opportunity to host a distinguished speaker as part of the Snyder Endowed Chair Seminar Series. We were fortunate to bring Dr. Casanova (MD/PhD), a premier clinician-scientist to Calgary from The Rockefeller University (NY, USA). Five current LIM members, a LIM alumni and myself had a highly engaging dinner with Dr. Casanova when he arrived. He provided very candid, but entertaining, advice for mentorship for everyone who attended. The following day, Dr. Casanova attended an informal lunch and open discussion with the entire LIM group. Most trainees found him refreshingly, but bluntly, honest and he provided the group with several provocative ideas concerning clinician scientist training and career paths. Finally, the LIM members attended the Snyder Institute seminar, were Dr. Casanova described two unpublished human research discoveries, both of which were subsequently published in the prestigious journal, SCIENCE.

Dr. Bryan Yipp

MENTORSHIP

Mentorship is a critical aspect of the Leaders in Medicine Program (LIM). This Program offers joint programs where students can pursue graduate work and medical school at the same time. The main program includes the MD/PhD, MD/MSc and MD/MBA Programs. The director (Dr. Beck), co-director (Dr. Hollenberg) and associate director (Dr Bryan Yipp) as well as our program administrator (Ms. Selman) frequently meet with students on a one on one basis. We are available to meet with students whenever they have and issue but also meet with students on a regular basis throughout their training. We developed a program where clinical clerks from the LIM Program return and talk to the 1st and 2nd year medical students to give them advice on clerkship. This has been an outstanding success. We have also started a program where we get LIM graduates (some residents some in junior staff positions) to discuss career development, balancing research career with residency/clinical work and family. We strive to set up "mentorship flow" where we help

identify mentors for the students to guide them through their graduate program, medical school, clerkship, residency and, ideally, into their first faculty position.

We identified LIM graduates and/or others at all universities across Canada and United States that can have (and are presently) mentoring students. A list of willing high level mentors is found on the LIM website and given to students on a yearly basis. Developing this list of mentors from across North America has been critical to aid students when they start in to a new position or university to allow them to quickly get involved in research groups and develop strong local/discipline specific mentorship. Many LIM students that have graduated still contact our program directors for advice, mentorship and career planning.

EDUCATIONAL EVENTS

Program Educational Events are intended to enrich the student research experience. LIM students and Affiliates are expected to commit to a minimum of 2 to 4 hours per month to the program and to attend up to an average of 60% of the monthly seminars. There are many opportunities to present research through seminars, the journal club, national conferences and the yearly LIM Research Symposium.

The program sponsors attendance at two main national symposiums. This year 21 students attended and presented abstracts at the Clinician Investigator Trainee Association of Canada (CITAC), this year held in November in Toronto in 2014. Five to 8 students are accepted to present at the annual Canadian National Medical Student Research Symposium (CNMSRS) held in Winnipeg in June.

Our students consistently win poster and/or oral research presentation awards at these events (see more information on specific events below). Students use their Leaders in Medicine CIHR or AI-HS MD/PhD research allowances and the program uses our anonymous donor funds and GSE MTF funds to reimburse student expenses for these trips.

Annual Leaders in Medicine Symposium

Each year the Leaders in Medicine students organize and run the annual Leaders in Medicine research symposium. Held in early November, the Annual Symposium is well organized and well attended. This year's 6th Annual Symposium was extremely well organized with a record number of presenters. See below and **Appendix A** for details.

Highlights from the 6th Annual University of Calgary Leaders in Medicine Research Symposium

The Leaders in Medicine Program at the University of Calgary hosted its 6th Annual Research Symposium on November 14, 2014, showcasing the breath of work performed by students in the program at the Cumming School of Medicine. Participation at this year's event was our most successful year to date, with a total of six oral presentations and 77 posters presented during the afternoon symposium. For a detailed description of the work presented at the symposium, please see the *Proceedings from the 6th Annual University of Calgary Leaders in Medicine Research Symposium* published in this issue of Clinical and Investigative Medicine.

We were honoured to host Dr. Danuta Skowronski as the keynote speaker for this year's Leaders in Medicine Research Symposium. Dr. Danuta Skowronski has served as the Epidemiology Lead for Influenza and Emerging Respiratory Pathogens at the BCCDC for the past 17 years. Her leadership in the fields of rapid response research and real time risk assessment is invaluable. She is widely recognized for her role in communicating of emerging public health issues to the public. Dr. Skowronski has more than 100 publications, primarily related to influenza, emerging respiratory pathogens and vaccine-preventable diseases. She has been the recipient of numerous awards, including the James M. Robinson Award for significant contributions to public health and the UBC President's Award for public education through media. Dr. Skowronski was also named among the 100 most influential women in BC by the Vancouver Sun.

Dr. Skowronski was chosen as this year's keynote speaker given her extensive work and expertise in epidemiology and rapid response research, coupled with her leadership in establishing partnership between basic scientists and epidemiologists across Canada. These partnerships have resulted in a national surveillance-research platform which provides real-time linking of genotypic, phenotypic and epidemiologic indicators of vaccine-virus relatedness and vaccine protection.

Attendees of the Annual LiM Research Symposium were fortunate to glean an inside view of the excitement and complexities of rapid response to public health crises from Dr. Skowronski. During her very engaging presentation on "*Rapid response research during emerging public health crises: influenza and reflections from the five year anniversary of the 2009 pandemic*", Dr. Skowronski highlighted some of the most precarious situations that she has faced thus far during her leadership at the BCCDC. These scenarios included the BCCDC response to the H1N1 pandemic, the SARS outbreak of 2003, and oculo-respiratory syndrome during the 2000-2001 influenza va

In addition to her keynote address at the symposium, Dr. Skowronski provided a light hearted discussion of her career path the day before the research symposium and relevant examples related to her work in epidemiology and rapid response research. In addition to interacting with and inspiring students in the Leaders in Medicine Program, Dr. Skowronski also presented some of her work to undergraduate students in the Bachelor of Health Sciences Program in the Cumming School of Medicine at the University of Calgary. *Jodie Roberts*
MD/MSc trainee

The Keynote Speaker, Dr. Danuta Skowronski sent the following comment: *"Many thanks for your wonderful hospitality and warm welcome in Calgary. I had a great time interacting with your terrific organizing committee and your impressive and fun students. Their presentation and posters really wowed me – they have so much great potential and I hope some of them will consider a research career in public health and emerging pathogens."* ***Danuta Skowronski***

RESEARCH IN PROGRESS (RIP) – STUDENT SPEAKER SERIES

Progress (RIP) meetings, held once a month are coordinated by student representatives. RIP presentations are typically short (5-10 minutes) allowing students to share a specific research passion. The sessions foster discussion, new ideas, and often collaboration. Three to five students do a presentation on their research at each monthly meeting, focusing on how the research ties to exciting work in their field.

Date	Name	Presentation
6-17-14	Jaysen Weslosky, Jaye Platnich, Jackie Williamson	Miscellaneous
9-9-14	New LIM members	Introductions: New LIM students do a short introduction of themselves.
10-7-14	Laura Palmer	An Evaluation of Model Systems in Animal Research
	Barbara Maciejewki	Viral-bacterial interactions and innate immune responses in the lung
	Sharita Manga	ECG use for Myocardial Scar Assessment.
11-4-14	Vadim Iablokov	Regulation of intestinal epithelial apoptosis through the G protein-coupled receptor PAR2
	Jenn Beatty	*Giardia duodenalis* cysteine proteases modify human microbiota biofilms: *A role in post-infectious epithelial dysfunction?*
	Alex Frolkis	Statistical Tests
12-2-14	Nabeela Nathoo	This is your brain on social media
	Ann Zalucky	For debate: the clinician scientist's role in disease prevention
	Vincent Vong	Risky Business
2-3-15	Kristen Barton	Your most important patient
	Laura Senst	Stress and synapses
	Helena Zakrzewski	Recent advances in pediatric ophthalmology: innovations in gene therapy for Leber's congenital amaurosis
3-3-15	Michael Keough	My experience publishing with a video protocol journal
	Alex Campbell	I, Physician: the Future of Artificial Intelligence in Medicine
	Heather Leduc-Pessah	The paradoxical effects of using opioids to treat chronic pain
4-7-15	Richard Xiang	Clinical Decision Making
	Jaye Platnich	NLRP6 in Kidney Injury and Inflammation
	Daniela Urrego	Regulation of Myometrial smooth muscle function: Implications for Preterm labour
5-5-15	Michael Peplowski	LIM Symposium Feedback
	James Cotton	Things I wished I knew about medical school before starting
	Allison McDonald	Viral-induced neurodegeneration – novel presentation of a perforin1 disorder

JOURNAL CLUB – SEMINAR SERIES

Designed to provide opportunities to learn about important research that may be outside the student's field of study, the LIM Journal Club is focused on new translational research that holds a broad medical interest. A number of students present research papers about whatever is of interest to them, so long as the topic is translational. Presentations average 45 minutes and are followed by a general discussion, usually moderated by experts from the Cumming School of Medicine.

Date	Name	Presentation
24-5-14	James Cotton	Discussion of the research article looking at an alternative approach to controlling multidrug resistant intracellular bacterial pathogens and a one-page critique of the paper.
30-9-14	Helena Zakrzewski	Presenting the article "Atropine vs Patching for Treatment of Moderate Amblyopia" from the May issue of JAMA Ophthalmology"
28-10-14	Jason Bau	Presenting the article "Topoisomerases facilitate transcription of long genes linked to autism."
25-11-14	Christina Thornton	Presenting the article "Artificial sweeteners induce glucose intolerance by altering the gut microbiota"
27-1-15	Kristine Woodward Jodie Roberts Craig Beers	Presenting "Mobile Phone Emissions Modulate Brain Excitability in Patients with Focal Epilepsy" Presenting "Dravet Syndrome Patient-Derived Neurons Suggest a Novel Epilepsy Mechanism" Presenting "Sudden unexpected death in epilepsy: Assessing the public health burden."
24-2-15	Nabeela Nathoo and Mike Keough	Debate discussion regarding "Multiple Sclerosis: Autoimmunity or Neurodegeneration"
31-3-15	Paul Adamiak	Presenting the article "The SIRT1 Activator SRT1720 Extends Lifespan and Improves Health of Mice Fed and Standard Diet"
28-4-15	Ceilidh Kinlin	Presenting the article "Efficacy of a devise to narrow the coronary sinus in refractory angina"

VISITING SPEAKER SERIES

A student-organized program, the Visiting Speaker Series brings educators from the University of Calgary or from other institutions, some jointly sponsored and others fully sponsored by LIM. This year the series included a Clerkship Panel, with 3rd year medical students speaking about the program and what to look forward in clerkship.

Date	Speaker
July and August 2014	No speaker series
Friday, September 19, 2014	Dr. Gill Kaplan, Associate Professor, Environmental Health Research Group, Cumming School of Medicine, University of Calgary
Wednesday, October 29, 2014	Dr. Peter Stys, Professor, Department of Clinical Neurosciences, Cumming School of Medicine, University of Calgary
Thursday, November 13, 2014	Dr. Danuta Skowronski, Physician Epidemiologist, BCCDC and Clinical Professor, School of Population & Public Health, University of BC
Tuesday, December 16, 2014	Dr. Paul Beck, Assistant Professor, Division of Gastroenterology, Gastrointestinal and Mucosal Inflammation Research Groups, Cumming School of Medicine, University of Calgary
Friday, January 9, 2014	Dr. Jean-Laurent Casanova, Senior Attending Physician and Professor, Howard Hughes Medical Institute, St. Giles Laboratory of Human Genetics of Infectious Diseases, Rockefeller University

Tuesday, February 10, 2015	Clerkship panel – Angie Karlos, Sarah Tulk, Mehrnoosh Aghaei. Leaders in Medicine students in 3rd year of medical school.
Friday, February 27, 2015	Dr. James Talbot, Chief Medical Officer of Health in Alberta
Friday, April 17, 2015	Dr. Marvin Fritzler, Professor, McCaig Institute for Bone & Joint Health, Cumming School of Medicine, University of Calgary

Canadian National Medical Student Research Symposium

Held in conjunction with the CIHR Canadian Student Health Research Forum, students are invited to attend this annual conference hosted by the University of Manitoba's Faculty of Medicine. Canadian National Medical Student Research Symposium invites MD and MD-plus students from other Canadian universities to present abstracts. This is a unique educational opportunity or trainees. Five students submitted abstracts: *Structural determinants for the catalytic inhibition of human topoisomerase IIα by salicylate-related compounds* submitted by Jason Bau. *Developing three-colour fluorescence cross-correlation spectroscopy* submitted by Megan Blades. *Influence of telomere dynamics on disease progression and therapeutic response in bone marrow failure syndromes* submitted by Erin Degelman. *Treating donor site pain in burn victims that have undergone autologous split-thickness skin grafting: A review of the literature* submitted by Amanda Eslinger. *Harmless Commensal Microbial Neighbors Synergistically Trigger Pseudomonas aeruginosa Virulence Genes in Cystic Fibrosis* submitted by Christina Thornton.

CITAC/CSCI Young Investigators Forum

Held for the past few years in Ottawa in September, this year the Canadian Society for Clinical Investigators (CSCI) and Clinician-Investigator Trainee Association of Canada (CITAC) was held in Toronto in November. The event allows students to meet with peers and clinical scientists from around Canada.

The conference includes presentation of oral and poster research by LIM joint and Affiliate students. Three LIM students were award winners this year: Alec Rogers (2nd in oral), Ryan Leigh (3rd in oral) and Laura Senst (1st in poster).

Funded by student research allowances, LIM and GSE this year a record of 21 students were able to attend. Five (5) used AIHS research allowances and the rest were paid from a combination of Medical Travel Funds through GSE, LIM CIHR research allowances and LIM anonymous donor funds. LIM funding from our anonymous donor was used to sponsor a portion of the event.

Leaders in Medicine Social Events

The student executive social committee plans and holds a number of social events each year. A welcome BBQ, a pot-luck and a graduate dinner among others.

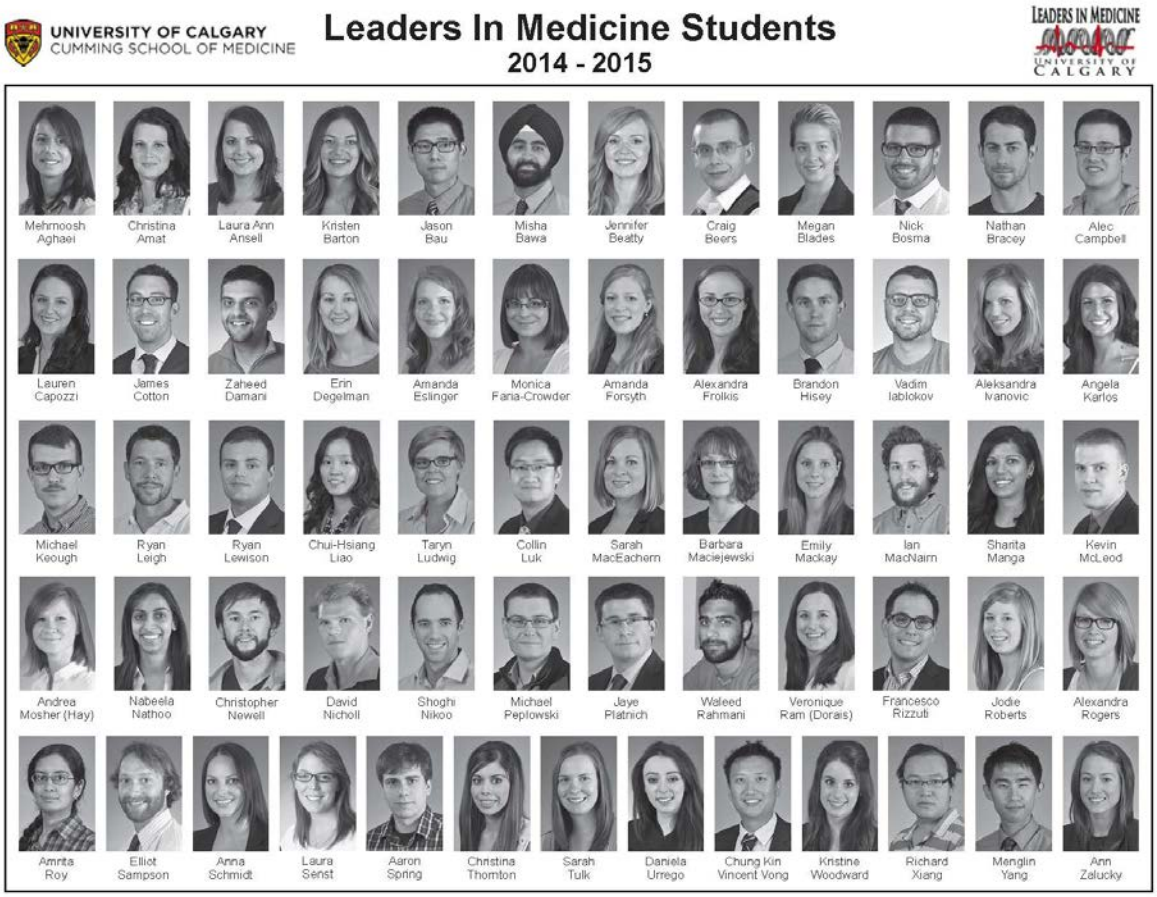
Student Comment

"I grew in my educational experience through the LIM program. The program gives me valuable exposure to fields of study other than my own. The Annual Research Symposium allowed for clinical scientists outside my field of study to critique my work which I found helpful and constructive."

Nabeela Nathoo, MD/PhD candidate

Leaders in Medicine Students

Current Students



STUDENT ACCOMPLISHMENTS

Leaders in Medicine trainees are high achievers in both in their personal and scholastic pursuits. These are a few of the special achievements. We also list these, when possible in our website, http://cumming.ucalgary.ca/lim/current-students/accomplishments

2014-15 ACCOMPLISHMENTS:-

SAMPLES OF SPECIAL ACCOMPLISHMENTS

Vince **Vong** was student lead (program director) in a student volunteer first-responder team the Student Medical Response (SMR) team. This is an innovative new student group on campus which will contribute to the health safety on campus. The team consists of volunteers who have trained higher than standard in first aid and is the first student team of its type in Western Canada

Ann Zalucky MD/MSc candidate listed as one of the Top 40 under 40 in Avenue. *"Ann Zalucky is pursuing both a master's degree and a medical doctorate, research and presenting findings on kidney disease and running the MicroMalaria Project, which she co-founded to help prevent the spread of malaria in sub-Saharan Africa."* http://www.avenuecalgary.com/Top-40-Under-40/Ann-Zalucky/

Chris Newell MD/PhD candidate awarded inaugural Mitochondrial Disease PhD Scholarship. *"Newell came to UCalgary after completing his BSc at St. Francis Xavier University where he did an honours thesis under Professor Daniel Kane. Newell says that it was Prof. Kane who first got him interested in mitochondrial research, and from there he developed a passion for this aspect of basic science. It was this newfound enthusiasm that brought Newell to UCalgary where he was accepted to the Cumming School of Medicine for his PhD and joined the* ***Leaders in Medicine*** *program."* (UToday article).

SAMPLE OF GENERAL ACCOMPLISHMENTS

Ryan **Lewinson,** MD/PhD candidate received the Most Outstanding Podium Presentation 3rd Price at the 15th Annual Alberta Biomedical Engineering Conference in Banff. His presentation was on the biomechanics of footwear orthotics.

Nabeela **Nathoo** MD/PhD candidate awarded 2nd Place in the 2014 Hotchkiss Brain Institute PhD Researcher of the Year.

Ian **MacNairn** MD/PhD candidate asked to be key speaker at the 2015 Adapted Physical Activity conference in March. He was asked to present regarding poster he presented at this year's Research Symposium and CITAC.

Ian **MacNairn** also presented tales of adventure and exploration of a truly unique region of the world at a Wild Mountain Calgary sponsored event. "Stories from the Field: Madagascar's Limestone Labyrinth."

Christine **Thornton** MD/PhD candidate received a Canadian Foundation for Infectious Diseases award for her paper on "Community-acquired Clostridium difficile infections"

Heather **Leduc-Pessah** MD/PhD candidate was finalist in the year's 3 Minute Thesis Competition.

Lydia Sikora Memorial Research Award - Congratulations to **Nabeela Nathoo** (1st place), **Sarah MacEachern** (2nd place), **Jodie Roberts** (honorable mention), **Jason Bau** (honorable mention)

Kristen Barton, MD/PhD Candidate - awarded the 2014 Vanier Canada Graduate Scholarship (2014-2017) as well as Kappa Gamma Foundation of Canada Scholarship.

Nathan Bracey and Collin Luk, MD/PhD Candidates - awarded the 2014 Achievement in Medicine award from the Leaders in Medicine program.

Andrea Mosher, MD/PhD Candidate - awarded the 2014 Leaders in Medicine Program Achievement Award.

Jason Bau, MD/PhD Candidate - received the David Proud Award for Research Excellence from the Department of Physiology and Pharmacology in July 2014.

Ryan Lewinson, MD/PhD Candidate - received the 2014 J.B. Hyne Research Innovation Award for excellence in Biomedical Engineering research.

LIM Students Award MD-PhD Studentship from Alberta Innovates Health Solutions

Awardee	**Supervisor** *(Department)*	**Institution**	**Project Title**
Ansell, Laura A.	Thompson, Roger J.*Cell Biology & Anatomy*	University of Calgary	A Novel Role for Amyloid Beta Protein during Hypoxia/Ischemia
*Degelman, Erin S.	Beattie, Tara L.*Biochemistry & Molecular Biology*	University of Calgary	Influence of Telomere Dynamics on Disease Progression and Response to Therapeutics in Bone Marrow Failure Syndromes
Rahmani, Waleed M.	Biernaskie, Jeffrey A.*Comparative Biology & Experimental Medicine*	University of Calgary	The Immunomodulatory Role of Macrophage on Hair Follicle Mesenchymal Stem Cells during Wound Healing

2014 Residency Results

Leaders in Medicine students continue to show success with matching their desired residency program. This is a critical point in all medical students' careers. Matching means that a student can follow his/her desired career a step toward following their passion.

MATCHES:

LIM Student Name		Joint or Affiliate	CARMS	Choice
Anderson	Dustin	Joint	Neurology/Edmonton	2nd due to Couples Match
Dykeman	Jonathan	Joint	Radiology/Calgary	1st
Hons	Ian	Joint	Family Medicine/London	3rd
Fralick	John	Affiliate	Internal/Toronto	1st
Huebner	Kyla	Joint	Ortho/Western Ontario	2nd
Jones	Tristan	Joint	Emergency/Victoria	1st
Luu	Judy	Joint	Internal Medicine/Saskatoon	1st Couples Match
Matthews	Graeme	Affiliate	Ortho Surgery/Saskatoon	1st Couples Match
Moser	Joanna	Joint	Anesthesiology/Calgary	1st
Redding	Nicole	Joint	Family Medicine/Vancouver	1st
Rowan	Sharon	Joint	Urban Fam Med/Calgary	1st
Shields	Ryan	Affiliate	Family Med/Toronto	1st
Wadhwani	Aman	Joint	Diag. Radiology/Calgary	1st
Williams	Kimberly	Affiliate	Psychiatry/Calgary	1st

ALUMNI:-

The LIM student executive this year explored how to track and stay in touch with Alumni, they are working with the UME Alumni program and LIM administration to set up a system to stay in touch. The desire is to have a system to contact former students in order to follow them through their career, their successes and to be able to ask them to stay involved where possible. It is planned to invite alumni to speak and judges, etc. either in the Speakers Series, the Research Symposium or other events where possible.

AWARDS/SCHOLARSHIPS

TYPES OF AWARDS (as listed in Student's 2012-13 Annual Reports)

1. Dr. T Chen Fong Doctoral Scholarship in Neuroscience $30,000
2. Achievers in Medical Science Research Excellence Award $3500
3. Achievers in Medical Science $25,000
4. Achievers in Medical Science Award, LIM $40,000
5. Alberta Innovates Health Solutions Studentship $30,000
6. Dr. Gary MacPherson Leadership Scholarship $2000
7. Queen Elizabeth II Graduate Award MSc $10,800
8. Queen Elizabeth II Graduate Award PhD $15,000
9. Leaders in Medicine Outstanding Achievement Award $1000
10. Medical Science Academic Productivity Scholarship $500
11. Leaders in Medicine's CIHR Stipend Scholarship $21,000
12. Lydia Sikora Award for Research Excellence $10,000
13. University of Calgary Eyes High Doctoral Research Excellence Award $5000

14. The Dr. Benno Nigg Distinguished Faculty Graduate Achievement Award $1000
15. Graduate Award, Association of Professional Engineers & Geoscientists of Alberta $5000
16. Canadian Graduate Students Masters Scholarship $17,500
17. Alberta Graduate Student FGS Fee Scholarship $3000
18. University of Calgary Faculty of Medicine International Elective Studentship $1500
19. GRS Graduate Student Scholarship $2000
20. Beverly Phillips Rising Star Award, Snyder Institute for Chronic Diseases $30,000
21. Dr. Gary McPherson Leadership Scholarship $2000
22. Nat Christie Foundation medical Entrance Award $5,000
23. BME Graduate Program Director's Prize for Leadership $2500
24. Alberta Graduate Citizenship Award $2000
25. AITF PhD Scholarship $26,000
26. Vanier Award $50,000
27. Alberta Cancer Foundation Graduate Studentship Award $40,000
28. Dawson Jarock Research Award in Pediatric Nephrology and Rheumatology $2500
29. Louise McKinney Award $2500
30. Professional Development Grant, University of Calgary $470
31. Biochemistry & Molecular Biology publication award $100
32. Cystic Fibrosis Canada Studentship $19,000
33. Persons Case Scholarship, Government of Alberta $2000
34. Geral Weber Cosmopolitan International Club of Calgary Graduate Scholarship $21,000
35. American Society of Nephrology Student Scholar Grant $7000
36. Alberta Heritage Graduate Student Scholarship Award $3000
37. Izaak Walton Killam memorial Scholarship $36,000
38. Medical Science Academic Productivity Scholarship $500
39. Kappa Gamma Foundation of Canada Scholarship $5000

2014-15 PUBLICATIONS

PUBLISHED: – TOTAL REPORTED **93**

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Motta, J.P., Flannigan, K., Agbor, T., **Beatty, J.K**., Blackler, R., Workentine, M., Da Silva, G., Wang, R., Buret, A., Wallace, J. **2015**. Hydrogen Sulfide Protects From Colitis and Restores Intestinal Microbiota Biofilm and Mucus Production. Inflammatory Bowel Diseases.

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Aghakhani Y, **Beers** CA, Pittman DJ, Gaxiola-Valdez I, Goodyear BG, Federico P. Co-localization between the BOLD response and epileptiform discharges recorded by simultaneous intracranial EEG-fMRI at 3 T. *Neuroimage Clinical* 2015;Mar 7;7:755-63.

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6th Annual
University of Calgary
Leaders in Medicine Research Symposium
November 14th, 2014

Distinguished Guest and Speaker:

Dr. Danuta Skowronski MD, MHSc

Physician Epidemiologist

UNIVERSITY OF CALGARY
CUMMING SCHOOL OF MEDICINE

Dear participants,

We are very pleased to welcome you to the 2014 Leaders in Medicine Research Symposium organized by trainees for trainees at the University of Calgary. The objectives of our 6th Annual Leaders in Medicine Research Symposium are to:

(1) showcase the impressive variety of projects undertaken by Leaders in Medicine Program Students, Leaders in Medicine Program Affiliates, and medical students at the University of Calgary;

(2) promote medical student participation in research and special projects and involvement in the Leaders in Medicine Program at the University of Calgary;

(3) highlight the diversity of opportunities and importance of pursuing research and special projects during medical school and beyond, and;

(4) engage our many Leaders in Medicine Program alumni in continued involvement and interaction with current students and the program to foster future mentorship opportunities.

Please take a moment to engage in all this research symposium has to offer, including presentations of novel results from vast fields of research, the opportunity to network with other trainees past and present and distinguished researchers, and celebrate the research successes of many.

This year we are pleased to extend our warmest welcome to our keynote speaker, Dr. Danuta Skowronski, as well as many faculty members representing the multidimensional scope of world class clinical and scientific directives currently underway here at the University of Calgary.

This symposium would not be possible without the efforts of countless volunteers that have generously provided their time and input. In addition, we would like to particularly thank Dr. Paul Beck, Dr. Morley Hollenberg, Dr. Bryan Yipp, and Ms. Michelle Selman for their invaluable advice and assistance in organizing this year's edition of the research symposium.

We look forward to an informative and interactive symposium full of networking and great science talk!

With best wishes,

Jennifer, Michael, and Jodie

6th Annual University of Calgary

Leaders in Medicine Research Symposium

November 14th, 2014
1:00 – 5:30 PM
Theatre Four and HRIC Atrium, Cumming School of Medicine

PROGRAM

12:30 – 1:00 pm: Registration and Poster Set-Up – HRIC Atrium

1:00 – 1:15 pm: **Welcome and Introduction of Keynote Speaker – Theatre Four**

1:15 – 2:15 pm: **Keynote Address – Theatre Four**

Dr. Danuta Skowronski

"Rapid response research during emerging public health crises: influenza and reflections from the five year anniversary of the 2009 pandemic"

2:15 – 2:30 pm: Refreshments – Outside of Theatre Four

2:30 – 3:30 pm: **Student Oral Presentations – Theatre Four**

3:30 – 3:45 pm: Reception (Food & Drink) – HRIC Atrium

3:45 – 5:15 pm: **Student Poster Presentations – HRIC Atrium**

5:15 – 5:30 pm: **Awards and Closing Remarks – HRIC Atrium**

The Leaders in Medicine Research Symposium Organizing Committee would like to thank:

Keynote Speaker: Dr. Danuta Skowronski

Oral and Poster Competition Judges:

Dr. Aman Wadhwani
Dr. Amy Metcalfe
Dr. Andrew Flynn
Dr. Aru Narendran
Dr. Chris Waterhouse
Dr. Daniel Miller
Dr. Danuta Skowronski
Dr. Duncan Nickerson
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Funding for this Symposium was generously provided by:

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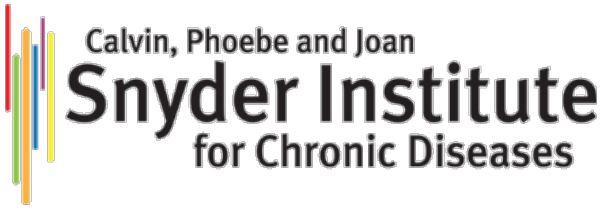

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Keynote Speaker

Dr. Danuta Skowronski, MD, MHSc

Physician Epidemiologist
British Columbia Centre for Disease Control
School of Population & Public Health, University of British Columbia

Dr. Danuta Skowronski has been Epidemiology Lead for Influenza and Emerging Respiratory Pathogens at the British Columbia Centre for Disease Control (BCCDC) for approximately 15 years. In this post, she is responsible for surveillance and rapid response research, a role for which she has been distinguished for her notable contributions around several major public health events.

Dr. Skowronski led the public health response to SARS in BC in 2003, and was responsible for human health recommendations during outbreaks of avian influenza in BC in 2004. In addition to being a member of Canada's National Advisory Committee on Immunization from 2008 - 2011, Dr. Skowronski has been involved in numerous provincial- and national-level pandemic planning activities and committees since 1998. Dr. Skowronski has more than 100 publications, primarily related to influenza, and has been recognized for her distinguished career in public health.

Dr. Skowronski is the recipient of numerous awards and accolades, including the UBC President's Award for Public Education through Media in 2007 and was named among the 100 most influential women of British Columbia by the Vancouver SUN in 2010. In 2011, Dr. Skowronski was awarded the James M. Robinson Award by the Faculty of Medicine at UBC for her significant contributions to public health.

Dr. Skowronski completed her medical degree and family medicine training at Queen's University in Kingston, Ontario and completed a Master's of Health Sciences degree and a Fellowship in Community Medicine at the University of British Columbia. She is further certified with the American Board of Preventive Medicine and completed additional training with the London School of Hygiene and Tropical Medicine. She worked for several years as an associate Medical Health Officer in Surrey, BC gaining practical experience in public health before joining the BCCDC in 1998 to pursue her interests in surveillance, applied public health research and policy development.

Adapted from Dr. Skowronski's BCCDC Profile

Past Symposia

1st Leaders in Medicine Research Symposium | 6 November 2009

Dr. Lorne Tyrrell, MD, PhD
University of Alberta

2nd Leaders in Medicine Research Symposium | 5 November 2010

Dr. Ramnik Xavier, MD
Harvard Medical School
Massachusetts General Hospital

3rd Leaders in Medicine Research Symposium | 4 November 2011

Dr. Douglas Hamilton, MD, PhD
NASA Flight Surgeon

4th Leaders in Medicine Research Symposium | 2 November 2012

Dr. Hugh Scully, MD
Professor of Surgery and Health Policy
University of Toronto
Toronto General Hospital

5th Leaders in Medicine Research Symposium | 8 November 2013

Dr. Jerrold Ellner, MD
Chief of Infectious Disease
Boston Medical Centre

Oral Presentation Schedule

The role of cell communication and 3D cell-matrix environment in a stem cell-based tissue engineering strategy for bone repair

Swathi Damaraju, John Matyas, Derrick Rancourt, and Neil Duncan

McCaig Institute for Bone and Joint Health, University of Calgary

Background: The use of stem cells for the repair of bone and cartilage is a primary research interest in modern tissue engineering strategies. The aim of this project was to determine the role of connexin containing gap junctions and confined compression on the biosynthetic activity of embryonic stem cells stimulated to form osteoblasts in a 3D collagen-I scaffold.

Methods: We used a previously determined preparation that induces osteoblast differentiation in a 3-dimensional collagen scaffold seeded with murine embryonic stem cells, and has been shown to have reduced teratoma formation upon implantation in vivo. Confined compression of gels was applied in the presence or absence of communication inhibitors, or a nitric oxide donor or scavenger. Experiments assessing gap junction-mediated cell communication, nitric oxide production, mineral production, immunofluorescence for integrin $\alpha 5\beta 1$, and the expression of connexin-43, osteoblast-cadherin, β-catenin, and various pluripotent and osteogenic markers were performed.

Results: These studies revealed that mechanical pre-stimulation could be used as a tool to prime this scaffold for bone healing applications. Cell communication and specific cell-cell and cell-matrix interactions within this scaffold were crucial in regulating osteoblast differentiation and function. Further, nitric oxide played a major role in regulating mineral formation within this scaffold, and exogenous nitric oxide increased mineral formation in early-differentiated gels, and stimulated cells towards osteoblast differentiation.

Conclusions: The results presented here represent a characterization of this *ex vivo* scaffold for factors known to be important in bone formation *in vivo*, and provide a greater understanding of the micro-scale mechanisms regulating bone remodeling.

The proteolytic activity of *Nepenthes* pitcher fluid as a therapeutic for the treatment of celiac disease

Yang, M[1,2], Rey, M[1], and Schriemer, DC[1]

[1]Department of Biochemistry & Molecular Biology, Faculty of Medicine, University of Calgary [2]Leaders in Medicine Program, Faculty of Medicine, University of Calgary

Background: Celiac disease (CD) is a highly prevalent autoimmune disorder that is triggered by the incomplete digestion of immune stimulatory peptides in the gliadin fraction of dietary gluten. The basis for gliadin resistance to digestion is due to the abundance of P (~15%) and Q (~30%) residues in its protein sequence. Currently, no therapeutic product for CD exists but oral proteases aimed at efficiently digesting gliadin throughout the gastrointestinal tract have shown promise in advanced clinical trials. In this study, we propose that the proteolytic activity of *Nepenthes* plant extracts will be suited for an oral protease therapeutic for CD.

Methods: Digests of an immunodominant 33-mer peptide of α-gliadin by the *Nepenthes* pitcher fluid was quantified by LC-MS. Digests of gliadin extracts from wheat by the *Nepenthes* pitcher fluid proteins was performed *in vitro* at a fixed dosage under simulated gastrointestinal conditions. Aliquots were taken at different time-points and analyzed by LC-MS/MS. In addition, all digests were performed with and compared to an equivalent dosage of pepsin.

Results: Quantification by LC-MS showed that *Nepenthes* pitcher fluid was able to digest the 33-mer peptide of α-gliadin fully and efficiently even at a 10-times lower concentration than that of pepsin, which was only able to digest ~7% of the peptide at a 1:10 molar ratio (enzyme: substrate). Quantitative and qualitative comparison of the LC-MS/MS data obtained from *Nepenthes* pitcher fluid digests of gliadin extracts appeared to show a net destruction of immunogenic peptides below initial levels and near minimal T-cell stimulatory levels with increased digestion times, whereas it appeared that no net destruction or further release of immunogenic epitopes into solution was observed with an equivalent dosage of pepsin.
Conclusions: Our data indicates that a novel protease formulation in *Nepenthes* pitcher fluid, appears to efficiently process immunogenic epitopes of gliadin under gastronintestinal conditions, thus, supporting the potential of the proposed protease formulation as an effective oral therapeutic candidate for CD.

Monitoring pediatric inflammatory bowel disease – A retrospective analysis of transabdominal ultrasound

Amelia Kellar[1], Gilaad Kaplan[1], Remo Panaccione[1], Jennifer DeBruyn[2], Stephanie Wilson[1,3], and Kerri L. Novak[1]

[1]Department of Gastroenterology, University of Calgary, [2]Department of Gastroenterology, Alberta Children's Hospital, [3]Department of Radiology, Foothills Medical Centre

Background: Poorly controlled inflammatory bowel disease (IBD) in children can lead to long- term complications in adulthood. There is a need for an imaging modality to effectively monitor IBD in the pediatric population. The current gold standard, ileocolonoscopy, requires anesthesia in children. Computed tomography (CT) is associated with a risk of radiation and is not recommended for repeated use. Magnetic resonance imaging (MRI) has proven to be effective, but may have limited availability. Transabdominal ultrasound is accessible, safe and well-tolerated in children; however, data to support its effectiveness in monitoring pediatric IBD is limited.

Methods: 57 children were retrospectively included from an established database of children with IBD, and cross-referenced with Picture Archiving and Communication (PACs) database. Patients that had endoscopy and sonography within 60 days were included for comparison. Ultrasound parameters included: bowel wall thickness, mesenteric fat, hyperemia and lymphadenopathy. The weighted kappa statistic was calculated to assess agreement between sonographic and endoscopic findings. Using ordinal logistic regression and proportional odds models, a grey-scale ultrasound (US) score was created to using parameters that best predict disease activity, compared to gold standard endoscopy.

Results: There was moderate agreement in disease severity between sonographic and endoscopic findings (weight kappa=0.55). Significant clinical predictors of pediatric IBD disease severity were bowel wall thickness and hyperemia ($p<0.05$). According to this novel scoring system, 66% of patients were classified correctly, disease severity was under-estimated in 14% of patients and over-estimated in 17% of patients. The AUC was 90% for normal versus active disease. Additional analysis will be conducted with 76 patients from the same database.

Conclusion: The parameters bowel wall thickness and hyperemia best predict disease severity in children with IBD. These parameters can be combined into an accurate predictive score, effective in the detection of inflammatory activity in children with inflammatory bowel disease.

The design and application of a molecular profiling strategy to identify polymicrobial acute sepsis infections

Monica M. P. Faria[2,4], John M. Conly[1-4], and Michael G. Surette[2,4,5]

[1]Departments of Medicine, Microbiology, Immunology & Infectious Diseases[2], Pathology & Laboratory Medicine[3], Snyder Institute for Chronic Diseases[4], Faculty of Medicine, University of Calgary, Calgary, Canada; Farncombe Family Digestive Health Research Institute, Departments of Medicine and Biochemistry and Biomedical Sciences, McMaster University, Hamilton, Ontario, Canada[5].

Background: Sepsis is a broad term used to describe a vast range of clinical presentations ranging from mild body dysfunction to multiple organ failure. These clinical signs are a result of a systemic inflammatory response to microbes or microbial products present in sterile sites such as blood. Current clinical diagnostics rely on culture techniques to identify systemic infections. However, culture lacks sensitivity and a positive result is only obtained in 40% of cases thereby limiting our knowledge of sepsis microbiology.

Methods: Disruption of blood cells with detergent and hypotonic shock was done to enhance recovery of the community. Efficiencies of recovery and limits of detection were determined for both viable cells and DNA using synthetic bacterial communities inoculated into whole blood. The method was applied to clinical samples collected from consented patients in both the intensive care unit (ICU) and emergency department (ED) from Foothills Medical Centre. Total DNA was extracted for bacterial community profiling using paired-end Illumina MiSeq sequencing of the V3 region of the 16S rRNA gene.

Results: Application of the paired-end Illumina 16S rRNA sequencing to saponin treated blood from ICU and ED patients indicated there were five common bacterial DNA profiles present in whole blood. These patterns were examined alongside the patient's clinical data and indicated common molecular profiling patterns correlated with the primary source of infection. Several case studies demonstrated the strength of molecular profiling to identify a principal pathogen that was not recovered using diagnostic blood culture. Bacterial DNA from *Streptococcus* and *Staphylococcus* were abundant in patients that died in the ICU. Polymicrobial DNA was present in the majority of blood samples with the taxonomic profiles suggesting commensal microbiota were implicated in addition to a principal pathogen. As such, a role for reduced mucosal barrier function was also hypothesized to play a role in the presence of bacterial DNA detected in the bloodstream.

Conclusions: Overall, common bacterial DNA patterns were identified in the blood of septic patients in both the ICU and ED. These profiles were associated with the patients' primary source of infection, implicated the commensal microbiota in systemic infection, and suggested that certain bacterial DNA profiles were associated with mortality in the ICU. Taken together, molecular profiling could be used to identify bacterial DNA profiles that provided clinically significant findings, not observed with diagnostic blood culture, when interpreted in conjunction with patient admissions data.

Hair follicle dermal stem cells regenerate the dermal sheath, repopulate the dermal papilla and modulate hair type

Waleed Rahmani, Sepideh Abbasi, Andrew Hagner, and Jeff Biernaskie

Faculty of Veterinary Medicine – Department of Comparative Biology and Experimental Medicine

Background: Dermal stem cells residing within the hair follicle mesenchyme have recently been identified and characterized as key multipotent cells that induce hair follicle growth and play a role in dermal maintenance. Moreover, the two dermal compartments of the hair follicle, dermal sheath (DS) and dermal papilla (DP), have been shown to express the stem cell gene Sox2 as well as generate skin-derived precursors (SKPs) when cultured. However, the primary source, migration pattern, and fate of these dermal stem cells remain a mystery. Here we hypothesized that αSMA+ dermal stem cells reside in the DS, regenerate the DS, and contribute cells into the DP.

Methods: To address this, we generated two inducible Cre-lox transgenic mice, αSMA-CreERT2:ROSA26^{eYFP} and αSMA-CreERT2:ROSA26^{confetti}, to perform in vivo genetic lineage tracing experiments. Tamoxifen treatment during early anagen (hair follicle growth phase) exclusively labeled DS cells and not the DP. We then documented the fate of these cells over multiple hair follicle cycles for up to 7 months.

Results: Our results identify a population of bipotent self-renewing hair follicle dermal stem cells (hfDSCs) that envelop the telogen DP, are activated at the onset of anagen to regenerate the DS and are retained at the end of each hair follicle cycle. More importantly, hfDSCs are capable of contributing cells into the DP that are in turn capable of exiting the DP and re-entering the hfDSC niche after hair follicle degeneration.

Conclusion: This work provides definitive evidence for the existence and location of a dermal stem cell within the adult hair follicle and provides new insights into the lineage relationships within the mesenchymal compartment of the hair follicle. Moreover, since human clinical studies suggest that DP cell loss is the primary contributor to androgenetic alopecia, our findings have direct implications toward understanding the pathological mechanisms that underlie hair loss.

A Novel role for amyloid beta protein during hypoxia/ischemia

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Background: Alzheimer's Disease (AD) is a progressive neurodegenerative disorder that is associated with genetic and environmental risk factors, including stroke (ischemia). AD involves the formation of deposits of the protein amyloid beta (Aβ). Interestingly, basal levels of Aβ are upregulated under hypoxic conditions. During ischemic stroke, neurons lose their ability to maintain ionic gradients, which leads to ionic dysregulation known as the anoxic depolarization (aDP). The ion channel pannexin-1 (Panx1) has been demonstrated to be integral to the aDP and is opened by *N*-methyl-*D*-aspartate receptors (NMDARs) through Src family kinases during hypoxia. We hypothesize that Aβ upregulation during hypoxia functions to protect brain tissue by interacting with Panx1.

Methods: Whole cell patch clamp electrophysiology was used in hippocampal slices from rats, which were continuously perfused with hypoxic artificial cerebral spinal fluid in order to mimic ischemia and induce the aDP. Various concentrations of Aβ protein were applied concurrently with hypoxia (pM to μM range). In a separate set of experiments, slices were incubated in a ɣ-secretase inhibitor to decrease production of Aβ prior to application of hypoxia. Finally, low concentrations of Aβ were applied with a Panx1 antibody, NMDAR antagonist, or Src inhibitor in order to observe if there are any additive neuroprotective effects of pharmacologically blocking these three targets in the presence of Aβ.

Results: Depletion of Aβ exacerbated the aDP, while application of low concentrations of Aβ attenuated the aDP. Interestingly, high concentrations of Aβ worsened the aDP. Concurrent application of Aβ and a Panx1 antibody, NMDAR antagonist, or Src inhibitor was not additive on the effect of Aβ alone.

Conclusion: These data suggest that Aβ acts as a neuroprotective agent during hypoxia/ischemia by interacting with Panx1 through NMDARs and Src. This gives insight into the physiological activity of Aβ and can provide better understanding of the underlying cause of stroke-induced AD.

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Unprofessional conduct in the health care profession: results from a qualitative study of disciplinary decisions against registered nurses in a Canadian province

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Introduction: Misconduct in the health care profession costs lives and money. It can be directed at patients, co-workers, or employers. The conduct of members of the health care profession, like that of many other professionals, is self-regulated. Although a serious issue, little is known outside of the regulatory bodies regarding the extent and types of misconduct in this field and the effectiveness of sanctions.

Methods: We analyzed the content of publicly available data on complaints of professional misconduct against registered nurses (RNs) and the resulting disciplinary actions, paying particular attention to variables such as complainants, alleged offenses, victims, offenders, and settings

Results: Preliminary findings. There were roughly two disciplined misconducts observed per discipline file (no gender difference[s]). 26% of the files are on men who make up 5% of the nurses in total. Thus, the number of disciplined misconducts were 5x higher for male than female nurses. The most common types of misconduct RNs were disciplined for are as follows: False documentation re client care (41/203); criminal conviction (22); negligent care (20); theft/fraud (19); drugs (18). Gender differences are as follows: Female nurse misconduct: false documentation (31/155); negligent care (20); theft/fraud (15); drugs (14); failed to assess client (14). Male nurse misconduct: criminal conviction (12/48); false documentation (10); theft/fraud (4).

Conclusion: The most common types of misconduct against patients that RNs were disciplined for included false documentation regarding client care and negligent care. Results have to be interpreted with caution as the data analyzed here only consist of incidents that were reported. Accordingly, the ‘dark figure’ of RN’s professional misconduct remains unknown. An alternative might be to conduct a self-report study. In the absence of longitudinal data, it is also impossible to determine the effectiveness of arguably weak disciplinary action administered through self-regulatory approaches. Future research needs to examine the root causes for the misconduct and also explore whether male RNs are in fact committing more acts of misconduct or are subject to higher scrutiny in this female-dominated profession.

“DOCS”: Donor Offer Call Simulation; a novel tool to evaluate nephrology and kidney transplant trainees in managing deceased donor kidney offers

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Introduction: Competence in accepting deceased donor kidney (DDK) offers for transplantation is a curricular expectation of nephrology/transplant trainees. Yet the current curriculum dedicates minimal formalized training to the refinement of this skill. We assessed trainees’ competence in accepting DDK offers by reviewing their performance following participation in a Donor Offer Call Simulation (DOCS) exercise.

Methods: A standardized DOCS rubric was developed for the purposes of assessing participants’ preparedness in accepting DDK calls. Seven categories, known to be relevant to decision making for organ allocation, graft outcome and acceptance or discard of an organ, were examined. One nephrology and two transplant trainees participated in two DOCS, typical of DDK offer. Two silent observers witnessed the simulations and scored participants using the DOCS rubric, with points awarded for probing and successfully acquiring key donor information.

Results: All three participants reported increased confidence and competence in participating in donor offer calls following completion of the DOCS. Mean scores for both simulation scenarios were 54.14% (Range 35.02%-7.9%, $p<0.05$). Performance was correlated with level of training; with the two transplant fellows consistently outperforming the nephrology trainee ($p<0.5$). Notably the transplant trainees at the end of the training year still missed between 25-50% of critical information.

Conclusions: DOCS identified important competency gaps in trainees for accepting DDK offer calls. This highlights the need for improved training practices implemented early in the nephrology-training curriculum. DOCS is a highly efficient and cost effective model that can be easily incorporated into current training practices. A potential exists to implement the DOCS scoring rubric into clinical practice to systemize the donor offer process thus ensuring complete information acquisition and enhance reproducibility between calls.

Working under knifepoint – perceived abuse and intimidation of medical students

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Introduction: The progression from classroom to clinical setting can be a challenging transition for medical students. The expectation and roles of medical students often vary between specialties. Experience in the operating room is anticipated as one of the most challenging environments for the novel medical learner. We sought to identify common concerns prior to exposure in this learning environment and examine the experience of final year medical students on their surgical clerkship rotation in an effort to identify areas where improvements can be made.

Methods: A twenty-question survey was developed after a focus group met to identify potential issues that medical students encounter during their surgical clerkship. Personal and anecdotal experiences guided the development of the survey. It was distributed to final year medical students and recent graduates (350 individuals) using SurveyMonkey. A quality improvement ethics application was completed prior to the commencement of the survey as were participant consent forms. Two investigators grouped responses and identified common themes in the experiences reported.

Results: Seventy-two individuals responded to the survey providing a 21% response rate. Subjects were asked how confident they were in their understanding of what was expected during a surgical rotation. Fifty-two (72%) responded that they were “unsure” or “very unsure” while only twelve and three felt “somewhat confident” and “very confident”, respectively. The majority of learners felt nervous (96%) and feared appearing incompetent (89%). Common concerns included insufficient knowledge and technical skill, anticipated negative experiences and feelings of uncertainty regarding medical student expectations.

Conclusion: We present common themes stemming from medical student experiences during their surgical clerkship. We comment on perception of intimidation and abuse, the rationalization behind such behavior, and perceived lack of guidance. The intention of this analysis was to identify weaknesses in our surgical training so that a quality improvement plan can be implemented.

Survey of physician willingness to provide methadone maintenance therapy among primary care physicians in Alberta

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Introduction: Methadone has been proven to be a cost-effective treatment for opioid dependence, but availability of treatment is often inconsistent. Currently in Calgary, Alberta, there is a wait-time in excess of three months to access Methadone Maintenance Therapy (MMT) in dedicated Opioid Dependency Programs operated by Alberta Heath Services for the treatment of Opioid Dependence. There are also relatively few primary care physicians in possession of a Methadone exemption. The aim of this study was to identify the reasons for which primary care physicians in Alberta are reluctant to obtain a methadone exemption.

Methods: We disseminated a survey to family physicians in Alberta in an attempt to identify barriers to obtaining an exemption to provide MMT. A statistical analysis including logistic regression analysis was performed to determine how perceived barriers were related to physician willingness to provide MMT.

Results: We found that physicians who perceived their practice as requiring modification or a shift in how they practiced were more willing to obtain an exemption ($p < 0.05$). They also felt less obligated to provide MMT. Somewhat counter-intuitively, feeling uncomfortable working with patients who have addictions was associated with greater willingness to obtain an exemption. The MMT exemption procedure was identified as a barrier. Among non-exempted physicians, barriers included the patient population being difficult (55%) and a lack of experience, training or education in MMT (63%).

Conclusions: Among primary care physicians in Alberta, issues of practice modification, the exemption procedure, a perceived difficult patient population and lack of training stand out as barriers to obtaining an MMT exemption.

A survey of mobile technologies used by medical trainees and staff at three Canadian institutions

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Introduction: The use of mobile technology is becoming increasingly prevalent in medical practice. The manner in which trainees and staff physicians utilize these technologies, however, remains unknown. The purpose of this study was to examine how medical students, residents and faculty members in three Canadian medical institutions use mobile technology in medical education and practice.

Methods: A cross-sectional survey was developed based on current literature and focus group discussions. Questions were aimed at assessing the prevalence of mobile devices in medical practice, reasons for usage, common programs or applications accessed, and the proportion of learning performed through mobile technology. The survey was sent online to medical students, residents, and faculty members at Western University, McMaster University, and the University of Calgary.

Results: 245 medical students, 75 residents, and 226 faculty members responded. 97% of medical students, 97% of residents, and 91% of faculty own a smartphone or tablet. The most common reasons for using a mobile device in a classroom or clinical setting was for communication, scheduling, and browsing the Internet for medical purposes. The most common medical app used was Medscape. 93% of respondents agreed that mobile technology has a positive impact on medicine and 80% agreed that mobile technology should be incorporated into medical curricula.

Conclusions: Mobile technology is widespread in medicine at all levels of education and practice. Medical students, residents, and faculty are using smartphones and tablets for a variety of functions and consider mobile technologies to have an overall positive impact on medicine. These technologies, however, are rarely incorporated into didactic experiences in the classroom and clinical setting. Because of its broad prevalence in learning and practice, mobile technologies may represent a strong opportunity for educational institutions to enhance medical education in an already familiar and accessible medium.

Alberta physicians' perspectives on vaccination and diagnostic testing for gastroenteritis in children: a survey of primary care providers

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Introduction: Worldwide, gastroenteritis contributes significantly to pediatric morbidity and mortality. The rotavirus vaccine has not yet been incorporated into Alberta's publically funded vaccination program, despite its use being recommended by Canada's National Advisory Committee on Immunization (NACI). We gathered primary care physicians' opinions regarding the implementation of a gastroenteritis vaccine, as well as their understanding of diagnostic tests used to identify gastroenteritis-causing pathogens.

Methods: Survey content was developed by experts from the fields of pediatrics, family medicine, emergency medicine, microbiology, and public health. The 30-item survey was distributed to physicians who are members of Alberta Primary Care Networks, the TARRANT network, and The Society of General Pediatricians of Greater Edmonton.

Results: The majority (73%) of respondent physicians support the incorporation of a gastroenteritis vaccine into the routine vaccination schedule for children. However, parental endorsement was perceived as being lower (54%). The majority (62%) of respondents perceived current methods of stool sample collection as being inconvenient for caregivers. Rectal swabs were perceived by most respondents (82%) as being convenient, with the potential to improve specimen collection rates. Physicians' understanding of which tests to order to identify causes of gastroenteritis infection were suboptimal.

Conclusion: Implementation of a gastroenteritis vaccine into the routine pediatric vaccination schedule is still under debate. Stool sample collection and diagnostic testing methods could be simplified, which could contribute to improved rates of testing and better knowledge of gastroenteritis disease burden.

Rare diseases and orphan drugs in Alberta: The landscape and the liability

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Introduction: During the past 30 years, research, development and availability of innovative drugs to treat rare diseases have been enhanced globally. Many of these drugs have been priced high causing public and private insurers around the world concern. There are questions about the sustainability of paying high prices that consume large proportions of health budgets to the detriment of other areas of health care.

Methods: A scoping review was conducted to understand the extent of the orphan drug issue here in Alberta, Canada and globally. News articles, government websites, and peer-reviewed journals were reviewed to understand the approval process. Finally, a legal analysis was conducted to assess whether the current process in Alberta was fair and whether it placed the government at risk of liability.

Results: Unlike many countries, Canada does not currently have any orphan drug legislation. In 2012, the federal government announced that a framework would be put in place, however to date, nothing has been implemented. In Alberta, the government has implemented a *Rare Diseases Drug Program* ("RDDP"). The RDDP's "Expert Committee" determines what drugs will be covered by the program, treatment guidelines and criteria for coverage. Some have deemed the process unclear and lacking in transparency, calling into question the fairness of the program and the potential legal liability to the government.

Conclusion: The threat of growing orphan drug costs to overall health budgets is real. Currently, there is no legislation in place in Canada or Alberta that addresses the subject. The RDDP in Alberta has turned its mind to the issue, however the lack of transparency and clarity around the decision-making process calls into question its fairness and poses a potential legal risk to the government.

Health communities and inequity: A content analysis comparing the Google domains of Fragile X Syndrome and Cystic Fibrosis

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Introduction: The communication of health is sociocultural as is the communication of pediatric developmental disorders. Internet displays are important in communicating health needs, promising research, and fundraising goals to the public on behalf of a health community. The purpose of this study was to compare the web content available for two pediatric developmental disorders in order to discern and explicate differences that privilege one condition over the other.

Methods: In addition to sharing a similar prevalence, Cystic Fibrosis (CF) and Fragile X Syndrome (FXS) are life-long, incurable, multi-systemic and genetic conditions. Content analysis was simultaneously conducted on the top 30 links in the Google domain for each condition on two occasions. Coding of web content retrieved via standardized search queries addressed website category, content, target audience and tone.

Results: Significant differences were seen between CF and FXS. The average number of total hits for CF (23,500,000) exceeded FXS (2,085,000). CF was found to have a higher proportion of National Organizations ranking in the top 30 hits, whereas the majority for FXS was dedicated to health databases. CF was found to offer a wider variety of content, including information, event promotion, and programs and services; the majority of FXS's top 30 hits were solely informational. A subjective analysis of tone was performed for each disorder with high inter-observer reliability; 21/30 websites for CF depicted an overarching positive tone while 23/30 websites for FXS were neutral.

Conclusions: Although these disorders share many attributes, CF presents a more comprehensive and positive approach to the condition, while FXS focuses more on dissemination of neutral, disorder-related information. Inequities observed in these two health communities include disparity in resources and access to information for providers and affected families, which are unwarranted and perhaps unfair given similar prevalences.

Inequity amongst children's developmental conditions: marketing tactics in a crowded field

Stephanie D'Agostini*, Jacqueline Harrison*, Jennifer Mateshaytis*, Dr. Lynn McIntyre

Introduction: Evidence suggests that caregivers use the Internet to find information and resources for their child's health condition, yet web presence differs in its ability to effectively sell information and resources. This study compares the Google domain web content available for five pediatric developmental disorders in order to explore any differences in health information and service access.

Methods: Cystic Fibrosis (CF), Fragile X Syndrome (FXS), Down Syndrome (DS), Duchenne Muscular Dystrophy (DMD), and Spina Bifida (SB) were selected based on specific inclusion criteria. Content analysis was conducted on pre-set dates, using a coding sheet to consistently evaluate the Google domain content retrieved via standardized search queries. The top 30 links were ranked and evaluated.

Results: The disorders differed significantly with respect to total number of hits, website category and website content. DS and CF had 101,300,000 and 23,500,000 hits respectively; with the other disorders totaling less than 5,100,000 hits each. The predominant website categories were national organizations for CF and SB, local organizations for DS, and health informational databases for DMD and FXS. In a subjective analysis of tone over 65% of the websites for CF and DS depicted an overarching positive tone, while at least 50% of each of SB, DMD and FXS's hits were neutral. Of note, websites targeted the public as their audience as opposed to those affected by the condition.

Conclusions: Although these disorders share many attributes, they present vast differences in their web presence and content. CF and DS present a more well-rounded, positive approach to disease, while FXS, SB and DMD focus on dissemination of disorder-related information. Physicians should be mindful that more activist disorders might receive inequitable attention from health care systems. Improvements to tools and information are necessary to provide reliable and useful online resources to families for FXS, SB and DMD.

TITLE: A problematic role of 'patient choice' in elective surgical decision-making

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ABSTRACT:

Introduction: In response to criticisms of paternalistic medicine, respect for patient autonomy has become a central principle in ethical medical practice. A key part of this principle is emphasis on patients' right to choose their treatment course. If patients are able to choose which treatment is best for them, the argument goes, then the patient's perspective will be preserved. However, recent evidence suggests that shifting the responsibility for medical decision-making onto patients introduces new problems. The present research investigates how 'patient choice' acts in the medical decision making conversations in a clinic that provides elective urogynecological surgery.

Methods: This research utilizes results of ethnographic observations of interactions between surgeons and patients. The researcher shadowed surgeons for six weeks and produced detailed fieldnotes about the interviews, examinations, tests, and discussions observed. The conclusions here are based on themes and categories developed using common procedures for analyzing qualitative data. Data were coded using Nvivo 10.

Results: Decisions regarding whether to have surgery and which surgery to have often arose smoothly out of conversations between doctors and patients. In these encounters, 'patient choice' did not arise as a central issue; instead, options emerged in such a way that one appeared more desirable than the others. Other times, however, the best course of action was unclear. In these encounters, after some discussion centered on success and complication rates, surgeons would tell patients it is their choice and often have them leave the clinic to make their decision.

Conclusions: 'Patient choice' therefore shifts responsibility for the decision onto to the patient. Rather than encouraging surgeons and patients to share the work of decision-making, emphasis on 'patient choice' may isolate patients from surgeons, making more difficult the tough act of choosing whether to have surgery, especially when it is elective.

Ethics and current practice in clinical photography

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Introduction: Clinical photography is a form of photography used in the medical care setting which captures a patient's physical appearance, either partially or fully. Digital technology has made it easier for health care providers to take their own photographs in a clinical setting. Producing, using, and distributing these images has ethical and legal consequences and it is important to understand current practices and attitudes towards clinical photography among health care providers.

Methods: A literature review was undertaken to gauge prevalence of clinical photography and current practice in terms of gaining consent, usage of images obtained, storage of clinical images, and awareness of relevant ethical principles and legal consequences.

Results: A significant number of health care workers in Canada, the United States, the United Kingdom, and Australia are using hospital digital cameras, personal digital cameras, and personal cell phone cameras to take clinical photographs. Most hospitals and jurisdictions have guidelines surrounding informed consent for clinical photographs (consent for use in education, publication, etc.) consent is often obtained improperly, not obtained at all, or undocumented. Policies governing the usage and distribution of clinical photographs as protected healthcare information exist, but health care workers are often unaware of how to apply these policies in practice. A detailed analysis of studies regarding consent for clinical photography, prevalence of clinical photography, patient responses, and historical and legal landmarks is presented in this paper.

Conclusion: This review found that while significant numbers of health care workers are using digital technology to take medical photographs, many are not obtaining proper informed consent or maintaining confidentiality and are thus violating ethical and legal principles. It is recommended that hospitals provide more education on the appropriate use and distribution of clinical photographs to health care providers to maintain patient trust and confidentiality, and to avoid violation of patient rights.

Fielding's Anatomy: Doctors, Drink, and Deformity

Veronique Ram

Introduction: Literary criticism highlights how contemporary novels portray medical practices as metaphors for social control. In fact, during the late eighteenth century, the rise of scientific knowledge over religious discourse shifts the image of the body as God's vessel to one increasingly represented in clinical terms. Medicine, which continues to grow into an elite profession, emphasizes the need to diagnose and label extraordinary bodies in order to understand their physical error. Indeed, the paternalistic physician characters express anxiety over non-normative bodies, labeling them as social illnesses requiring isolation, for they disrupt social order. All bodies must assimilate to the proper body norm – one that proves legitimate and civilized – or else they trouble the universality of *the* human.

Methods: A literature review of databases (MLA Bibliography, Medline) was performed to explore previous research on doctors as literary characters, and to consider theories on the body, the nation, and the representation of medicine as paternalistic in literary texts. A summary of the results was drafted and included over 300 texts. After reading said texts, the literature review was narrowed to deformity in contemporary Canadian fiction (post 1960).

Results: I chose to focus on the Canadian novel, rather than non-fiction or poetry, because the genre remains historically recognized as one that provides a rich avenue for social commentary and questions of nationalism. My annotated bibliography includes 100 texts published since 1960 that include a physician character that plays a role in defining the normative and non-normative physical health of the nation. The data was subsequently narrowed to focus on 6 novels in which children were the deformed figures intended as symbolic challenges of the medicalization of Canadian society.

Conclusions: For the purposes of this presentation, I focus on two novels, *The Colony of Unrequited Dreams* and the sequel, *The Custodian of Paradise*, in order to demonstrate how women's bodies, as a popular and potent metaphor, must remain healthy and meet normative expectations to act as vessels for the health of the nation. The main character, Fielding, is subjected to continuous incarcerations as a result of deviant drinking, disease, and deformity, which threaten the health of the nation. My central thesis considers such deviance, however, a contestation of paternalistic models of medical practices. Contrary to some critics, who perceive Canadian society as in a palliative state, subject to pharmaceutical care and the failure of the human body, I argue that deformity avoids a defining diagnosis.

Correlations amongst mental health, cognitive flexibility, and zinc status

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Introduction: Cognitive flexibility impairment has been seen in both anorexia nervosa (AN) and commonly comorbid disorders, as have symptoms overlapping with those of zinc depletion. Risk groups for zinc depletion and AN also have distinct overlap, and zinc has been found to play a role in neuroplasticity, which affects cognitive flexibility. Zinc supplementation has shown benefit in treatment of AN, with unclear mechanism. This study's primary aim was to investigate correlations amongst mental health, cognitive flexibility, and zinc status, in order to better understand if zinc supplementation benefits in AN are due to metabolic alterations or to mental health changes which impact behaviour. It was hypothesized that that lower zinc status (as measured by the Bryce-Smith zinc taste test (ZTT) and reported symptoms of zinc depletion) would be associated with decreased cognitive flexibility and with increased depressive, anxiety, obsessive-compulsive, and eating disorder symptoms. The secondary aim was to better characterize the ZTT via score comparison with reported seasoning usage and reported zinc depletion symptoms.

Methods: The Perceived Stress Scale, Mental Health Inventory-38 anxiety subscale, Inventory of Depressive Symptoms-SR30, Compulsiveness Inventory, Obsessive Compulsive Inventory-R, Eating Attitudes Test-26, Trail Making Tests A/B, Berg's Card Sorting Test, Haptic Illusion Test, Bryce-Smith ZTT, and a zinc-related factors questionnaire were administered to all participants.

Results: 12 females aged 18-50 were tested and results analyzed using Spearman's and Mann-Whitney U tests. No significant correlations were found between ZTT scores and measures used; however trends in directions that would support the hypothesis were observed.

Conclusion: Due to small sample size and trends observed, it is suggested that the number of participants be increased to better determine potential correlations and that a rough estimate of intake of foods with high zinc levels be introduced for further comparison purposes.

Transnational farm workers, local health inequities: A role for physicians in supporting migrant farm worker well-being

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Introduction: Each year, BC employers hire over 6,000 farm workers through the federal Temporary Foreign Worker Program. These migrant farm workers, who are predominantly male and Mexican, often report barriers to accessing health services. This is of particular concern because they work in one of the province's most hazardous industries.

Methods: We conducted a review of the barriers and health concerns of migrant farm workers, gathered through existing literature and original interviews.

Results:

Migrant farm workers face barriers to healthcare access due to long working hours, language difference, fear of deportation, and geographic isolation. Specific health concerns of migrant farm workers include: musculoskeletal issues due to repetitive and stressful ergonomic positions, and dermatological and ocular problems due to exposure to agrochemicals, soil, insects, sun, and climatic extremes.Due to the structure of the migrant farm worker program, physicians could unintentionally have a negative impact on a worker's employment and legal status in Canada, with implications for continuity of health care (e.g. a farm worker is diagnosed with cancer in Canada, a doctor's office phones their employer to seek information about the worker's health coverage and discloses details about the patient's health, the patient is repatriated to Mexico and fails to receive quality health care, and is not "named" to return to the farm in future years).

Conclusion: This information is intended to provide a practical guide to respond to the health needs of this vulnerable population, particularly through translation services, navigating insurance status, and acting with cultural sensitivity. In the process of providing health care, physicians may unintentionally have a negative effect on migrants' employment and legal status. It is therefore imperative for physicians to understand the context under which farm workers are employed in order to ensure they do not exacerbate their precarious working and living conditions.

Improving primary care access in rural Alberta through a community engagement effort to decrease no shows

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Introduction: Timely access to primary healthcare is an ongoing issue in Canada and Internationally, particularly in rural communities where physician supply is limited. In Rocky Mountain House, Alberta, patients' average wait for the third next available appointment is 27 days. The downstream effects of poor access are numerous and include decreased continuity of care, poor patient satisfaction, increased visits to the emergency department, and burnout of physicians. This study aims to engage the community to develop strategies to decrease missed appointments to ultimately improve appointment supply.

Methods: An infographic poster was displayed throughout the clinic to bring awareness regarding the importance of keeping or cancelling all appointments. An anonymous survey was used to gather feedback from patients regarding what changes they feel would help decrease missed appointments. Run charts were used to track weekly no show rates over the course of the study.

Results: There were 34 respondents to the survey, of which 30% had missed a clinic appointment without cancelling. The largest contributing factor was transportation difficulties, followed closely by not being able to get through via phone to cancel, and forgetting about the appointment. Fifty-eight percent of respondents preferred to cancel their appointment via phone, thirty percent via text message, and thirteen percent via e-mail. The majority of respondents thought they would benefit from an automated reminder prior to appointments, a service that is not currently offered. Thus far there has been no change to the weekly no-show rate, which fluctuated around ten percent over the past six months.

Conclusions: In a town with poor access to primary care, patients have identified several areas for improvement with potential to decrease the rate of missed appointments. Future initiatives that should be pursued include addressing barriers to transportation, improving the phone system to facilitate cancellations, and implementing automated appointment reminders.

Orthostatic hypotension, frailty and falling risk in elderly care home residents

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Introduction: Orthostatic hypotension (OH; a significant fall in blood pressure when upright) is a deficit that increases in incidence with age as autonomic dysfunction becomes more common. An accumulation in physiological deficits results in frailty, regarded as a state enhanced vulnerability to adverse outcomes. Here, we quantified a frailty index (FI) and hypothesized that this index would serve as an objective predictor of OH and falling in a group (n=54) of older adults living in long-term care.

Methods: From the minimum data set document (MDS), a frailty index (FI) was generated from a list of 57 deficits, ranging from 0 (no deficits) to 1.0 (57 deficits). A passive seated orthostatic stress test was used to measure cardiovascular responses to orthostatic stress. Falling rates (falls/year) were extracted from fall incident report forms.

Results: The mean FI was 0.27±0.02 (range 0.07-0.64), and was correlated with age ($r=0.441$; $p<0.001$). Those who were frail (FI≥0.25) were significantly older, had a larger orthostatic reduction in diastolic arterial pressure ($p=0.05$), along with a poorer ability to recover the upright decline in systolic arterial pressure ($p=0.06$). FI was greater in women (0.31±0.13) than men (0.25±0.12; $p=0.07$). OH was present in 47% of subjects. Women were more likely to have OH than men ($p=0.05$). Those who were frail had higher prospective and retrospective rates of falling than the non-frail. Multiple regression analysis predicted prospective falling ($r=0.9$; $p<0.001$) based on FI and whether an individual had a fall in the past year.

Conclusion: The risk of falling in a cohort of elderly long-term care residents can be predicted using a frailty score based on MDS data. Frailty is also related to markers of OH. Risk measurement using this FI offers a potential means to single out individuals for intensive prevention measures in the long-term care setting.

Historical compliance rates for providing postoperative radiotherapy in oral cavity squamous cell carcinoma

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Introduction: Squamous cell carcinoma (SCC) is the most common oral cavity cancer (OC) with a 5-year overall survival rate of 50-60%. Recently the Alberta Health Services released updated guidelines for the treatment of OCSCC, which provide recommendations for treating early and advanced-stage OCSCC. Primary treatment is surgical resection of the tumour; treatment with post-operative radiotherapy (PORT) is dependent on the pathological features of the tumour.

Methods: We performed a retrospective study, determining the historical compliance rate of the Tom Baker Cancer Centre (TBCC) and the Richmond Road Diagnostic Centre Head and Neck Clinic (RRDC) with current guidelines. Using our database, Otobase, we analyzed the treatment of 236 patients who presented to the TBCC and RRDC from January 1, 2009 – December 31, 2013.

Result: Of the 236 patients, there were 44 discordant cases; 2 patients received PORT against guideline recommendations and 42 patients did not receive PORT against guideline recommendations. We further looked into each of the discordant cases to determine the reason for the discordance. The reasons for discordance included: patient refusal (N = 7), patient medically unfit/unable to tolerate PORT (N = 8), patient lost to follow-up/unknown (N = 3), post-operative complication (N = 1), and other (N = 25). Within the other category, there were 10 cases the Tumour Board Team (surgeons, oncologists, pathologists, and radiologists) disagreed with the guidelines.

Conclusion: The guidelines are largely based off of retrospective studies and emphasize the importance of a multidisciplinary team making case-by-case treatment decisions. The Tumour Board Team reviews each case and decides on the best treatment; however, the results show there are patients who are not receiving their intended care (patient lost to follow-up/unknown). Given the results, it would be prudent to further investigate the survival rates of those who received surgery alone compared to those who received PORT.

International Surgical Outcomes Study: A Look at Local Outcomes

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Introduction: The International Surgical Outcomes Study (ISOS) was designed to assess multiple outcomes in all types of elective surgery. Several hospitals in Canada have elected to participate, including three centers in Calgary. This presentation will discuss the local outcomes of this observational study.

Methods: The Calgary arm of this cohort study looked at patients having surgery during the period of May 26 and June 13, 2014. Preoperative, perioperative, and postoperative data were collected from all patients aged 18 years and older undergoing elective surgery at the Foothills Medical Centre (FMC), Peter Lougheed Centre (PLC), or South Health Campus (SHC). All patients spending at least one day in hospital post-operatively were eligible and included in the analysis. Patients were followed for a maximum of 30 days or until discharge from hospital, whichever came earlier.

Results: 281 patients were included; 36 at the SHC, 95 at the PLC, and 150 at the FMC. Of 281 patients, 2 (0.71%) died in hospital within 30 days of their surgery, and 54 (19.2%) patients experienced one or more complications, with 39 (26%) of these patients having had surgery at the FMC, 12 (12.6%) at the PLC, and 3 (8.3%) at the SHC. Complications ranged in severity and included hematoma, ileus, surgical site infection, pneumonia, acute kidney injury, arrhythmia, anemia requiring blood transfusion, anastomotic leak, sepsis, and death, among others.

Conclusion: The 30-day in-hospital mortality rate in Calgary (0.71%) is lower than quoted in recent literature. The overall complication rate of 19.2% reinforces that surgery is not a benign treatment and risks should be thoroughly discussed with all patients beforehand. The FMC had the greatest number of complications, likely due to the fact that cardiac, thoracic, and neurosurgical procedures are performed at that site.

Effects of After-Hours Utilization of Ultrasound at Foothills Medical Centre

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Introduction: Sonography is a valuable method for imaging the body. It is the preferred imaging modality for many acute presentations in the Emergency Department such as ectopic pregnancy and abdominal pain in young females. An impediment to more widespread use is the limited availability after hours. Just over one year ago, ultrasound has been made available in house, until 2300hrs at the Foothills Medical Centre (FMC). The purpose of this study is twofold. First, to characterize the types of studies being performed after-hours and second, to examine whether increased availability of ultrasound has decreased the number of Computed Tomography (CT) scans after-hours.

Methods: The PACs system was used to determine the number of ultrasound studies completed after hours. After-hours was defined as 1600hrs - 0700hrs. Data was gathered from 8 weeks before and after implementation of after-hours ultrasound. Data on age, gender, study indication, time of study and whether a technician was called back was gathered (technicians called back after 2300hrs). Studies in the Emergency Department as well as relevant studies from Maternity Triage and Inpatients were included.

Results: The number of studies pre and post implementation increased from 75 to 389. The portion of callback cases decreased from 58.6% to 8.5%. The number of urgent cases decreased from 41.3% pre to 25.2% post implementation. After implementation a larger variety of studies as well as more inpatients were being scanned. Data on the effect of after hours ultrasound on the number of CT scans performed is still being collected.

Conclusions: The availability of after-hours ultrasound has resulted in a decrease in the acuity and number of call back cases. Increased availability of ultrasound resulted in more inpatient studies after-hours. Effects on the number of CT scans are still pending.

Sexually Transmitted Infections in Immigrants and the Canadian Immigration Medical Exam

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Background: Nearly 250,000 immigrants enter into Canada each year. Immigrants who were born in countries with higher prevalence of sexually transmitted infections (STI) and who subsequently apply for immigration can impact the epidemiology of infectious diseases in Canada. Moreover, recent immigrants underutilize the healthcare system, attributing to higher health risks. To assess the populations at risk, we conducted a literature review to examine the current screening requirements for STIs in new immigrants as well as current rates of infection.

Method: A thorough literature review was conducted in PubMed, Medline, and government publications on the current STI screening requirements under the Immigration Medical Exam (IME), current rates of infection among immigrant applicants, and demographics on those infected.

Results: Canadian immigration requires mandatory HIV and syphilis serological screening on all applicants who are ≧15 years old. Results summarized below:

HIV - From 2002 to 2003, 634,958 were ≧15 years old and were tested for HIV. From this applicant pool, 932 were found to be HIV-antibody-positive (146 per 100,000). Of those who tested positive, 67% were born in Africa and 22% in the Americas. The national rate for HIV in Canada for the 2-year period from 2010 to 2011 is 15.7 per 100,000.

Syphilis – From 2000 to 2004, 2,001,417 were screened for syphilis. From the screening pool, 2,209 applicants were found to be syphilis-positive (110 per 100,000). Of those who tested positive, 54.5% were from Asia and the Pacific region and 16.7% from Africa and the Middle East region. The national rate for infectious syphilis in Canada for the 5-year period from 2007 to 2011 is 23.3 per 100,000.

Conclusion: With the recent cuts to refugee healthcare in Canada, information on the prevalence and demographics of HIV and syphilis immigrants may influence and modify policy and management programs at a regional and national level. In the clinical setting, this information can help practitioners identify at-risk populations and make positive strides to immigrant health outcomes.

Shelter-based health service delivery targeting chronically homeless populations: A systematic review & recommendations

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Introduction: The deinstitutionalization of the mental health system and lack of affordable and supported housing options have increased the representation of individuals experiencing substance abuse and serious mental health illness in the chronically homeless population living in emergency shelters. This population is also likely to report numerous chronic health conditions, developmental disability, and chronic physical illness and are more likely to die prematurely. In order to develop evidence-based policy recommendations, a systematic review of the literature was conducted to characterize the provision shelter-based health care services relative to traditionally accessed services. Outcomes included mental health, economic, and community related indices.

Methods: Data sources included (1) computerized databases: Medline, Elsevier's Embase, the Canadian Public Policy Collection, The International Encyclopedia of the Social and Behavioural Sciences, Cumulative Index to Nursing and Allied Health Literature (CINAHL); (2) citations in articles reviewed; and (3) references provided by the expert panel.

Results: Fifteen articles were identified for review that met the inclusion and exclusion criteria. Most (71%) were from the United States. Interventions offered were heterogeneous and ranged from a medically managed alcohol intervention to holistic health services coordinated across various agencies. Evidence was summarized for an expert panel and the quality of the data was graded.

Conclusion: Interventions targeting the chronically homeless are diverse and likely influenced directly by the social and environmental factors of any given community. Due to the complex needs of this subgroup, integrated services are likely required and recommendations are developed based on the quality of the evidence and expert opinion. A delineation of services offered in the city of Calgary is articulated and policy recommendations are discussed.

Post dural puncture headaches in the emergency department: a GRADE-based evaluation of the research evidence and recommendations for practice

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Introduction: Spinal subdural access is commonly indicated to acquire cerebrospinal fluid (CSF) in provision of diagnostic information, to administer anesthetic agents, or perform specialized imaging studies. Occasionally, inadvertent dural puncture also occurs as a complication of the administration of epidural anesthesia. Resultant decrease in CSF volume may lead to intracranial hypotension and subsequent cerebral vasodilation, with traction of pain sensitive intracranial structures and vessels. The resulting symptom is a headache. These post dural puncture headaches (PDPH) are the most common complication of lumbar punctures, occurring in up to 70% of patients post-LP. At present, no consensus exists for the appropriate treatment of those patients presenting to the emergency department with a PDPH. This study employs the GRADE methodology to evaluate the quality of evidence and develop recommendations for standard treatment practices for those patients with PDPHs presenting to the emergency department.

Methods: The OVID Medline research database was used as the primary source for identifying studies. Secondary searches were conducted on PubMed, EMBASE, and the Cochrane Database of Systematic Reviews. The Guideline Development Tool (GRADE Working Group) was used to create evidence profiles.

Results: A total of 292 papers were identified comparing alternative treatment options for PDPH, from which 31 papers met all inclusion/exclusion criteria. Results indicated a weak to moderate quality body of evidence in support of epidural blood patching, however with potential for significant effect. Weak, low quality evidence for other interventions was also described, including caffeine, gabapentin and triptan class medications.

Conclusion: Post dural puncture headaches of significant severity warrants epidural blood patching (moderate evidence, strong recommendation). Further trials are required to provide sufficient evaluation of the potential benefits and harms of epidural blood patching and other therapeutic interventions.

Prenatal programming of mental Illness: possible mechanisms and links to poverty

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Introduction: Maternal adversity experienced during pregnancy is a significant risk factor for poor long-term health outcomes in offspring, including chronic diseases such as diabetes or cardiovascular disease. Recent evidence suggests that this linkage may extend to mental illness. Detrimental prenatal conditions including undernutrition, exposure to alcohol/drugs, or maternal stress are more common in mothers of lower socioeconomic status. This relationship may explain the association of poverty with higher rates of psychopathology.

Methods: A literature review was undertaken examining the association between prenatal adversity and poverty with psychological outcomes. Using the PubMed database, a total of 101 papers were reviewed.

Results: Animal models have found that animals exposed to prenatal stressors are more likely to develop anxious and depressive behaviours, as well as increased behavioural and neurological abnormalities. Human studies have found significant links between in-utero stress and psychopathology; specifically, externalizing disorders, internalizing disorders, schizophrenia, and cognitive defects.

Conclusions: Children of mothers exposed to stress and poverty in pregnancy are at a high risk for developing psychopathology later in life. Mechanisms of this association may be explained by fetal programming, predictive adaptive responses, or epigenetic hypotheses. Interventions to improve prenatal conditions may help to reduce the incidence of future psychopathology.

A Cross-cultural Perspective on Tuberculosis in Tanzania: Parallels and Prophesies. Based on an International Medical Elective in Tanzania

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Introduction: Tuberculosis continues to be among the major public health concern in Tanzania. The number of tuberculosis cases detected has steadily increased six-fold from 1983 to 2006, due to not only improved screening mechanisms, but also the growing HIV epidemic, urban overcrowding and population growth. The largest cohort of patients is between 15 and 45 years, the same age group affected by HIV/AIDS. Within the past ten years, great steps have been taken to improve the network of TB clinics in Tanzania, with greater access to affordable treatment.

Methods: A review was undertaken to identify the challenges in addressing Tuberculosis in Tanzania, the role of the culture and coexisting epidemics such as HIV/ AIDS, and the effect of the disease burden from social and economic perspectives. Using a predefined search strategy, 43 articles were identified, 19 describing tuberculosis public health interventions in Tanzania. A proposal was constructed to strengthen existing prevention strategies and screening tools.

Results: Tanzania's Ministry of Health and Social Welfare established a strategy for their National Tuberculosis and Leprosy Program that outlines the interventions available to screen, diagnose and treat tuberculosis, with a focus on equity, gender mainstreaming, and accessibility to those most susceptible. Community-based projects in parallel to this framework supplement existing strategies and provide promising models tailored to the needs to particular communities.

Conclusions: The advantages of tailoring Tuberculosis public health interventions to the needs of each community are clear, as are the strategies that are streamlining information and services nationally. Considering that the fastest growing cohort of tuberculosis patients also have HIV/ AIDS, a proposal outlines including specific diagnostic screening protocols in HIV/AIDS clinics, a model that is in its infancy stages at the PASADA HIV clinic. Future research points to developing cost-effective analysis to direct the best combination of local measures.

Systematic review of pediatric Type 1 Diabetes RCTs

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Introduction: Many pediatric trials are published each year but criticism has been raised regarding the validity of the outcome measures used and the adequacy of reporting of the outcomes, measurement tools and their psychometric properties. Type I diabetes affects many pediatric patients worldwide and many pediatric Type I diabetes randomized controlled trials (RCTs) have been published. However, the extent of reporting problems in this area has not yet been evaluated. We aimed to identify gaps in outcome reporting and heterogeneity of outcomes and outcome measurement tools in pediatric Type I diabetes RCTs and to develop a database of outcome measures for diabetes researchers.

Methods: We searched Medline, Embase, CINAHL, Cochrane Central, and Cochrane SR for pediatric Type I diabetes RCTs. Two independent reviewers screened and extracted data on identified references. Variables extracted included: journal, sample size, participant age, type of study, intervention, control, and details of primary outcome and outcome measurement tools.

Results: While searches identified 8350 unique references, only 164 papers were included. Participant age ranged from 1-20 years. Of the included trials, 32% were of insulin-based interventions, 10% of diet-based treatments, 18% of education-based interventions. Approximately one third of trials **did not** identify a primary outcome. Of those that did, 62 trials (38%) reported at least one primary outcome and of these, 76% described one outcome as primary and 24% identified more than one. Of the 164 included trials, 74 (46%) failed to address safety or harms of their intervention of interest.

Conclusions: This project has identified gaps in the quality of outcome reporting in pediatric Type I diabetes trials published over the past 10 years, leading to recommendations for improvements in reporting standards.

A Broad Differential Diagnosis for Amyotrophic Lateral Sclerosis

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Introduction: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder involving primarily motor neurons in the cerebral cortex, brainstem and spinal cord. While ALS uniformly causes muscle weakness, respiratory failure and death within 3-5 years, the initial presentation can vary and be difficult to differentiate from other diseases early on in its course. ALS is diagnosed through careful history taking, neurological examination, neuroimaging, laboratory and electrophysiological studies. Although an early diagnosis is important, ensuring that other diseases are considered and ruled out is critical.

Methods: A systematic review of the literature was completed using Pubmed, Medline, Embase and the Cochrane Database of Systematic Reviews. All english, human studies were included with no time restrictions. Information extracted included all diseases that can be mistaken for ALS. The first phase of this review consisted of a pilot search to formulate a broad differential diagnosis of ALS based on studies reporting diseases initially misdiagnosed as, or presenting similar to ALS. Each reported case will undergo full text review to confirm that the presentation resembled ALS.

Results: Using this criteria we identified 35 diseases with similar presentations to ALS. Further information pulled from the literature included common and distinguishing features seen in each disease compared to ALS. One such disease, Kennedy's disease shares features with ALS such as atrophy, weakness and fasciculations in the limbs and face. Lack of upper motor neuron findings, endocrine and distal sensory symptoms can distinguish it from ALS.

Conclusion: The formation of an accurate differential for ALS will allow physicians to rule out appropriate conditions, ensure a thorough work up is completed and reduce the risk of misdiagnosis. The next phase in this study will consist of a systematic review that will establish an appropriate group of differential diagnoses for the clinician to consider when diagnosing ALS.

Methadone, patient education, and Vancouver's downtown eastside: A patient workbook.

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Background: Methadone maintenance treatment (MMT) was introduced almost 40-years ago as a means to treat opioid withdrawal symptoms (Health Canada, 2008). Vancouver's downtown eastside (DTES) neighborhood houses about 40% of all BC's injection drug users and, it is also home to several MMT programs. Patients that are prescribed methadone treatment for opioid dependence have many educational needs related to their treatment. People that reside in the DTES are confronted with many complex issues such as a higher prevalence of mental illness and physical disabilities, increased rates of communicable diseases, increased drug use, poverty, lower levels of education, inadequate housing and food shortages (Poh et al, 2007; Barbolet et al, 2005). The community represents a population that is complex and has multiple barriers, and special consideration should be taken when applying concepts of health care, including patient education.

Conclusion: The purpose of this project was to create a patient workbook for patients in the DTES that gives specific information to what methadone is, its common side effects, and safety measures while taking methadone. The goal was to present the material in a comprehensive and useful format for persons with a range of intellectual ability and cultures, with an interactive component that allows patients on MMT to actively participate in their treatment and health.

Tuberculous osteomyelitis/arthritis of the first costo-clavicular joint and sternum

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Background: The most common pyogenic causes of osteomyelitis are *Staphylococcos aureus* and *Pseudomonas aeruginosa*, whilst *Mycobacterium tuberculosis* (TB) is a rare causative pathogen in healthy individuals in the world. Risk factors for tuberculous sternal osteomyelitis include but are not limited to: being in or from an endemic area, poor access to health care, immune suppression, and nosocomial exposure to TB. Approximately 25 cases of TB sternal osteomyelitis have been reported in all peer-reviewed journals to date. Bone and joint TB infections account for approximately 6-10% of all extra-pulmonary TB cases and about 1% of all TB cases in the United States. Sternal TB osteomyelitis accounts for less than 0.3% of all osteomyelitis cases and 1% of all skeletal TB.

Case Presentation: A young Somali immigrant presented with a two-year history of a large, firm, painful right anterolateral chest wall sternal mass. The patient denied any history of trauma or infection at the site and was asymptomatic. A lateral chest radiograph demonstrated a low density mass isolated to the subcutaneous soft tissue overlying the sternum, ribs and clavicle. Computed tomography (CT) with contrast demonstrated a cystic lesion in the right anterolateral chest wall. Enhanced-CT of the chest demonstrated sclerosis and destruction of the rib and costochondral joint/manubrio-sternal joint narrowing. Ultrasound-guided biopsy and aspiration returned 500cc of purulent, cloudy yellow, foul-smelling fluid. Acid-fact bacilli stain and the nucleic acid amplification test (NAAT) identified and confirmed *Mycobacterium tuberculosis*. A diagnosis of tuberculous osteomyelitis/septic arthritis was made and anti-tuberculosis therapy was initiated.

Conclusion: TB infections may cause severe damage, which can be mitigated if detected with appropriate imaging and treated early. Recognizing that tuberculosis affects up to one third of the world’s population should compel physicians to consider a diagnosis of TB in patients with aforementioned risk factors.

Giant arachnoid granulation in a pediatric patient with a history of focal seizures

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Background: Arachnoid granulations are growths of arachnoid membrane that project into the dural sinuses. These sinuses are responsible for draining venous blood and cerebrospinal fluid from the subarachnoid space into the internal jugular vein. Although they are normally found as incidental findings measuring a few millimeters in the transverse and posterior superior sagittal sinus, arachnoid granulations may sometimes grow to fill and dilate the sinuses or expand the inner table of the skull. They normally do not cause symptoms from venous hypertension as a result of partial sinus occlusion.

Case presentation: An 8 year-old boy presented with a one year history of focal seizures and secondary generalization. Investigations were performed to rule out other causes of headaches and complications. Electroencephalography was conducted and was normal. Visual field and acuity was unaffected and a fundoscopic examination revealed a sharp optic disc with no arteriovenous nicking. Imaging studies including computed tomography [CT], magnetic resonance imaging [MRI] and magnetic resonance venography [MRV] were performed. Findings demonstrated a giant arachnoid granulation in the posterior third of the superior sagittal sinus.

Conclusion: The seizures were treated prophylactically with medical therapy and the patient responded well.

EGFR mutation and estrogen receptor positive lung adenocarcinoma in a male to female transgender patient following estrogen therapy: a case report.

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Background: Epidermal growth factor receptor (EGFR) mutation positive non-small cell lung cancer (NSCLC) is known to be prevalent in non-smoking women. A significant correlation exists between EGFR mutation and ER expression in patients with lung adenocarcinoma (LA). Studies suggest a relationship between high NSCLC tumour estrogen receptor β (ERβ) expression and poor prognosis. Higher ERβ expression has been shown in men with NSCLC and has been associated with metastasis in patients with LA and EGFR mutations. Further, targeting of ER and EGFR in vitro and in vivo models of LA demonstrated anti-proliferative effects when receptors were targeted in tandem.This is a case of a male to female transgender patient with an EGFR mutation and ER positive LA who received estrogen therapy for their transition. The standard dose of estrogen for sex reassignment results in circulating levels of estrogen that are greater than 10 times that of a male.

Case Presentation: A previously healthy 50-year-old male to female transgender patient presented to the ER with a seizure. Magnetic resonance imaging (MRI) suggested metastatic brain disease. Computed tomography (CT) showed a large primary tumour with widespread nodules bilaterally. The diagnosis of primary NSCLC was confirmed with bronchoscopy and biopsy. Pathology showed invasive LA. Bone-scan confirmed metastatic disease. Immunohistochemistry indicated the tumour was EGFR mutation positive and sensitive to the EGFR small molecule inhibitor, Gefitinib. The tumour was found to express high levels of the ER. Chemotherapy with Gefitinib was successful in limiting progression of the disease for several months. The patient passed away a year after diagnosis from progressive disease.

Conclusion: There is evidence that ER plays a role in lung cancer onset and that its expression has negative implications for prognosis, especially in EGFR mutant LA. This case highlights the potential cooperative role of ER and EGFR in NSCLC progression.

Minimizing the peri-induction risks of hypertrophic obstructive cardiomyopathy: a case report.

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Background: Hypertrophic obstructive cardiomyopathy (HOCM) is a cardiac condition that is especially susceptible to hemodynamic changes during the peri-induction period. There are no current guidelines for the anesthetic management of HOCM. We present a case of HOCM that was diagnosed following a peri-induction cardiac arrest.

Case Presentation: A 54 year male was brought to the emergency room (ER) of a tertiary hospital by paramedics after striking a car while riding his motorcycle at high speed. The patient was responsive, alert and oriented, and complained of pain in his thoracic spine and difficulty breathing. He was able to respond to commands with his upper limbs. He had normal sensation, but no motor function to his lower limbs. The patient's heart rhythm was atrial flutter at a rate of 160, blood pressure 96/45, respiratory rate 28. Chest xray showed no pneumo/hemothorax or widened mediastinum. Pelvic xray showed an acetabular fracture. Bedside ultrasound identified no significant source of blood loss. The decision was made to secure the airway and obtain a computed tomography (CT) scan. The patient was given rocuronium, propofol and fentanyl, and intubated successfully on the first pass. After initiating ventilations with a transport ventilator the patient deteriorated and had no palpable pulse. The patient received bilateral chest tubes and return of spontaneous circulation was achieved following 2 rounds of cardiopulmonary resuscitation and 1mg epinephrine. CT was obtained, which identified a T9-10 vertebral dislocation, a large heart, and no additional source of bleeding. After admission to ICU the patient deteriorated again, and a TEE demonstrated HOCM, which was determined to be the cause of his arrest.

Conclusion: If there is a known diagnosis of HOCM, measures can be taken to minimize the risks of induction and intubation. These include maintaining adequate preload and afterload, maintaining sinus rhythm, and minimizing increases in sympathetic tone.

Arteriovenous malformation of the upper lip: a case report and literature review

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Background: Arteriovenous malformations (AVM) are congenital malformations of abnormal connections between arteries and veins. Most occur intracranially. However, the case presented here involves the face. Initially AVMs are asymptomatic, but they progress, causing ischemic pain, ulceration, and bleeding, disfiguration and psychological distress. Ultimately, they must be fully resected to prevent disfiguration, dysfunction and recurrence.

Case Presentation: A 6-year-old girl was referred to the vascular birthmark clinic for an upper lip mass. On examination, the lip appeared swollen and the lesion felt soft and pulsatile. We noted red-purple discoloration of the hard palate and abnormal dentition. Clinically, speech was affected. Imaging showed the AVM to be supplied mainly by the left facial artery. No bony involvement has been shown but the maxillary bone is thinned. The location of the lesion is a challenging area to resect an AVM and perform a reconstruction, as it is a crucial subunit of the face both in terms of functionality and aesthetics. Consequently a literature review was performed to determine current standard of care for lip AVM.

Literature Review: Eighteen articles were found of which a majority were case reports. The review determined current standard of care for lip AVM was embolization with surgical resection 24-72 hours post-embolization. The majority of articles mentioned the key role of a multi-disciplinary team and the value of pre-intervention diagnostic imaging. Knowledge of the anatomy of the lesion was of utmost importance in embolization and excision.

Conclusion: Following extensive pre-operative imaging and consultation with two pediatric plastic surgeons and an interventional radiologist at the Alberta Children's Hospital and an external consultation with the Boston Children's Group we plan for the patient to undergo embolization of the main AVM feeding vessels, followed by resection 24-48hrs later through an inner lip mucosal approach with no removal of palate, teeth or skin of the upper lip.

Exploring linkages of access to drinking water, sanitation and mortality in children under 5 years old in Africa

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Introduction: Access to water and sanitation are paramount to health: research has shown that inadequate water supply, sanitation and hygiene was the second leading cause of disease following malnutrition. This research aims to quantify the linkages between water and sanitation and its impact on child mortality.

Methods: Data, collected through the United Nations database, was captured for % population with access to clean drinking water, % population with access to improved sanitation and child mortality under five. Data was captured for countries in Africa from 1990 to 2012. Linear regression analysis was conducted in Prism.

Results: Initial analysis shows a trend between improved access to water and decreasing child mortality (R^2=0.51, $p<0.0001$), improved access to sanitation and decreasing child mortality (R^2=0.40, $p<0.0001$) and improved access to both water & sanitation and decreasing child mortality (R^2=0.55, $p<0.0001$). Between 1990 and 2012, Malawi had the biggest increase in % access to water (43% absolute increase). During this time period, child mortality dropped by 174.8 deaths per 1,000 live births. Rwanda had the highest increase in access to improved sanitation (34% absolute increase), and also showed a decrease in child mortality of 96.9 deaths per 1,000 live births.

Conclusion: Diarrheal disease incidence would be a better indicator but data was currently unavailable. Mortality was used as a marker since diarrheal disease is one of the leading causes of death in post-neonatal children. While these results appear to show a correlation between water, sanitation & child mortality, the issue is multifactorial and other variables are linked to mortality and may be exacerbated by lack of access to water and sanitation. Further multivariate analysis would be ideal to discern these relationships as well as efforts should focus on collecting data on diarrheal disease incidence and mortality.

A global health radio show as a novel method of participatory group reflection on an international medical elective: Insights from the University of Calgary Global Health Concentration

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Introduction: The increasing interest in global health has prompted a number of medical schools to develop and diversify opportunities for international exposure. There is better awareness of the ethical implications of medical students completing clinical training abroad. Consequently, it becomes more important that medical students can reflect appropriately on their participation in clinical electives.

Methods: The authors formed the current cohort of GHC students and completed electives in internal medicine and primary care in Tanzania in July 2014. We developed a novel method of reflecting upon our experiences. First, ethical issues were discussed in site-specific groups and then brought to the larger group at daily meetings. Next, we developed questions in key areas including health equity, contribution to medical care, reciprocity, and ethical medical practice. These questions were refined and researched amongst the student group. Then, we identified Tanzanian and Canadian preceptor mentors and sought consent to record structured interviews on our topics of interest to create a two-part radio show. The show aired on CKUT 90.3FM in Montreal on August 12, and August 19, 2014**,** and ongoing feedback continues via an associated blog.

Results: We utilized a group participatory and goal-oriented approach to unpack the ethical issues that arose with the participation of our local and international mentors. The collaborative discussions were pivotal in contextualizing the insights gained and fostered a unified approach to effect change in this setting. Additionally, interviewing local physicians allowed the GHC to improve relationships with these partners..

Conclusion: We recommend that medical students be guided to complete frequent and ongoing participatory group reflections in addition to individual introspective reflections. Key components of successful participatory group reflection include: i) site-specific group debriefs; ii) whole group debriefs; iii) development of key areas of concern or potential learning; iv) group research on these issues; v) development of structured questionnaires; vi) engagement with local and international mentors; and, vii) producing a tangible reflective outcome such as a documentary, audio, or written piece centered around the key themes identified and previously researched as a group.

“There is a lot of embarrassment”: Reflections of students and educators on sex education in West Bengal, India

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Introduction: Open discussion of sexuality is largely taboo in Indian society. In 2005, in response to the spiraling AIDS epidemic in India, the West Bengal government introduced a sex-education program called Jeebon Shoili Shikhya (Lifestyle Education) for implementation in secondary schools in the state. This research, conducted in the early stages of the program’s implementation, sought educator and student reactions on the design, content, execution and effectiveness of the Lifestyle Education program.

Methods: Personal interviews with 10 educators and one public official, and focus-group interviews with a total of 298 youth, were conducted during July and August 2006 in Kolkata (Calcutta) and the neighbouring Hooghly and Howrah districts of the state of West Bengal. Bilingual (Bengali and English) semi-structured interview guides were designed and pilot-tested before use. Interviews were audio-recorded with permission, transcribed, and coded for a thematic analysis.

Results: Educators described the challenges in implementing the program, including negative reactions of community members, parents and teachers. This widespread opposition led to the dilution of program content; very little information about sexuality and sexual health was ultimately conveyed to youth. Students expressed considerable dissatisfaction with the program. They were particularly frustrated at teachers’ palpable discomfort, which in turn caused students to also feel embarrassed. Students also expressed disappointment with the minimal information provided, and at the lack of written reference material.

Conclusion: Properly-designed and properly-executed sex education programs for youth are an important component in sexual health promotion, and in public health efforts to combat the global AIDS epidemic. In the years since the conduction of this research, intense debates have raged in West Bengal over the Lifestyle Education program; youth voices have been largely excluded in such discussions. This research suggests that youth strongly desire objective information and accessible resources, delivered without stigma, judgment or embarrassment.

Prevalence of myopia in school children in rural and urban regions of the Island of Cebu, Philippines

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Introduction: Prevalence studies in various ethnic populations and geographical regions have increased the understanding of the impact of genetic predisposition and environmental exposure on the development of myopia. This study aimed to determine the prevalence of myopia in school children in rural and urban regions of the Island of Cebu, Philippines and to compare the prevalence of myopia between these two settings.

Methods: Children at five selected schools were randomly sampled. Those children with amblyopia, strabismus or active eye infection and those children not of Pilipino ethnic origin were excluded. Eye examinations were conducted by five teams of senior optometry students under supervision. Visual acuity was assessed through use of Snellen, Lea's Symbols, or Tumbling E Charts. Objective refraction was performed using a streak retinoscope. Subjective refraction was then performed on each child whose uncorrected visual acuity was less than 20/20. Myopia was defined as a spherical equivalence $\leq$ 0.5 diopters.

Results: A total of 1272 children were included in this study. The mean age of the rural cohort was 10.6 ± 2.8 years and that of the urban cohort was 9.9 ± 1.9 years. The proportion of male children was 51.5% in the rural cohort and 51.7% in the urban cohort. The overall prevalence of myopia was 5.0%. The prevalence of myopia in the rural cohort (3.0%) was observed to be significantly less than that in the urban cohort (12.5%, $p = 0.00$). Myopia was associated with increased age.

Conclusion: The prevalence of myopia was significantly less in school children in rural regions than those in urban regions supporting the significant role of environmental exposure in the development of myopia.

Prevalence of Chronic Mountain Sickness in India

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Introduction: Chronic Mountain Sickness (CMS) is a maladaptation condition that can affect people who reside permanently at high altitude (HA). It is characterized by polycythemia, hypoxemia and dyspnea and can be fatal. Over 140 million people live permanently at HA around the world. Unfortunately, research into CMS is lacking and accurate data on prevalence of this condition do not exist for many regions around the world. In this study we sought to examine prevalence of CMS in the Indian Himalayas.

Methods: We surveyed 83 individuals (69 males) in eight towns across the HA districts of Sirmaur, Kinnaur and Lahaul and Spiti in Himachal Pradesh, India. Altitudes ranged from 2350m to 4150m. We used an adapted Qinghai CMS Scoring System to diagnose CMS. Information related to subject demographics, medical history, socioeconomic status and geography were collected to identify risk factors for CMS. Physiologic recordings of SpO_2 and pulse rate were made via pulse oximetry.

Results: Overall CMS prevalence was 6.17% and mean altitude was 3281m. At altitudes above 3000m, CMS prevalence rose to 13.73%. All cases of CMS were mild and there was a significant positive correlation between CMS scores and altitude ($R=0.784$, $p=0.0213$). Mean SpO_2 was 90.7% ± 0.4% and mean pulse rate was 80.3bpm ± 1.3bpm. SpO_2 significantly correlated with altitude ($R=-0.929$, $p<0.001$). In our study age, gender, and tobacco use were not independent risk factors for CMS. Individuals with CMS lived at higher altitudes than their non-CMS counterparts (3736.00m ± 113.30m versus 3279.80m ± 69.50m, respectively; $p=0.017$).

Conclusion: CMS prevalence in HA towns of the Indian Himalayas of Himachal Pradesh is 6.17% and 13.73% for towns above 3000m. Further research is required to determine prevalence of CMS in other regions of the world and to determine risk factors associated with CMS.

Global trends in the rate of cleft lip and palate: bridging the gap

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Introduction: Orofacial clefts are the most common craniofacial malformation of the newborn. Worldwide rates vary based on ethnicity and geography. We aimed to assess trends in the rate of cleft lip and palate (CLP) in a large number of countries across several world regions.

Methods: Preferred sources for data collection included national registries, regional registries, health ministries, and academic centers. When available, we captured the number of infants born with (1) cleft lip with or without palate (CL±P), and (2) isolated cleft palate (CP) from 1990 to 2013. Annual rates per 10,000 live births were calculated and countries were grouped according to World Health Organization (WHO) regions (Americas, Europe, South East Asia, Western Pacific, Africa and Eastern Mediterranean).

Results: Data was captured from 52 countries. According to most recent data, the highest total rates of CLP were reported in Venezuela (38 cases/10,000 births), Iran (36 cases/10,000 births) and Japan (30 cases/10,000 births). In total, 64% of infants had CL±P and only eight countries reported a higher proportion of CP compared to CL±P. Preliminary analysis of temporal trends were assessed within WHO regions from 1990 to 2013. The Americas reported significant increases in the rate of CL±P from 10.3 cases/10,000 births to 12.37 cases/10,000 births ($p = 0.01$) and total CLP from 13.5 cases/10,000 births to 15.3 cases/10,000 births ($p = 0.02$). No other WHO region demonstrated a significant change in CLP rate.

Conclusion: The rate of CLP has remained stable throughout much of the world, with an increase noted in the Americas. Analyses are limited by a paucity of data from certain regions (Africa, Eastern Mediterranean and Asia). Future efforts to develop comprehensive registries will allow for a more accurate assessment of the global burden of CLP.

What factors predict the fertility intentions and unmet need for contraception among young people in Kenya?

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Introduction: Kenya demonstrates high rates of fertility, teenage pregnancy, unsafe abortion, maternal mortality, and unmet need for contraception. Young people in Kenya demonstrate variable fertility intentions. To improve reproductive and sexual health services and the health outcomes of young people in Kenya, this report identifies the predictors associated with the desire to have children and with unmet need for contraception.

Methods*:* Kenyan data from the Integra Initiative 2012 household surveys was used. From the surveys, four groups of predictor variables were identified: socio-demographic, socio-economic, cultural/environmental, and individual life events. To assess associations between these predictors, young Kenyans' fertility intentions, and unmet need for contraception, multivariable logistic regression analyses were completed.

Results: Older age and having previous children was associated with higher odds of desiring children in two or more years among males and females. Males with a partner or an income above 1,000 Ksh/month had higher odds of desiring children within two years, than single males or those with lower income. Males who had experienced forced sex had higher odds of desiring children in two or more years. Females living with at least three people had higher odds of desiring children in two or more years. Older age and larger household sizes were associated with higher odds of unmet need for contraception among sexually active females.

Conclusion: Age, having previous children, and household size were predictive of females' fertility intentions. Age, having previous children, income, and experience of forced sex were predictive of males' fertility intentions. Reproductive and sexual health services should therefore target sub-groups of young people according to these gender-specific factors. Older age and larger household size were associated with unmet need for contraception, indicating contraceptive programs should target these women. Despite further research needed, evidently there are gender-specific and shared factors that predict Kenyan's fertility intentions.

Postictal Phenomena Affect A Return to Normal Activity in Children with Epilepsy

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Background: Following a seizure, patients with epilepsy have reported a multitude of symptoms in the postictal period, ranging from headache to psychosis, with varying degrees of frequency, duration, and severity. However, these phenomena have not been well characterized in children, and their impact on patient well-being is not understood. Therefore, the aim of this study is to characterize postictal symptoms in a population of children with epilepsy.

Hypothesis & Methods: We propose that in a subset of epilepsy patients, postictal symptoms will affect their ability to return to normal childhood behavior. To test this hypothesis, we used a questionnaire-based approach to characterize postictal symptoms, including type, frequency, and duration, in a population of children with epilepsy and we evaluated the impact these symptoms had on the ability of these children to perform their regular activities. Additionally, we sought to identify aggravating and alleviating factors.

Results: Our study aims to include 500 subjects. Data will be presented at the symposium.

Conclusions: With this preliminary study, we hope to further our understanding of symptoms experienced in the postictal period and gain a better understanding of how these symptoms impact the ability of children with epilepsy to perform their regular activities. To the best of our knowledge, this is the first prospective study of this type in the pediatric population.

Incidence of Clobazam associated behavioural changes in patients with Lennox-Gastaut syndrome: a single center case series.

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Introduction: Clobazam, a 1,5-benzodiazepine has been used in Canada for over thirty years to treat multiple seizure types in children. In 2011, Clobazam was approved by the FDA as adjunctive treatment for Lennox-Gastaut syndrome (LGS). LGS is a devastating childhood epilepsy syndrome characterized by the occurrence of multiple types of seizures and cognitive decline. Two randomized, controlled studies and a follow-up open-label study of Clobazam demonstrated impressive efficacy and safety, with behavioural abnormalities occurring in less than 10% of patients. The aim of this study was to investigate the use of Clobazam, and the incidence of behavioural side effects amongst patients with LGS at the Alberta Children's Hospital (ACH).

Methods: Data from all patients identified with LGS in the EEG database at ACH, between March 2000 and April 2012, were retrospectively extracted from medical records. Factors of interest for Clobazam discontinuation included: age, gender, starting dose, maximum dose, number of concomitant antiepileptic drugs, and MRI findings.

Results: 44 patients with LGS were identified and complete charts were available for 29 patients (69%) which comprised the study population. 19 (66%) of these patients were prescribed Clobazam at some point in their care. Of this group, 9 (47%) patients maintained therapy, 4 patients doing so despite negative behavioural changes. Behavioural changes leading to discontinuation occurred in 6 patients (30%). Starting dose was significantly higher in the group which experienced side effects ($p=0.04$) than the group that did not. Also of note, though not significant, was the higher incidence of MRI lesional findings and simultaneous AEDs in the group which experienced behavioural changes.

Conclusion: This study identified the incidence and variables associated with behavioural abnormalities in LGS patients who are treated with Clobazam. The incidences of aggression and hyperactivity in this study are much higher than that previously reported by other studies. Lower starting doses should be considered to avoid behavioural changes.

Using fMRI to image sensory networks in children with perinatal stroke

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Introduction: Perinatal stroke is a cerebrovascular event that occurs between 20 weeks gestation and 28 days of age. It is known to cause life long impairments including gross and fine motor difficulties, language and speech problems, behavioural abnormalities, and frequent seizures. Perinatal stroke is the most common cause of hemiparetic cerebral palsy, attributed primarily to disruptions within cortical motor regions in the brain. However, disturbances within sensory regions may be equally as important in contributing to functional deficits. Previous research has investigated resting-state motor networks using fMRI, and determined significant differences in connection strength between patients with perinatal stroke and controls. Therefore, we will attempt to determine if similar differences occur in resting-state sensory networks, and identify if there is a relationship between connection strength and sensory impairments.

Methods: Children are being recruited through the Alberta Perinatal Stroke Project based at the Alberta Children's Hospital. Resting-state data is collected on the 3T research scanner at the ACH. Children are asked to lie still with their eyes closed for a total of 5 minutes. Data is analyzed using the FEAT tool of FSL. Functional connectivity is computed between the primary sensory cortex (S1) of the non-lesioned hemisphere of the brain and every other brain voxel, given the intact structure of the region, to determine sensory network connectivity. The S1 of the lesioned hemisphere is also being used to determine connectivity with the non-lesioned S1, and will be reported as a correlation coefficient between the two.

Results: Data analysis is currently in progress and preliminary results will be discussed at the symposium.

Conclusion: Patients with perinatal stroke frequently present with hemiparetic cerebral palsy, which can cause motor and sensory impairments that negatively impact their daily functioning. By determining the underlying cause of these impairments, there is the potential to identify novel targets for therapeutic intervention. Similar research in motor networks has been translated into trials of brain stimulation, which has had a positive impact on motor function in patients with perinatal stroke. Studies of sensory networks have the potential to further these gains, and significantly improve patients' quality of life.

Predicting *PIK3CA* gene mutation based on gene expression in cervical cancer: a model for targeting gene sequencing to high yield samples

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Introduction: As novel gene mutations are identified as drivers of cancer using DNA sequencing, existing gene expression data can be repurposed if it can be used to identify those samples that are more likely to contain mutations. Using existing gene expression data to identify samples more likely to yield valuable sequence information can reduce the cost of further genetic analysis. We therefore propose a method for predicting the mutation status of specific genes based on transcriptome-wide gene expression.

Methods: Our training dataset included *PIK3CA* mutation status for 43 patients with locally advanced cervical squamous cell carcinoma (26 wild-type, 17 mutation carriers) along with corresponding Almac Xcel microarray(c) gene expression data. The classification to nearest centroids (ClaNC) method was used to rank genes by standard t-statistics and select class specific genes that form a signature used to differentiate those tumors with *PIK3CA* mutations. Error rates were predicted using 5-fold cross-validation. Validation of the method was not possible due to the absence of a test dataset.

Results: 14 specific gene expression probes were identified for each class (mutation carriers and wild-type) from 110,961 probes on Almac Xcel arrays. Error was estimated at 0.29 with 5-fold cross-validation.

Conclusion: Classification to nearest centroids is a promising method for predicting the mutation status of a specific gene based on gene expression microarray data. Predicted error rates may not be sufficiently low but are limited by small sample size. A larger training set may confirm this as a viable method for targeting resources to sequence samples more likely to contain mutations. A second dataset is required to validate the method and more accurately quantify error rates.

The Cartilage Boundary Lubricating Ability of Synovial Fluid Constituents

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Introduction: Articular cartilage is the tissue covering the ends of long bones that promotes the load bearing, wear resistant and low friction properties of a joint. Within the joint capsule, the constituents of synovial fluid adsorbed to the cartilage surface are in part responsible for facilitating the low friction environment and preventing osteoarthritic degradation. Dipalmitoyl phosphatidylcholine (DPPC) and hyaluronan (HA) are synovial fluid constituents that are yet to have their friction reducing properties fully clarified. Thus, the purpose of this study was to determine the *in-vitro* cartilage boundary lubricating properties of DPPC alone and in combination with HA at physiological concentrations.

Methods: Cartilage explants (n=6) were harvested from the patellofemoral groove of bovine stifle joints. Lubricants of interest were saline (control), DPPC, HA and DPPC+HA in a cartilage-on-cartilage friction test to determine static ($\mu_{static,\ Neq}$) and kinetic ($<\mu_{kinetic,\ Neq}>$) friction coefficients for each. A 2x2 factorial ANOVA was used to determine the effect of lubricant and pre sliding duration on $\mu_{static,Neq}$ and a one-way ANOVA to determine the effect of lubricant on $<\mu_{kinetic,\ Neq}>$ with Tukey post hoc testing.

Results: DPPC alone and HA alone both significantly ($p<0.05$) reduced friction ($<\mu_{kinetic,\ Neq}> = 0.089$ and 0.068, respectively) compared to saline ($<\mu_{kinetic,\ Neq}> = 0.156$). DPPC+HA also significantly reduced friction ($<\mu_{kinetic,\ Neq}> = 0.078$) compared to saline, but was not significantly different from DPPC or HA alone.

Conclusions: At physiologic concentrations, both DPPC and HA act as boundary lubricants at opposing articular cartilage surfaces. Their combination, however, does not create a synergistic effect to reduce friction further than either one independently. These results provide insight into the lubrication of articular cartilage by synovial fluid constituents and their potential application to biotherapeutic treatments for osteoarthritis.

Integrin α1β1 Regulates Chondrocyte Intracellular Smad2 and Smad3 Activation

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Introduction: The collagen receptor integrin α1β1 is utilized by chondrocytes to respond to and influence their extracellular matrix. We have shown that in its absence, chondrocytes are hypersensitive to fibrotic transforming growth factor-β (TGF-β) and insensitive to the inflammatory interleukin-1 (IL-1). It is currently unknown how the activation levels of signaling pathways downstream of TGF-β are affected. The purpose of this study was to measure the levels of Smad2/3 proteins in integrin α1-null chondrocytes.

Methods: Isolated femora and tibiae from wild type (BALB/c) or integrin α1-null mice were processed for immunohistochemical analysis of frozen sections. Antibodies against phosphorylated Smad2/3 (Ser465/Ser467, 1:100; Alexa Fluor® 647 secondary) and the nucleic acid stain Hoescht 33342 (0.1 mM)) were applied. Slides were imaged on an LSM 7 DUO (Carl Zeiss Ltd) confocal microscope prior to evaluation for pSmad2/3 presence by three experienced blinded graders.

Results: pSmad2/3 staining was punctate and colocalized to both the chondrocytic cytoplasm and nucleus. In the thicker tibial integrin α1-null sections, the domain of staining included chondrocytes in the superficial and deep layers in addition to the middle layer. More integrin α1-null chondrocytes stained positively for pSmad2/3 compared to wild type in both femoral (78% vs 73%) and tibial (78% vs 68%, $P<0.0001$) cartilage.

Conclusion: Our results suggest that integrin α1β1 suppresses the Smad2/3 pathway. Osteoarthritis observed in integrin α1-null mice is qualitatively similar to joints injected with excess TGF-β. Together with integrin α1β1's role in IL-1 and TGF-β signal transduction, our results may help to explain this phenotype The hypersensitivity to TGF-β of integrin α1-null chondrocytes translates into downstream pathways; nuclear colocalization suggests altered transcription. Harnessing the influence of integrin α1β1 on the canonical Smad2/3 pathway downstream of TGF-β may be crucial to the development of novel therapeutics for the treatment of osteoarthritis.

Laquinimod reduces neuronal caspase-6 activation and axonal degeneration in vitro

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Background: Laquinimod is an immunomodulatory compound that reduces relapse rate, brain atrophy and disability progression in multiple sclerosis. It has well-documented effects on inflammation, is widely distributed in the CNS and has been shown to ameliorate axonal damage in vitro and in vivo through an unknown mechanism. We have shown recently that caspase-6 is an important mediator in axonal degeneration, since sympathetic neurons derived from caspase-6 -/- mice do not degenerate when cultured in the absence of neuronal growth factor (NGF). We therefore investigated whether the beneficial effect of Laquinimod on axonal damage is mediated by caspase-6.

Methods: Cell-free and cell-based enzymatic activity assays were used to determine whether Laquinimod directly inhibits caspase-6. To investigate an effect on intraneuronal caspase-6 activity, primary cortical neurons were treated with camptothecin in the presence or absence of Laquinimod, and cleavage of the caspase-6 specific substrate lamin A was quantified by ELISA. Axonal degeneration of primary sympathetic neurons from the superior cervical ganglion (SCG) was induced by NGF withdrawal in the presence or absence of Laquinimod.

Results: Laquinimod did not directly inhibit caspase-6 activity in cell-free or transfection-based cellular systems. However, the presence of Laquinimod in camptothecin-stressed primary cortical neuron cultures led to a significant decrease in caspase-6 activation. In cultures of primary SCG neurons, Laquinimod partially protected axons from degeneration after NGF withdrawal, a process that is specifically dependent on caspase-6 activity, in agreement with the reduction of caspase-6 activity observed in stressed cortical neurons.

Conclusions: The beneficial effects of Laquinimod described so far involve neuroprotection through the downregulation of glial activation, whereas our findings represent a novel, purely neuronal mechanism of action. We propose that by preventing neuronal caspase-6 activation and axonal degeneration, Laquinimod might also provide benefits in other neurodegenerative disorders associated with excessive activation of caspase-6, such as Huntington’s disease.

Circulating Tumor Cells: Potential Prognostic and Predictive Virtual Biopsy --Enumeration and Biomarker Analysis of Circulating Tumor Cells

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Introduction: Circulating tumor cells (CTCs) are tumor cells that are disseminated in the blood. The number of CTCs enumerated using CellSearch (Veridex, LLC) has been FDA approved for predicting prognosis of patients with metastatic breast cancer, colorectal cancer, and prostate cancer. CTCs can also be used as a liquid biopsy which can be easily obtained from patients' peripheral blood to evaluate biomarkers.

Methods: We have set up the CellSearch system for enumerating CTCs and developed methods of quantitative protein biomarker analysis on CTCs. Due to the qualitative nature of the CellSearch system for biomarker analysis on CTCs, we developed quantitative biomarker analysis of CTCs using ficoll separation followed by fluorescent immunocytochemistry staining and AQUA analysis.

Results: Since interindividual variability in interpretation of CellSearch results has been previously reported, we completed a concordance study for our CellSearch System and result interpretation with Veridex using control samples. Our local enumeration results are similar to the Veridex results [Tom Baker Cancer Center (22±6) versus Veridex (22±3), n=7]. The CTCs were identified based on cytokeratin positive and CD45 negative staining. Biomarker quantification was performed by AQUA analysis of biomarker signals on the cytokeratin mask and CD45 mask. Using these methods, we have developed three markers for breast cancer CTCs, including Estrogen Receptor, Receptor Activator of Nuclear Factor κ B, and the Prolactin Receptor.

Conclusions: In conclusion, with these valuable platforms of CTC analysis established, we can evaluate novel prognostic and predictive factors for cancer metastasis.

Fatty acid synthesis in colorectal cancer: characterization of lipid metabolism in serum, tumour, and normal host tissues

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Introduction: Reprogrammed energy metabolism is one of the central hallmarks of cancer cells. Morbid obesity has been linked to colorectal cancer (CRC), and CRC is in turn associated with changes in fat metabolism. Our objective was to survey the serum fatty acid profile in CRC, and to identify contributory alterations in enzymes involved in fatty acid metabolism that reside in tumour and normal host tissue.

Methods: Gas and liquid chromatography-mass spectrometry were employed to characterize fatty acid metabolite abundance in serum from individuals with CRC (stage I-IV) and age- and gender-matched disease-free controls. Transcription of the IGF-1 signaling axis and the downstream lipogenic pathway were quantified using real-time PCR in liver metastases and non-cancerous liver tissue from a subset of the same patient population.

Results: Serum metabolites central to endogenous fatty acid synthesis were increased in individuals with CRC, generally increasing with stage. IGF-1 levels were significantly higher (p-value = 0.004) in non-cancerous liver from individuals with CRC. The receptor, IGF-1R, was highly expressed within tumour tissue. Tumour expression of the fatty acid synthetic transcription factor, SREBP1c, was also high. SREBP1c expression was significantly correlated with tumour expression of fatty acid synthase ($R^2=0.71$, p-value < 0.0001), a downstream enzyme central to fatty acid synthesis. However, expression levels of other lipogenic enzymes were variable and did not correlate with SREBP1c.

Conclusion: Circulating fatty acids are altered in CRC. Tumour contributes to this abnormal pool of fatty acids, due in part to increased expression of SREBP1c transcription factor. We speculate that this is driven by host-derived IGF-1, which in turn is stimulated by a tumour-derived factor. Further mechanistic studies will be required to understand the associations reported and to understand the clinical implications of these observations.

Reverse Remodeling and the Relationship to Survival in Patients who have Undergone Cardiac Resynchronization Therapy: A Systematic Review and Meta-analysis

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Introduction: Cardiac resynchronization therapy (CRT) uses low voltage stimulation to facilitate efficient contraction of the ventricles and has been shown to reduce morbidity and mortality among select heart failure (HF) patients. Favourable left ventricular reverse remodeling is often used to assess CRT benefit post implant. However, the current literature on left ventricular reverse remodeling and its relationship to reduced mortality in patients who have undergone CRT has yet to be evaluated in a review. Hypothesis: Left ventricular reverse remodeling promotes survival and can be used as a reliable prognostic marker of CRT benefit.

Methods: 6 electronic databases were searched from 1950 to January 2014 for randomized trials reporting left ventricular reverse remodeling with CRT versus control therapies in HF patients. Left ventricular reverse remodeling is predefined as a relative reduction in left ventricular end systolic volume (LVESV) and/or an absolute increase in left ventricular ejection fraction (LVEF) with CRT versus control, assessed via echocardiography (echo).

Results: The pooled mean increase in LVEF was 3.5% (9 studies, p-value <0.001) and the pooled relative reduction in LVESV was 13% (7 studies, p-value<0.001). A greater increase in LVEF and larger percent reduction in LVESV were both associated with a lower risk of death.

Conclusion: Cardiac resynchronization therapy (CRT) produces a significant increase in left ventricular ejection fraction and reduction in left ventricular end systolic volume (relative to control therapies). The clinical implication is that left ventricular reverse remodeling is not only increased post CRT, but this increase is associated with lower risk of death. As such, left ventricular reverse remodeling assessed using echo may be a clinically useful surrogate marker of improved survival and help prognosticate patients in the early stages of CRT recovery. Additional studies, including meta-analyses utilizing individual patient data may provide further insight into this relationship.

Obstructive Sleep Apnea Treatment Improves Arterial Stiffness and Alters Vascular Sensitivity to Angiotensin II in Humans

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Background*:* Obstructive sleep apnea (OSA) is a recognized risk factor for the development of vascular disease, particularly hypertension. Limited studies suggest a prominent role for the renin-angiotensin system (RAS), activation of which is deleterious to kidney and cardiovascular function. We sought to determine the effect of continuous positive airway pressure (CPAP) therapy on arterial stiffness and the RAS at baseline and in response to Angiotensin II (AngII), in humans with OSA.

Methods*:* Sixteen newly diagnosed (12 men, 4 post-menopausal women; 50±3y) OSA subjects (respiratory disturbance index [RDI]>15hr^{-1}) with nocturnal hypoxia [oxyhemoglobin saturation {SaO_2} <90% for >12% of night]) who were otherwise healthy were studied pre- and post-CPAP therapy (1 month of adequate therapy [>4h/night]). Subjects were studied in high salt balance, a state of maximal RAS suppression. Arterial stiffness (aortic augmentation index [AIx] and carotid femoral pulse wave velocity [PWV]) was measured by applanation tonometry at baseline and in response to a graded AngII infusion (3ng/kg/min·30min, 6ng/kg/min·30min, recovery·30min). The primary outcome was the effect of CPAP treatment on the AIx and PWV responses to AngII at 60 min and the recovery period.

Results*:* CPAP corrected OSA (RDI: 44±5 vs 4±1hr^{-1}, p=0.005; duration SaO_2<90%: 35±5 vs 5±2% of night, p=0.005) and reduced baseline AIx (20.6±1.7 vs 15.9±3.1%, p=0.024), but did not affect baseline PWV (8.44±0.53 vs 8.29±0.42m/s, p=0.6). There was a significant increase in AIx (8.8±1.1 vs 12.7±2.1%, p=0.044) and a non-significant decrease in PWV (1.16±0.37 vs 1.09±0.39m/s, p=0.6) sensitivity to AngII (all values pre- vs post-CPAP). There was no change in how quickly AIx returned to baseline after AngII challenge (1.3±1.6 vs 1.3±2.6%, p=0.8), but a more rapid recovery was observed with PWV post-AngII challenge (1.11±0.45 vs 0.41±0.21m/s, p=0.055).

Conclusions*:* Our preliminary observations suggest OSA treatment with CPAP may improve arterial stiffness through changes in vascular sensitivity to AngII.

Novel stress rescues homotypic stress-induced cannabinoid receptor downregulation

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Background: The paraventricular nucleus lies at the apex of the hypothalamic-pituitary-adrenal (HPA) axis stress response, and displays bi-directional plasticity. Synapses here respond to retrograde messengers including the ubiquitous endocannabinoids (eCBs). Both eCB and cannabinoid type-1 receptor (CB1R) signaling modulates the output of the HPA axis in response to stress. Our lab has previously demonstrated that in adolescent male rats, repetitive exposure to homotypic stress functionally downregulates CB1R signaling at synapses on parvocellular neuroendocrine cells (PNCs) in the paraventricular nucleus. Following stress exposure, CB1R function passively recovers over several days. Here, we hypothesized that recovery of CB1R signaling would be sensitive to synaptic and behavioural manipulations.

Methods: Experiments were performed using male Sprague-Dawley rats (post-natal day 21-35). The stress paradigm used was a mixed psychological and physical stressor, 30-min immobilization. In the novel stress condition a different stress paradigm (forced swim or predator odor) was substituted on the last day. Coronal hypothalamic brain slices were prepared for in-vitro whole-cell patch clamp recordings of PNCs. Depolarization-induced suppression of inhibition (DSI) at GABAergic synapses was used to identify retrograde short-term plasticity and activation level of CB1R.

Results: GABA synapses in PNCs of naive animals show robust depolarization-induced suppression of inhibition (45.2 ± 4.9% inhibition of post-synaptic currents, $n=28$, $p<0.01$), which is eliminated following 5-day immobilization stress (10.6 ± 2.5%, $n=26$, $p<0.01$). Interestingly, exposing an animal to a novel forced swim stress on the fifth day causes a robust recovery of CB1R signaling (63.1 ± 9.3%, $n=7$, $p<0.01$). eCB signaling is also completely recovered with low frequency stimulation (1Hz, 10 min) of PNCs following 5D stress, suggesting that novel stress may modify CB1 signaling through alterations to presynaptic activity state.

Conclusions: These observations indicate that eCB signaling is labile and can be regulated in a bi-directional manner by homotypic and novel stressors.

Administration of a cannabinoid receptor 1 agonist rescues learning and memory behaviors after a traumatic brain injury in male rats.

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Introduction: TBI is one of the major causes of central nervous system dysfunction leading to cognitive impairments. Nearly 1.7 million people in United States suffer from traumatic brain injury (TBI) annually. To date, there is no effective treatment to rescue or recover the learning and memory functions following a TBI. Previous studies have elucidated several pathological consequences of TBI which include excitotoxicity, neuroinflammation, and disrupted metabolic functions. The cannabinoid receptor 1 (CB1R) is a G-protein coupled receptor that can reduce excitotoxicity and neuroinflammation, and can modulate mitochondrial functions.

Methods: We tested the hypothesis that administration of a CB1R agonist (arachidonyl-2'-chloroethylamide, ACEA) after a TBI would rescue learning and memory-linked behaviors. To test this hypothesis, we randomly assigned young adult male Sprague-Dawley rats (n=33) into five groups i.e. TBI + drug (n=8), TBI + vehicle (n=8), sham + drug (n=6), sham + vehicle (n=7), or naïve (n=4). All the groups were subjected to either a controlled cortical impact (CCI) injury or sham injury followed by the administration of ACEA (1 mg/kg) or vehicle daily for one week. We conducted Morris water maze (MWM) and novel object recognition task (NOR) to determine the post injury memory retention.

Results: The results showed that CCI-injured (TBI + vehicle) rats exhibit significant deficits in the memory-associated Novel Object Recognition and Morris Water Task tests. In contrast, the CCI-injured rats that received the ACEA treatment showed no deficits in their ability to do these tests, and their behaviors were indistinguishable from naïve animals despite an obvious brain lesion.

Conclusion: The results presented here suggest that cannabinoid agonist treatment could potentially be beneficial for the treatment of traumatic brain injuries. However, future studies should focus more on the risks of a cannabinoid treatment plan and its implications to justify its use in patient population.

The Role of CIC in Neural Progenitors

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Introduction: Oligodendrogliomas (ODG) are distinctive brain tumors composed of cells resembling oligodendrocytes. Recently, the gene encoding the transcriptional repressor Capicua (CIC) was identified as mutated in most ODGs with concurrent 1p/19q loss and IDH1/2 mutation – a genetic signature rare in other cancers. Mutation of the retained 19q CIC allele is likely functionally important, but how it contributes to ODG biology is unknown. We hypothesize that CIC, through its transcriptional repressor function, may restrict OPC proliferation, migration, or differentiation to the correct time and place in neurodevelopment. The aims of this study are to characterize the temporal and spatial expression of CIC in the normal cerebrum, and to determine the effect of CIC loss on neural progenitors.

Methods: To characterize temporal and spatial expression of CIC in the normal mouse cerebrum, we examined CIC expression throughout development using immunofluorescence staining. Double labeling was performed to determine which cells types express CIC. CIC biologic functions were examined using loss-of-function approaches *in vitro* and *in vivo*. CIC-knockout and CIC-wild type cell lines were created *in vitro* from CIC conditional knockout mice, and used to study cell growth, proliferation, and cell fate specification. As well, CIC or control shRNAs were co-electroporated with GFP into neural progenitors *in vivo* using *in utero* electroporation. Brains were harvested at 2 and 4 days post-electroporation, and GFP+ cells were examined for location, proliferation, and cellular identity.

Results: CIC was found to be widely expressed throughout normal murine brain development, with expression becoming increasingly nuclear between postnatal days 0 (P0) and 7 (P7). CIC co-expressed with markers of progenitor fate in both embryonic and adult progenitor pools, as well as markers of neuronal and astrocyte fate at P7. However, CIC did not predominately co-express with markers of oligodendrocyte fate at this age. In functional studies, ablation of CIC *in vitro* resulted in an increase in cell number, viability, and sphere volume when compared to controls. *In vivo*, transient transfections of CIC shRNA resulted in increased proliferation in the murine cortex. Analysis of cell fate showed a decreased expression of early neuronal and oligodendrocyte markers *in vitro* following CIC ablation, and an increased expression of glioblast markers *in vivo*. As well, significant abnormal cellular localization was found in CIC shRNA electroporations when compared to controls.

Conclusions: Our data supports a role for CIC in regulating several processes in neural progenitors that are relevant to cancer – proliferation, migration and, cell fate specification. CIC loss due to mutational inactivation may bias progenitors to a precursor cell fate and de-repress proliferative controls, resulting in conditions that promote oligodendroglioma formation.

Vaccinia Virus B4R-Null Mutants Exhibit Decreased Virus Spread

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Introduction: The *Poxviridae* is a large family of viruses whose members infect a wide variety of hosts. The most well-known member, variola virus, is the causative agent of smallpox, a disease that killed more humans in recorded history than all other infectious diseases combined. Though smallpox was eradicated in 1977, other poxviruses cause clinically relevant infections, and recent outbreaks of monkeypox underline the importance of studying these viruses. Vaccinia virus (VACV), the prototypic poxvirus, produces two types of infectious virions: mature virions and extracellular virions. Extracellular virions undergo additional membrane-wrapping steps compared to mature virions, and remain associated with the cell until they stimulate actin rearrangement. This work characterized the role of the VACV ankyrin/F-box protein B4R in virion morphogenesis, release, and spread.

Methods: Recombinant viruses devoid of B4R were generated and compared to parental viruses using the functional assays described below.

Results: Viruses devoid of B4R had a reduced plaque size in tissue culture, and decreased ability to spread, as assessed by multiple step growth analysis. Electron microscopy indicated that B4R-null viruses still formed mature and extracellular virions; however, there was a decrease of virions released into the media following deletion of B4R. Notably, confocal microscopy revealed that deletion of B4R did not affect the ability of the virus to rearrange actin; however, the VACV large deletion mutant, VACV811, which is missing 55 open reading frames, had decreased ability to produce actin projectiles, suggesting that additional mediators of actin rearrangement exist in VACV. Using an *in vivo* mouse model, we demonstrate that ectromelia virus devoid of EVM154, the homologue of B4R, was unable to spread to organs following infection of C57BL/6 mice.

Conclusion: Our results indicate that B4R is a mediator of virus spread, and suggest that additional unidentified mediators also exist in VACV.

Determining the downstream signaling pathways involved in the prostaglandin E_2-mediated repression of inflammatory mediator output in human myometrial cells

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Introduction: While prostaglandin production is increased in human labour, the precise role remains unclear. Our group has previously shown that prostaglandin E_2 (PGE_2) inhibits spontaneous myometrial contractions and represses interleukin-1 -1 -induced inflammatory mediator output by human myometrial cells. The biological effects of PGE_2 occur via activation of the G protein coupled receptors EP_1-EP_4. The EP_1 and EP_3 subtypes are coupled to G q and G of cAMP production, respectively. In contrast, both EP_2 and EP_4 couple to G s and stimu cAMP production. Subsequently, cAMP may activate multiple pathways, including protein kinase A (PKA) and/or exchange proteins directly activated by cAMP (Epacs). The objective of this study is to determine the downstream signaling pathways involved in the PGE_2-mediated repression of inflammatory mediator output.

Methods: Lower segment myometrial biopsies were collected from term elective Caesarean deliveries prior to labour onset and used to isolate myometrial cells (n=5, 37-40 weeks gestation). Cultured myometrial cells were treated with IL-1 esence or absence of PGE_2, specific EP agonists or PGE_2 +/- cAMP analogues selective for PKA or Epacs. Inflammatory mediator output (CXCL8, CCL2, CSF2) was measured by ELISA.

Results: IL-1 0.001). The CXCL8, CCL2, a mediated effect was repressed by pre-treatment with PGE_2, an EP_2 selective agonist, an EP_4 selective agonist, and PKA-selective cAMP analogues ($p<0.05$), but not Epac-selective cAMP analogues.

Conclusion: The PGE_2-mediated repression of IL-1 -induced inflammatory mediator output in human myometrial cells occurs through activation of the EP_2 and EP_4 receptor subtypes, but not EP_1 or EP_3. Based on the use of selective pharmacological agents, the downstream signaling pathways involved in this effect are likely mediated by PKA, but not Epacs.

Synergistic effects of human rhinovirus and bacterial infections in induction of CCL20 from human bronchial epithelial cells

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Introduction: Human rhinovirus (HRV) infections trigger acute attacks of lower airway diseases, such as chronic obstructive pulmonary disease (COPD). These attacks are life-threatening and lead to loss of lung function. HRV-infected airway epithelial cells release both proinflammatory mediators, and antiviral/host defense molecules that regulate viral growth and reproduction. CCL20 stimulates innate and adaptive immune responses by recruiting immature dendritic cells to airway mucosa. COPD patients' airways are often chronically colonized by bacteria, such as nontypeable *Haemophilus influenzae* (NTHI) and *Pseudomonas aeruginosa* (PAO). Few studies have examined the effect of bacterial infection on epithelial response to HRV. We hypothesize that the combination of HRV and bacterial infection will modulate CCL20 production relative to that of either stimulus alone.

Methods: Human bronchial epithelial cells were isolated from donor lungs and cultured in Bronchial Epithelial Growth Medium. Cells were grown to near-full confluence, and stimulated with medium containing either HRV, bacteria (NTHI or PAO), or a combination of HRV and bacteria. After 6, 12, and 24 hours, supernatants and cells were collected for CCL20 protein and mRNA quantification, respectively.

Results: While both HRV and the bacteria alone induced production of CCL20, the combination of bacteria and HRV caused synergistic expression of both protein and mRNA levels. Time-course data obtained for NTHI and HRV indicated that HRV induced maximum CCL20 steady-state mRNA production at 6 hours, which then dropped off at 12 and 24 hours, while protein levels increased gradually through the time-course. When HRV and NTHI were combined, CCL20 mRNA levels were maintained across all three time-points.

Conclusion: HRV and bacteria synergistically induce CCL20 mRNA and protein expression. NTHI appears to stabilize CCL20 mRNA induced by HRV**.** This study should provide new insights into the immune response to HRV in airways already colonized by bacteria and may identify novel therapeutic targets.

The Scavenger Receptor CD36 Recruits $\alpha_5\beta_1$ Integrin to Promote the Cytoadherence of *P. falciparum* Infected Erythrocytes

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Introduction: The adhesion of Plasmodium falciparum-infected erythrocytes (IRBC) to receptors on different host cells plays a divergent yet critical role in determining the progression and outcome of the infection. Based on our ex vivo studies with clinical parasite isolates from adult Thai patients, we have previously proposed a paradigm for IRBC cytoadherence under physiological shear stress that consists of a recruitment cascade mediated largely by P-selectin, ICAM-1 and CD36 on primary human dermal microvascular endothelium (HDMEC). In addition, we detected post-adhesion signaling events involving Src family kinases and the adaptor protein p130CAS in endothelial cells that lead to CD36 clustering and cytoskeletal rearrangement which enhance the magnitude of the adhesive strength, allowing adherent IRBC to withstand shear stress of up to 20 dynes/cm^2. In this study, we addressed whether CD36 supports IRBC adhesion as part of an assembly of membrane receptors.

Methods: We examined the interaction between HDMEC and Plasmodium falciparum isolates using flow chamber's, atomic force and confocal microscopy in combination with loss and gain-of-function assays.

Results: The integrin $\alpha_5\beta_1$ does not support adhesive interactions between IRBC and HDMEC. Upon IRBC adhesion to CD36, the integrin is recruited either passively as part of a molecular complex with CD36, or actively to the site of IRBC attachment through phosphorylation of Src family kinases, a process that is Ca^{2+}-dependent. Clustering of β_1 integrin is associated with an increase in IRBC recruitment as well as in adhesive strength after attachment (~40% in both cases).

Conclusions: The adhesion of IRBC to a multimolecular complex on the surface of endothelial cells could be of critical importance in enabling adherent IRBC to withstand the high shear stress in the microcirculations. Targeting integrins may provide a novel approach to decrease IRBC cytoadherence to microvascular endothelium.

Giardia duodenalis cysteine-like cathepsin proteases disrupt and cleave a key homeostatic cytoskeletal protein, villin.

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Introduction: Disruptions of intestinal epithelial barrier and epithelial maintenance are implicated in the pathophysiology of a variety of intestinal disorders. *Giardia duodenalis*, a non-invasive protozoan parasite of the upper small intestine, closely associates with intestinal epithelial cells to induce pathophysiological effects resembling chronic inflammatory GI diseases, including intestinal epithelial barrier dysfunction via mechanisms that remain obscure. The *Giardia* genome contains genes for cathepsin B-, C-, and K/L-like cysteine proteases; however, their roles are largely unknown. The aims of this study were to characterize *Giardia* cathepsin activity as they infect human intestinal epithelial cells, and characterize their pathophysiological effects, particularly on cytoskeletal and tight junctional proteins.

Methods: *G. duodenalis* trophozoites (Assemblage A isolates NF, S2 or Assemblage B isolate GS/M) were co-incubated *in vitro* with human colonic monolayers (Caco-2) for 2 or 24 hours. *Giardia* trophozoite lysates, supernatants, and host cell monolayers lysates were isolated and incubated with cathepsin fluorogenic substrates to measure cathepsin activity. *Giardia* trophozoites pretreated with a broad spectrum cysteine protease inhibitor (E64d) were co-incubated with Caco-2 monolayers. Co-incubation of *Giardia* trophozoites with Caco-2 cells was also done in the presence of an MLCK inhibitor, ML-9. Caco-2 lysates were also incubated with *Giardia* trophozoite lysates in the presence of E64d. Host cell lysates were processed for Western blotting to assess effects of *Giardia* cathepsins on tight junctional integrity (ZO-1) or cytoskeletal proteins (Villin).

Results: *Giardia* trophozoites express intra-trophozoite as well as secretory/excretory cathepsin activity, in the presence or absence of Caco-2 monolayers, and in an assemblage-independent manner. No changes in cathepsin activity within host cells were detected in the presence of *Giardia* from either assemblage. Pretreatment of *Giardia* NF trophozoites with E64d inhibited *Giardia* cathepsin activity, but failed to block *Giardia*-induced ZO-1. However, pretreatment of *Giardia* trophozoites with E64d prevented the breakdown of villin, a key actin-bundling protein that is responsible for the homeostatic maintenance of epithelial microvilli. Co-incubation of Caco-2 and *Giardia* NF trophozoite lysates with E64d prevented villin breakdown. In addition, ML-9 prevented *Giardia*-induced cleavage of villin after 24 hours but not 2 hours of incubation.

Conclusion: *Giardia* trophozoites express and release cathepsin-like cysteine proteases. *Giardia*-induced villin, but not ZO-1, breakdown is mediated in part by cathepsin-like proteases, which may later be propagated by an MLCK-dependent pathway. This suggests that *Giardia* cathepsins at least in part contribute to this parasite's pathogenesis through a disruption of cytoskeletal proteins.

Intestinal Mucus in Giardiasis, and Effects of *G. duodenalis* on MUC2

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Introduction: *Giardia duodenalis*, a common non-invasive parasite of the human small intestine, causes malabsorptive diarrhea, and leads to post-infectious irritable bowel syndrome (PI-IBS) and extra-intestinal complications via unestablished mechanisms. We hypothesized that, while the mucus barrier plays a protective role in giardiasis, *Giardia* may disrupt this barrier by either depletion or degradation of mucin proteins, which may contribute to acute and chronic disease. The aims of this study are to characterize how *G. duodenalis* interacts with host mucus and assess its effects on the primary constituent of the mucus layer, mucin-2 (MUC2).

Methods: *Giardia* trophozoites were orally gavaged to C57BL/6 wild-type (WT) mice and $Muc2^{-/-}$ mice. Mice were weighed daily and sacrificed at the peak of infection. Intestinal tissues were collected and processed for trophozoite counts and histological staining. The liver and spleen were collected aseptically, homogenized, and plated on Columbia blood agar to assess bacterial translocation. Secreted products obtained from a 3hr incubation of *Giardia* trophozoites in PBS were co-incubated with purified human mucin, and MUC2 integrity was assessed by western blotting.

Results: $Muc2^{-/-}$ mice infected with *Giardia* had a higher parasitic load and failed to gain weight compared to the infected WT mice. Periodic acid-Schiff and Alcian blue staining showed that *Giardia* induced goblet cell mucin depletion in the WT mice, whereas it induced an aberrant hypersecretory response in the $Muc2^{-/-}$ mice. Staining with wheat germ agglutinin (WGA) confirmed these results. Infected mice showed increased bacterial translocation of aerobic and anaerobic species into the liver and spleen. Co-incubation of purified human mucin with *Giardia*'s secreted products showed degradation of MUC2 comparable to a positive control.

Conclusion: Mucus protects the host against parasite accumulation and *Giardia*-induced inhibition of weight gain. *Giardia* causes goblet cell mucin depletion and degrades MUC2. The disruptions are associated with increased bacterial translocation. These mechanisms may contribute to PI-IBS.

Comprehensively evaluating stakeholder experiences during the implementation of a single-entry model for elective surgery in Winnipeg: a multi-stakeholder national project under the CIHR Evidence-Informed Healthcare Renewal (EIHR) Roadmap Signature Initiative

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Introduction: With single-entry models (SEMs) for elective surgery, referrals are pooled, assessed and patients can see the next-available surgeon through a central intake process. The Winnipeg Central Intake Service (WCIS) is a SEM to manage patients awaiting hip or knee replacement surgery. We will elucidate the development, implementation and impact of the WCIS on health/health services. We used a pre/post mixed-methods case study approach to measure impact on six dimensions of quality: acceptability, accessibility, appropriateness, effectiveness, efficiency and safety.

Methods: Assessment of experiences, changes in viewpoints and acceptability towards SEMs were elicited using semi-structured interviews with patients, family physicians, orthopaedic surgeons, surgical office assistants and WCIS team members (policy-makers, managers and planner). Anticipated/unanticipated, desirable/undesirable implications of the WCIS were assessed at macro (provincial), meso (regional), micro (clinical/patient) levels.

Results: Seventy pre-implementation stakeholder interviews are complete: expectations have been divergent and acceptance of SEMs has been conditional not universal. Policy-makers and patients favour the WCIS for reduced wait times and better availability of patient care information (appointment dates, preparation for surgery etc.). Family physicians and surgeons appreciate the streamlined referrals but are concerned about loss of autonomy and potential to permanently improve access. While initially opposed due to increased workload, surgical office assistants remain optimistic as they work with the WCIS team to adapt to and simplify processes. Greater assessment of capacity and readiness for change would have improved initial uptake/awareness among stakeholders. Continual improvement based on stakeholder feedback will be critical for sustained success through better identification, assessment, response to patient and system needs.

Conclusion: Through collaboration with national partners/knowledge-users including Winnipeg Regional Health Authority and Manitoba Health, findings will be translated into policy and practice to improve the WCIS, patient experience and system performance while strengthening other existing SEMs and informing the design and implementation of future SEMs across practice areas and Canadian jurisdictions.

Smoking's influence on the risk of surgery for Crohn's disease is dependent on age at diagnosis

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Introduction: Crohn's disease (CD) is an incurable condition of the gastrointestinal tract that may result in surgery. The most commonly studied environmental risk factor, which worsen prognosis, is smoking. While smoking is decreasing in the general population, it is unclear if the prevalence of smoking is decreasing in the CD population, and if this influences prognosis. Therefore, we assessed the effect of smoking at CD diagnosis on the need for early surgery. We hypothesized that the prevalence of smoking is decreasing in CD and that this may be partially responsible for decreased need for surgery.

Methods: The Health Improvement Network was used to identify an inception cohort of adult CD (n=1519) patients from 1999-2009. Poisson regression explored temporal trends for the proportion of CD patients who never smoked prior to their diagnosis, and the risk of surgery within 3 years of diagnosis. Cox proportional hazard models assessed the association between smoking (current, ex-smoking, and never) and intestinal resection after adjusting for covariates. Effect modification was explored for age at diagnosis according to the Montreal Classification (17-40 years old, >40 years old).

Results: The proportion of patients without a history of smoking increased (incidence rate ratio [IRR]=1.03; 95% confidence interval [CI]:1.02-1.05). The rate of surgery within 3 years of diagnosis decreased among patients diagnosed from 17-40 years (IRR=0.96; 95% CI:0.93-0.98). Smoking at diagnosis increased the risk of surgery (hazard ratio [HR]=2.99; 95% CI:1.52-5.92) for patients diagnosed after 40, but not for those diagnosed from 17-40 years.

Conclusion: Our data support the hypothesis that the decrease in smoking prevalence may contribute to the decreased need for surgery. The proportion of newly diagnosed CD patients of all ages who never smoke is increasing over time. Interestingly, the effect of smoking on surgery is dependent on the age at diagnosis of CD.

Diffuse Myocardial Fibrosis and Early Strain Abnormalities in Asymptomatic Type 2 Diabetics Without Overt Cardiovascular Disease

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Background: In a cohort of type 2 diabetic patients without overt cardiovascular disease, we sought to explore the capacity of quantitative T1 mapping and feature-tracking based strain analysis to identify the presence of diffuse fibrosis and related pre-clinical systolic dysfunction.

Methods: Nineteen Type 2 diabetes patients with no prior cardiac disease and 13 age-matched healthy volunteers underwent a standardized imaging protocol on a 1.5T MRI Scanner (Avanto, Siemens, Germany) with cine imaging, native and post-contrast T1 mapping, and late gadolinium enhancement. T1 mapping was performed using saturation recovery single shot acquisition (SASHA) pulse sequence in basal and mid short axis views. Cine images were analyzed using a prototype feature tracking strain analysis tool (cvi42, Circle Cardiovascular Inc. Canada) for peak global circumferential and longitudinal systolic strain and peak longitudinal diastolic strain rate. Segmental T1 values were determined using custom software (MATLAB), averaged to a global mean T1 value per subject, manually excluding segments with artifact.

Results: Among diabetic subjects, mean age was 57±9 years, 7 (39%) female, and Hb_{A1c} range 7.5-9.9%. The mean age of healthy volunteers was 52±12 years, 2 (15%) female. The left ventricular ejection fraction was normal for diabetics and controls (57.9±2.6% versus 57.8±2.9%, respectively, p=NS). Strain analysis showed trends towards reduction among diabetics in peak longitudinal systolic strain (-15.2±1.5 vs -16.1±1.3%, p=0.08). Late enhancement was visually normal in all subjects. There was a significant increase in native myocardial T1 values in diabetics compared to controls (1176±32 ms vs 1149±20ms, p=0.0096) and decrease in post-contrast T1 values (578±64 ms vs 628±41 ms, p=0.019), consistent with diffuse myocardial fibrosis.

Conclusions: Quantitative T1 mapping in asymptomatic type 2 diabetic patients showed changes consistent with increased myocardial fibrosis, as compared to controls. A trend towards reduced systolic strain indices was also seen, despite preservation of ejection fraction. These markers show promise for the detection of pre-clinical cardiomyopathy in type 2 diabetes.

High frequency oscillations detected during simultaneous intracranial EEG-fMRI studies reveal localized epileptogenic tissue

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Background: Using current neuroimaging techniques, seizure cure is achieved in less than 50% of patients undergoing epilepsy surgery, often due to difficult localization of the epileptic tissue. In the past decade, high frequency oscillations (HFOs) have emerged as key biomarkers of epileptogenic tissue. Recorded via intracranial EEG electrodes (iEEG) on the cortical surface, HFOs emerge as brief, rapid oscillations at 80-500Hz, and appear to better predict positive surgical outcome than traditional localization techniques. We sought to determine whether HFOs could be detected when recording iEEG with simultaneous functional magnetic resonance imaging (fMRI), a technique that has never been performed before due to the harshness of the MR environment for recording EEG. Our aim was both to detect HFOs, and to characterize the fMRI activity associated with these events.

Methods: We recruited two patients undergoing intracranial video-EEG monitoring for seizure focus localization. Subjects studied with simultaneous iEEG-fMRI. HFOs were identified using an automated detection algorithm and used to generate parametric maps of active brain regions. These data were compared to maps generated by traditional analysis of epileptic spikes alone.

Results: HFOs were detected in both patients. Maps of fMRI activity associated with both epileptic spikes and with HFOs can be seen in Figure 1. In both subjects, analysis with HFOs provided new localization information: the widespread fMRI activity seen with traditional analysis became significantly more localized to the area adjacent to the active iEEG electrode when examining HFOs alone.

Conclusions: We found that HFOs could be detected when recording iEEG-fMRI, and the fMRI activity associated with these events is more localized than with epileptic spikes. We hypothesize that HFOs may serve as a more discrete source of fMRI activity than epileptic spikes, and this novel technique may open new avenues for seizure focus localization and ultimately significantly improve patient outcomes from epilepsy surgery.

Susceptibility weighted imaging detects early venous deoxyhemoglobin changes in a model of multiple sclerosis

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Introduction: Susceptibility weighted imaging (SWI) is a magnetic resonance imaging (MRI) method sensitive to deoxyhemoglobin. SWI has shown altered deoxyhemoglobin content in the venous vasculature of multiple sclerosis (MS) patients. Previously, using SWI, we had shown elevated deoxyhemoglobin content in mice with experimental autoimmune encephalomyelitis (EAE) during peak disease. Here, the aim was to investigate changes to deoxyhemoglobin content of the venous vasculature over time in the EAE model using serial in vivo SWI.

Methods: Mice induced with EAE (*n*=9) were imaged at 9.4T with 3D gradient echo with flow compensation for SWI at four time points: baseline, day 7 (pre-motor dysfunction), day 12 (onset of motor dysfunction) and day 16-18 (peak disease). Naïve control mice (*n*=3) were matched with EAE for imaging time points.

Results: Hypointensities (dark spots) on SWI, corresponding to changes in venous deoxyhemoglobin content, were observed at day 7 in EAE mice, before motor dysfunction was present. The number of SWI hypointensities did not change substantially amongst naïve controls over the imaging time points, but there was great heterogeneity amongst EAE mice over the disease course. In all EAE mice, the number of SWI hypointensities was at a maximum either before or at the same time as maximum motor dysfunction (maximum EAE clinical score), but never after.

Conclusion: These data support the theory that increased oxygen extraction fraction and hypoxia may take place early in the EAE disease course, which can be detected with SWI. The cause and significance of these alterations in venous deoxyhemoglobin content require further investigation.

Wild Wellness: A review of the health implications of play in natural spaces on childhood development and well-being

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Introduction: The last thirty years has seen increased attention on inquiry into the role of play and activity in green, natural spaces and its relation to childhood health and development. Previous studies have focused on a variety of topics including physical, mental, emotional and social health outcomes in children and adults. Here, I hypothesize that time spent in play and activity in natural spaces during childhood correlates with myriad positive health outcomes both in childhood.

Methods: This paper is a meta-analysis of existing literature and research that has examined the role of activity in natural spaces with concurrent and subsequent implications for individual and population-level health outcomes. Focus is placed on changes that activity in natural spaces, when compared with inactivity as well as activity in human-created spaces, have on physical, mental, emotional (individual-level) and social (population-level) outcomes for children's health. The paper concludes with an overview of public and private initiatives focused on encouraging activity in natural spaces implemented in Canada along with corresponding preliminary results in terms of participation and health outcomes.

Results and Conclusions: Cumulative insights shared in the field suggest that increased time spent in play and activity in natural spaces results in lowered morbidity both during childhood as well as in later adolescence and adulthood. The myriad positive health changes include reduced symptoms of attention deficit disorder (ADD), decreased reliance on antidepressant prescription medication, reduced stress and anxiety, reduced rates of obesity and high blood pressure, increased concentration and creativity, and improved self-esteem and body-image. Additionally, children who spend time playing in outdoor, natural spaces have improved interpersonal communication as well as improved social interaction and social cohesion during childhood and adulthood.

Harmless Commensal Microbial Neighbors Synergistically Trigger *Pseudomonas aeruginosa* Virulence Genes in Cystic Fibrosis

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Introduction: Cystic fibrosis (CF) is the most common lethal genetic disease among Caucasians. 90% of CF patients succumb to pulmonary failure from chronic respiratory infections. Traditionally, research has focused on a narrow spectrum of microorganisms as principal pathogens such as *Pseudomonas aeruginosa* (PA). The oropharyngeal flora (OF) have been implicated in enhancing pathogenesis of PA while acting as benign commensals, otherwise known as “synergens”. These interactions may skew the balance between clinical stability and acute pulmonary exacerbation, leading to hospitalization. The objectives here were to evaluate these interactions and construct synergen mutants to identify the pathway(s) involved.

Methods: Seven oropharyngeal-derived microbes were isolated from sputum of adult CF patients (*Streptococcus*. sp, *Rothia*. sp and *Actinomyces*. sp) and screened *in vitro* for affecting PA virulence gene expression in co-cultures. The ability of these ‘benign’ microbe ‘synergens’ to stimulate PA virulence genes was evaluated using transformed PA reporters harboring luciferase constructs for known virulence gene promoters. The luciferase light production caused by the co-culture vs. monoculture of PA was monitored to quantify 'synergen' activity by measuring changes in light production. Transposon libraries in the synergens were constructed with 8000 mutants screened.

Results: Up-regulation of PA virulence gene expression was seen for all 7 synergens tested. The virulence pathways affected were for quorum sensing or bacterial communication. The highest up-regulation was by *Streptococcus*. sp, with 1800-fold increased virulence gene expression in co-culture as compared to PA alone. From 8000 synergen mutants, 526 were isolated as hits involved in co-culture. 61 of these mutants were conserved in all PA reporters, suggesting common interaction pathway(s) triggered by the synergens. 35 mutants displayed 10-fold or greater activation in co-culture as compared to the wild-type, demonstrating a gain-of-function mutation.

Conclusion: We have found that seemingly harmless non-pathogenic oropharyngeal ‘synergen’ microbes can trigger virulence genes in PA found in CF patients. The production of secondary signaling molecules have been shown to influence pathogen virulence profiles by modulating bacterial cell-cell communication pathways. Understanding the way in which commensal microbes synergistically trigger virulence will lead to better treatment and management of CF.

Human macrophages provide a replication niche for B. cenocepacia to escape neutrophil killing and enhance bacterial replication

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Introduction: Pulmonary innate immunity protects against inhaled pathogens through a combination of defenses that include tissue-resident macrophages and recruited neutrophils. *B. cenocepacia* is an opportunistic pathogen that causes severe respiratory infections in immunocompromised individuals, particularly those with cystic fibrosis or chronic granulomatous disease. Infections are characterized by neutrophil infiltration and excessive inflammation. The ability of the bacteria to survive and replicate within macrophages may contribute to their ability to evade host inflammatory response and cause chronic infections.

Methods: The collaborative effects of human macrophages and neutrophils in controlling survival of *B.* cenocepacia were investigated by co-culture experiments. The number of bacterial colony-forming units was measured in cultures with and without macrophages and/or neutrophils over time. The profiles of inflammatory mediators produced from co-culture experiments were also examined.

Results: While neutrophils were more efficient than macrophages in phagocytosing *B. cenocepacia*, the bacteria were able to quickly replicate within primary monocyte-derived macrophages, which offered a large survival advantage compared to bacterial growth in media alone. Proliferation required entry into macrophages and neither macrophage-released factors nor macrophage lysates were capable of enhancing bacterial growth. Only when neutrophils were co-cultured in great excess of macrophages were they able to control the growth of *B. cenocepacia* and to dampen the release of inflammatory mediators from macrophages.

Conclusion: This study suggests that macrophages have a dominant effect over neutrophils in the ability to affect *B. cenocepacia* growth and that an excess of neutrophils is required to abrogate this effect. These observations are consistent with the massive infiltration of neutrophils during respiratory infection with *B. cenocepacia* and may explain the skewing of host defense toward neutrophilia in an attempt of the host to control infection.

The presence of a TRP-NCX signaling complex in the regulation of endothelial function

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Introduction: Appropriate release of nitric oxide (NO) is critical for normal physiological functioning of the cardiovascular system. Although changes in intracellular Ca^{2+} concentration ($[Ca^{2+}]i$) in endothelial cells (ECs) is thought to play an important role in the coordination of NO release, the molecular mechanism underlying this influx is poorly understood. Sustained Ca^{2+} influx in ECs has been widely assumed to be due to the presence of transient receptor potential (TRP) protein-containing non-selective cation channels (NSCC) in the PM. However, the non-selective nature of TRP channels for cations indicates that TRP channels can also act as a Na^{+} entry pathway. Na^{+} accumulation under the plasma membrane could then facilitate sodium-calcium exchanger (NCX) activity in the reverse, Ca^{2+} entry mode. The role of NCX as a Ca^{2+} entry pathway has yet been studied in detail in ECs.

Methods: Intracellular Ca^{2+} measurements were made with FURA-2AM fluorometry. The effect of luminal flow on arterial diameter was studied using pressurized myography in endothelium-intact rat cerebral arteries (RCAs). Co-localization of proteins was assessed using proximity ligation assay (PLA). A three-step method of western blotting was utilized to detect eNOS phosphorylation at Ser1177.

Results: We identified the presence of a signaling complex comprised of stromal interaction molecule 1 (STIM1), transient receptor potential protein (canonical subtype) 1 (TRPC1), and the Na^{+}/Ca^{2+}exchanger 1 (NCX1) in cultured ECs. Inhibition of NCX by KB-R7943 significantly impaired agonist-induced phosphorylation of endothelial NO synthase (eNOS) at serine 1177 (S1177-eNOS). Recruitment of the NCX in reverse mode was also shown to play an important role in flow-mediated dilation (FMD) and the corresponding phosphorylation S1177-eNOS.

Conclusions: Our findings suggest that a TRP-NCX signaling complex mediates Ca^{2+} influx leading to a rise in $[Ca^{2+}]_i$, NOS activation and NO release to evoke FMD in cerebral artery.

The myeloid derived suppressor cell chemoattractant, MCP-1, is upregulated in the absence of TLR4 in the IL-10 deficient colon

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Introduction: The myeloid derived suppressor cell (MDSC, Gr1+CD11b+) is a protumorigenic cell type with immunosuppressive and pro-angiogenic functions. Our previous work has established that MDSC are recruited to the gut in the interleukin-10 deficient mouse (IL-$10^{-/-}$). In the absence of Toll like receptor 4 (TLR4) in the IL-$10^{-/-}$ mouse we find elevated MDSC levels and increased cancer development in the colon. The aim of this work was to study the recruitment of MDSC in this model.

Methods: MDSC chemotaxis was studied *in vitro* using transwell chambers. MDSC were isolated via percoll gradient centrifugation of bone marrow cells isolated from IL-$10^{-/-}$ and IL-$10^{-/-}$TLR$4^{-/-}$ mice at 3 months of age (purity: 80-95%). $5x10^5$ MDSC were placed in the upper chamber, chemoattactants in the lower chamber and the chambers are placed in 37*C for 3 hours. Migrated cells were cytospun onto slides and labeled with Gr1 and CD11b antibodies and double labeled cells were counted as MDSC.

Results: fMLP (5-100nM) and KC (10-150nM) are not MDSC chemoattractants. MDSC are chemoattracted to monocyte chemotactic protein 1 (MCP-1, 100ng/ml) and stromal derived factor 1 (SDF-1, 150ng/ml). Chemotactic response towards MCP-1 and SDF-1 was comparable in MDSC derived from IL-$10^{-/-}$ and IL-$10^{-/-}$TLR$4^{-/-}$ mice. MCP-1 protein level as determined via western blot analysis and standardized over actin protein levels. MCP-1 protein was detectable in the ascending and descending colons of IL-$10^{-/-}$ at 6 weeks and 6 months of age. Interestingly, MCP-1 protein levels were higher at both age 6 weeks (0.43 ± 0.05 vs 0.14 ± 0.03) and 6 months (0.75 ± 0.20 vs 0.14 ± 0.06) in IL-$10^{-/-}$TLR$4^{-/-}$ mouse colons compared to IL-$10^{-/-}$.

Conclusions: Our data show that MCP-1 and SDF-1 are chemoattractants for MDSC in the IL-$10^{-/-}$ model. The elevated MCP-1 protein levels in the absence of TLR4 in this model may explain the enhanced recruitment of these cells and increased cancer development.

Rapid degradation of the macrophage cytoskeleton upon contact with the gastrointestinal parasite Entamoeba histolytica

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Introduction: *Entamoeba histolytica* (*Eh*) is the causative agent of amebiasis, a disease responsible for ~100 000 deaths/year. In most cases, *Eh* colonizes the mucus layer of the colon without causing symptoms, however in some individuals *Eh* invades the colonic mucosa causing amebic colitis. The first response of the host at sites of *Eh* invasion is a robust acute inflammatory response mediated by macrophages. *Eh*-macrophage interaction is thus a critical first step in determining how the innate immune response will be shaped; yet the mechanisms that regulate this interaction remain largely unknown. In this study, we investigated the early cellular events triggered in macrophages in response to *Eh* and the putative virulent factors involved.

Methods: The cytoskeletal modulation of THP-1 macrophages was assessed by confocal microscopy and biochemical techniques following stimulation with *Eh* trophozoites. The contribution of *Eh* virulence factors and macrophage intracellular pathways and enzymes was evaluated with the use of specific inhibitors.

Results: We found that only live *Eh* in direct contact with human naive macrophages triggered an instantaneous degradation of the cytoskeletal-associated proteins Pyk2 and paxillin. This event was critically dependent on the major surface virulent factor, cysteine proteinase 5 (*Eh*CP5) as revealed using *Eh*CP5-deficient *Eh* and protease inhibitors. As macrophage cytosketal proteins are critically involved in cell adhesion, migration and inflammation, we surmise that *Eh* has evolved mechanisms to "stun" macrophages during infection to dampen the innate immune response.

Conclusion: Taken together, our findings advance a unique mechanism by which *Eh* modulates immune cells by interfering with the cell cytoskeleton, which may favour parasite colonization and/or altering pro-inflammatory responses in *Eh* pathogenesis.

Infections reduce granulocyte infiltration in an *in vivo* model of bacterial toxin-induced colitis and in human intestinal tissues: a role for *Giardia* cathepsin B proteases

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Introduction: *Giardia* infections are a leading cause of diarrheal disease and can occur concurrently with other gastrointestinal pathogens. *Giardia* infections have been shown to reduce the development of diarrhea and fever during co-infection with other gastrointestinal pathogens via unknown mechanisms. Secretion of interleukin-8 (CXCL8) from intestinal epithelial cells (IECS) recruits neutrophils (PMNs) to the basolateral membrane of the intestinal epithelium and occurs prior to induction of PMN-mediated diarrheal disease. The *Giardia* genome contains cathepsin B (catB) protease genes that have no described function. This study hypothesized that *Giardia* catB proteases attenuate IEC signals that recruit PMNs into intestinal tissues.

Methods: C57BL/6 mice infected with *Giardia* trophozoites for 7 days and were intra-rectally administered 100 µg of *Clostridium difficile* toxin A/B (TcdA/B) for 3 hours. *Giardia* trophozoites were co-incubated with *ex vivo* human colonic mucosal biopsy tissues from patients with active Crohn's disease (CD) for 6 hours. *In vitro* Caco-2 monolayers were co-incubated with *Giardia* trophozoites and subsequently administered pro-inflammatory interleukin-1β (IL-1 β), CXCL8, or *Salmonella* typhimurium. Samples were processed for qPCR, PMN chemotaxis assays, Luminex, or cathepsin activity assays.

Results: *In vivo Giardia* infections attenuated granulocyte infiltration and expression of several PMN cytokines induced by pro-inflammatory TcdA/B in an isolate-dependent manner. *Giardia* trophozoites decreased expression of PMN cytokines from *ex vivo* inflamed human descending colon mucosal biopsy tissues collected from patients with active CD. *Giardia* trophozoites reduced supernatant levels of intestinal epithelial CXCL8 induced by IL-1β or *S.* typhimurium; this was caused by the secretion of *Giardia* catB proteases that degraded CXCL8 post-transcriptionally. Furthermore, the degradation of CXCL8 by *Giardia* catB proteases attenuated CXCL8-induced PMN chemotaxis.

Conclusion: *Giardia* infections attenuate PMN recruitment into intestinal tissues induced by a potent bacterial pro-inflammatory toxin. This is, at least partially, mediated by the release of *Giardia* catB proteases that degrade intestinal epithelial CXCL8.

Kinematic Gait Patterns in Individuals with Mild-to-Moderate Hip Osteoarthritis

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Introduction: Hip osteoarthritis (OA) is a leading cause of pain and loss of function in affected individuals. Understanding the precise walking mechanics in non-surgical hip OA patients may provide valuable insight on how to clinically manage this population. Therefore, the purpose of the present study was to provide a comprehensive description of gait kinematics in individuals with radiographic evidence of mild-to-moderate hip OA as compared with matched controls.

Methods: 23 individuals with mild-to-moderate radiographic hip OA (as per the criteria of the American College of Rheumatology) and 22 healthy age and BMI matched subjects participated. Kinematic gait data were collected using an 8-camera 3D motion capture system (Vicon, Mx). Joint angles were calculated using the decomposition methods of Soderqvist et al. (1993). Peak joint angles were obtained in all three planes (sagittal, frontal, transverse) across the pelvis, hip, knee, and ankle during mid-stance (the time point corresponding to 30% of the gait cycle), terminal hip extension, and toe off of the affected side hip.

Mean differences in gait kinematics between groups was calculated using a two-way repeated measures ANOVA with group and time as the independent variables.

Results: Significant differences were observed between groups. Hip OA subjects hiked their unsupported hemi-pelvis compared with controls (CON: 0.76° (1.46) drop; HOA: 0.64° hike, P=0.00) and demonstrated an increased anterior pelvic tilt compared with controls (CON: 0.79° (3.50); HOA: 3.86° (3.64), P=0.01). Across the hip, OA patients demonstrated increased peak hip abduction (CON: 2.64° (3.59) adduction; HOA: 1.66° (3.50) abduction, P=0.00) and decreased peak hip extension (CON: 12.53° (7.05); HOA 3.96° (5.77), P=0.00).

Conclusion: Individuals with hip OA demonstrated significantly altered walking gait biomechanics as compared to healthy controls. These adaptations may be considered by clinicians working with this population. Understanding the underlying patho-anatomic changes that lead to these changes requires further investigation.

Dr. Scholl's Active Series Footwear Insoles for Running Injuries – A Biomechanical Analysis of Manufacturers Claims

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Introduction: The Active Series insole by Dr. Scholl's claims to help to prevent and treat running injuries such as patellofemoral pain, plantar faciitis, and tibial stress syndrome. If this is true, then it would be expected that the insole would influence biomechanical variables associated with developing these injuries. Thus, the purpose of this study was to determine if the Active Series insole alters biomechanical variables associated with patellofemoral pain, plantar faciitis, and tibial stress syndrome.

Methods: Fifteen participants completed 5 trials running at 4m/s along a 30m runway with each of two conditions: (1) their own running shoe, and (2) #1 with the Dr. Scholl's Active Series insole placed within the shoe. As participants ran, 3D trajectories of the participant's right lower leg and foot, and 3D ground reaction force data were recorded. Kinetic and kinematic data were used to calculate the following biomechanical variables: (1) knee abduction angular impulse during stance phase (associated with patellofemoral pain), (2) peak foot eversion angle during stance phase (associated with plantar faciitis and tibial stress syndrome), and (3) peak eversion velocity during stance (associated with tibial stress syndrome). Two-tailed paired-samples t-tests were used to compare the control and Dr. Scholl's conditions.

Results: As a group, no significant differences were observed between the control and Active Series conditions for peak ankle eversion angles (p=0.64) or knee abduction angular impulses (p=0.26). A trend was noticed where peak eversion velocity during stance phase increased in the Active Series condition (p=0.06). Individually, many participants experienced biomechanical changes greater than ±10% for each variable.

Conclusions: Dr. Scholl's Active Series insoles have an influence on biomechanical variables associated with patellofemoral pain, plantar faciitis, or tibial stress syndrome for individual runners; however, their influence is not systematic across participants. Consequently, the Dr. Scholl's insole may offer benefit to some runners, but be detrimental to others.

Does physical activity impact health status of head and neck cancer patients at diagnosis?

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Introduction: Head and neck cancer (HNC) and related treatments affect a multitude of basic physiological and psychological functions leading to decreased nutritional status, impaired physical functioning and decreased quality of life (QOL). There is a growing body of literature to support the use of physical activity (PA) in managing these side effects. The purpose of this paper is to investigate the relationship between PA levels pre-radiation and specific health outcomes, including nutrition status, physical functioning, workability, and QOL pre-treatment.

Methods: Patients were recruited in clinic as part of a year-long randomized controlled trial evaluating the impact of PA during or after radiation treatment. Assessments before the start if radiation and at 3, 6, 9, and 12 months post diagnosis included screening for demographic information, PA levels, QOL, nutritional status, and functional performance. Data from the first assessment is discussed in this paper. Raw data was analyzed using IBM SPSS Version 20.0. Descriptive analysis and Person's correlations were conducted to assess relationships between PA levels and health outcomes (significance level, $p<0.05$).

Results: A total of 60 HNC patients completed the first assessment (49 male, 11 female). Of the 60 participants, only 14 (23.3%) were meeting the recommended 150 minutes of moderate intensity aerobic exercise per week. Average weekly PA minutes at the first assessment were moderately correlated with decreased PG-SGA score (r=-.483, p=.000), and increased physical wellbeing (r=.312, p=.027), functional wellbeing (r=.373, p=.022), overall QOL (r=.365, p=.009), HNC patient specific QOL (r=.463, p=.001), perceived ability to work (r=.343, p=.015), and total distance traveled in a 6-minute walk test (r=.326, p=.021).

Conclusions: Results from this study indicate a relationship between weekly PA minutes and improved overall functioning and QOL. An intervention study is necessary to determine a causal relationship between PA and these health outcomes.

Hierarchical difference in active and passive force production at long lengths in skeletal muscle

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Introduction: According to the sliding filament and crossbridge theories of contraction, the amount of active force produced by a muscle is dependent upon the overlap of the myofilaments actin and myosin. As muscle length increases, filament overlap decreases and therefore active force decreases while passive forces become greater. However, Leonard *et al.* (2010) showed that activated myofibrils stretched to lengths beyond myofilament overlap produce much higher forces than myofibrils stretched passively. This observation cannot be explained under the current framework of muscle contraction. The purpose of this study was to examine how this phenomenon scales to higher levels of muscle hierarchy. It was hypothesized that the divergence in active and passive force with increasing length would be reduced in isolated fibres, and further diminished in whole muscles.

Methods: Three separate preparations from the semitendinosus muscle of the frog *Rana pipiens* were used: whole muscles, skinned fibres, and myofibrils. Muscles were positioned at the optimal length of their force-length relationships and then stretched until failure, defined by a drop in force during stretch. Force and length data were collected throughout the stretch protocol, and forces at discrete sarcomere lengths were calculated.

Results: A two- to three-fold augmentation in active stress above the passive stress was observed in myofibrils stretched beyond myofilament overlap. Moving up in hierarchical level to isolated fibres and whole muscles resulted in progressive decreases in the difference between active and passive conditions at long sarcomere lengths. We suggest that at the myofibrillar level, the protein titin plays a crucial role in modulating force at long sarcomere lengths. As higher structural levels are examined, effects of passive structural elements outside the cell may mask some of the effects observed at subcellular levels.

Conclusion: The large divergence between active and passive stresses observed in myofibrils does not occur at higher levels of muscle hierarchy.

Gross Morphological and Histological Analysis of Articular Cartilage after Anterior Cruciate Ligament Reconstructive Surgery with Dexamethasone Treatment

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Introduction: Anterior cruciate ligament (ACL) tears and/or menisci damage often results in accelerated development of osteoarthritis (OA). It is thought that there may be an injury-induced, mechanical abnormality of the injured joint and subsequent interplay between altered mechanics and/or biological changes, such as inflammation, which may lead to cartilage damage. Dexamethasone (DEX) is a synthetic steroid with anti-inflammatory properties, which could possibly be a treatment strategy for controlling inflammation. The purpose of this study was to characterize cartilage damage following idealized ACL reconstruction (ACL-R) surgery after DEX injection.

Methods: Six skeletally mature, female sheep were allocated into three groups: ACL-R+DEX (n=2), surgical sham (n=2), and non-operated controls (n=2). Surgeries involved an arthrotomy to the right stifle joint. DEX was given by an intra-articular injection (0.5 mg/kg body weight). For the surgical sham, a similar arthrotomy and surgical approach to the ACL-R was used, but there was no injury to the ligaments. Animals were sacrificed 2 weeks after surgery and gross morphological grading was conducted. The patella (PAT), femoral groove (FG), lateral femoral condyle (LFC), medial femoral condyle (MFC), lateral tibial condyle (LTC), and medial tibial condyle (MTC) cartilage locations were evaluated for histological changes. ANOVA with Bonferroni post-hoc analysis was used to determine differences between groups.

Results: Combined gross morphological score in the ACL-R group was slightly higher than that of the control, ACL-R+DEX, and the surgical sham groups. Of interest, there was no osteophyte damage to the ACL-R+DEX group in comparison to both the ACL-R+DEX and sham surgery groups. Histological observations of all locations showed no significant differences between the sham surgery, ACL-R+DEX surgery, and control group.

Conclusion: Preliminary results demonstrate that one injection of DEX immediately after ACL-R surgery mediated induction of cartilage damage at 2 weeks post surgery.

Temporal Effects of Intra-Articular Hyaluronan and/or Corticosteroids on Osteoarthritic Synovial Fluid Boundary Lubricant Composition: A Case Series

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Introduction: Proteoglycan 4 (PRG4) and hyaluronan (HA) are critical boundary lubricants present in synovial fluid (SF). Deficiency of either lubricant may lead to compromised boundary lubrication and increased cartilage wear. Intra-articular (IA) corticosteroid (CST) injections can provide short-term pain relief for patients with osteoarthritis (OA), and IA HA can provide pain relief for up to 6 months; however, the effects of IA treatment on SF boundary lubricant composition over time remain unclear. The purpose of this study was to measure PRG4 and HA content in SF aspirated from the same OA patient knee joint over time during the course of treatment with IA CST and/or HA.

Methods: In an ongoing study, knee SF was aspirated from chronic OA patients prior to IA treatment. Patients were included in this case series if 3 or more SF aspirations were available for analysis. In total, 4 knees (3 patients) with 3-5 aspirations were available for analysis. PRG4 and HA concentration was measured by sandwich enzyme linked immunosorbent assay. HA MW was measured by 1% agarose gel electrophoresis. SF boundary lubricant composition data from 29 normal cadaveric SF samples are included for comparison.

Results: No consistent trends in SF boundary lubricant composition after IA HA or CST treatment were observed over time. PRG4 concentration, HA concentration, and HA MW variably increased, decreased, fluctuated, or remained stable over time with IA treatment.

Conclusions: This study suggests that response to IA CST or HA treatment appears to vary between individuals. Other factors including joint loading, activity level, and inflammation may also influence SF lubricant composition over time. The outcome of future analysis of SF lubricant composition, boundary lubricating function, and pain relief provided by IA PRG4±HA might ultimately be beneficial for chronic, symptomatic OA patients with compromised SF boundary lubricant composition.