

Progress from the Past: Dr. Nathan Goluboff



Dr. Nathan Goluboff
1914-1997

Dr. Nathan Goluboff served the children of Saskatchewan for 45 years as a general pediatrician. He was respected for his dedicated and expert care of Saskatchewan children and acknowledged for his scholarly approach to diagnosis and management, his visionary and uncompromising commitment to evidenced-based decision making, and his excellent teaching.

Dr. Goluboff was born in Winnipeg. At the young age of 21 years and after completing

his internship at Saskatoon's City Hospital, he graduated from the University of Manitoba medical school in 1936. After completing a post-graduate internship at Saskatoon's St. Paul's Hospital he conducted a general practice in Lake Lenore, Saskatchewan from 1937-1939 and then in Rosthern, Saskatchewan from 1939-1941. He had a distinguished career as a member of the Royal Canadian Air Force during World War II. He met his future wife while he was on leave in Brooklyn, New York and married in 1943. Following the war Dr. Goluboff undertook post-graduate pediatric training in New York. In 1946 he returned to Saskatchewan to establish his pediatric practice.

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Featured Child Health Researcher

Dr. Daniel MacPhee

Dr. Daniel MacPhee is a Reproductive Biologist in the Department of Veterinary Biomedical Sciences at the Western College of Veterinary Medicine and an established scientist within the One Reproductive Health Group (<http://www.usask.ca/groups/onereproductivehealth>). Dr. MacPhee received his PhD in Zoology from the University of Western Ontario in 1990 where his work contributed significantly to our understanding of mammalian pre-implantation development, specifically on how the blastocyst forms. He then conducted Postdoctoral research on uterine myometrium function during pregnancy and labour and human placental development at the Samuel Lunenfeld Research Institute at Mt Sinai Hospital in Toronto, Ontario. Dr. MacPhee was an Assistant and then Associate Professor in the Faculty of Medicine at Memorial University of Newfoundland from 2001-2012. In 2012, Dr. MacPhee joined the University of Saskatchewan as an Associate Professor.



His research interests include the role of cell signaling protein networks in human placental development and stress proteins and their role in uterine function during labour. The uterus contains a smooth muscle component named the myometrium and during pregnancy the myometrium goes through a program of development. This process is characterized by changes in the muscle cells at the molecular and cellular level. Overall, the consequence of this whole differentiation pathway is the production of a tissue that can generate precisely coordinated and powerful contractions (labour) to

ensure the timely delivery of a term fetus whose organ systems are sufficiently mature for survival outside the uterus. Unfortunately, myometrial programming is still a poorly understood process. When the myometrium does not develop and/or function properly it can lead to a significantly increased risk of preterm birth, which accounts for the vast majority of all infant deaths, neonatal morbidity, and an increased risk of diseases in the future adult.

Small stress or heat shock proteins (sHSPs) have important housekeeping roles in cells acting as chaperones. In this role, sHSPs can surround stress damaged, non-functional proteins, protect them from destruction if possible and help them to regain proper function. Recent research in the field though has clearly shown more roles for this group of stress proteins. They can regulate smooth muscle contraction and relaxation and also can be involved in signaling between cells through their transport as cargo in extracellular vesicles called exosomes. Dr. MacPhee's basic research program examines the presence (expression) and regulation sHSPs and associated proteins in myometrial cells during pregnancy. His lab has discovered that many sHSPs are found in the myometrium. Ms. Jessica Nicoletti is an MSc candidate in the MacPhee lab and her work was presented at the recent Pediatrics Child Health Research Trainee Day (see abstract on page 8). She has found that an sHSP known as HSPB5 is particularly abundant in the myometrium during late pregnancy and labour. The exact role of HSPB5 in the myometrium is still unknown, but the scientific literature has indicated it could be a powerful regulator of immune system activation. Physiological uterine inflammation is now considered to be a likely contributor to the onset of labour raising important possibilities for sHSPs to play a vital role in regulating parturition.

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Our Partners: Children's Hospital Foundation of Saskatchewan

The Children's Hospital Foundation of Saskatchewan has demonstrated its ongoing commitment to improving the health and well-being of children through research by very generously supporting six research projects in the 2015 competition. The Foundation received a dramatic increase in high quality applications this year, a reflection of the increase in child health research at the University of Saskatchewan. The continuing support of the Children's Hospital Foundation of Saskatchewan is greatly appreciated.



Congratulations to the following researchers who are recipients of the Children's Hospital Foundation of Saskatchewan research grants for 2015!

- **Dr. Darryl Adamko**, *Pediatric Asthma - Metabolomic analysis*
- **Dr. Krista Baerg**, *Testing of JM-105 Janudice Meter*
- **Dr. Marta Erlandson**, *CHAMPS: Children's Healthy Heart Camp in Saskatchewan*
- **Dr. Richard Huntsman**, *Cannabidiol in Children with Refractory Epileptic Encephalopathy*
- **Dr. Alan Rosenberg**, *Uveitis & Arthritis in Children*
- **Dr. Hassan Vatanparast & Dr. Alan Rosenberg**, *Vitamin D in Children with Juvenile Idiopathic Arthritis*

health education to this underserved group. Myself, from the College of Nursing, in partnership with Red Cross RespectED, Greater Saskatoon Catholic Schools (GSCS) and Saskatoon Sexual Abuse and Information Center (SSAIC) for over 10 years, have developed and implemented a safe environments and healthy relationships program for adolescents with developmental disabilities attending GSC High Schools. This program entails the provision of educational resources to increase personal safety, including: promotion of emotional health, provision of healthy sexuality education, provision of knowledge regarding personal rights and responsibilities in relation to safe environments, body ownership, establishment of personal boundaries, and prevention knowledge and skills in order to stay safe. The promotion of healthy peer relationships focuses on assertive communication, expression of personal feelings, sensitivity to others feelings and attitudes, and knowledge of helping resources. Additionally this project provides education, awareness, tools, and supports to parents and teachers, enabling them to further educate and support the adolescents in healthy relationships and healthy sexuality education. Parents and teachers learn about the myths and misconceptions surrounding sexuality and adolescents with developmental disabilities and develop the skills to proactively promote healthy sexuality, prevent abuse, and work with adolescents to develop risk-management strategies. Currently a peer-to-

peer training model is being implemented to train and educate typical high schools students and university students to deliver the program to youth with developmental disabilities. Approximately 3-4 high school students from each of the five GSC high schools in Saskatoon and 8-10 interprofessional university students involved in their senior practica on the interprofessional clinical team receive the training and education to deliver this program. This includes an understanding of the content, methods of engagement and delivery, and techniques of puppeteering. This research project demonstrates best practices in Community-Engaged Scholarship, contributes to the potential for ongoing collaboration in providing experiential learning opportunities for students, and contributes to the sustainability of the project developed over the course of the 10-year partnership.

References: Health Canada: Canadian Incidence Study of Reported Child Abuse and Neglect Final Report (2000). Ottawa: Health Canada. • McCreary Centre Society, (1993). Sexual abuse and young people with disabilities project: Summary report. Vancouver McCreary Centre Society. • National Clearinghouse on Family Violence (1993). Family violence and people with mental handicap. Ottawa: Health Canada. • Public legal education (1993). Abuse of people with disabilities: Information for service providers. Retrieved May 20, 2009 from <http://www.publiclegaled.bc.ca/able/providers.html>.

Dr. Lee Murray is an Associate Professor, College of Nursing, U of S. Please see P8 for an abstract on this work presented by Tara Leson and Megan Weber at the Child Health Research Trainee Day.

Recent Child Health Publications from U of S Faculty

- Janzen B, **Karunanayake C**, Pahwa P, **Dyck R**, **Rennie D**, **Lawson J**, Pickett W, Bryce R, Hagel L, Zhao G, Dosman J; Saskatchewan Rural Health Study Team. Exploring diversity in socioeconomic inequalities in health among rural dwelling Canadians. *J Rural Health*. 2015;31:186-98.
- Khamis MM, **Adamko DJ**, **El-Aneed A**. Mass spectrometric based approaches in urine metabolomics and biomarker discovery. *Mass Spectrom Rev*. 2015 Epub ahead of print.
- Marsh NM, Wareham A, White BG, Miskiewicz EI, Landry J, **MacPhee DJ**. HSPB8 and the Co-Chaperone BAG3 are highly expressed during the synthetic phase of rat myometrium programming during pregnancy. *Biol Reprod*. 2015 Epub ahead of print.
- Mukker JK, Singh RS, Muir AD, Krol ES, Alcorn J. Comparative pharmacokinetics of purified flaxseed and associated mammalian lignans in male Wistar rats. *Br J Nutr*. 2015 Mar;113(5):749-57. doi: 10.1017/S0007114514004371. Epub 2015 Feb 26.
- Jetha A, Badley E, Beaton D, Fortin PR, **Shiff NJ**, Gignac MA. Unpacking early work experiences of young adults with rheumatic disease: An examination of absenteeism, job disruptions and productivity loss. *Arthritis Care Res*. 2015 Epub ahead of print.
- Johnston DL, Keene D, Kostova M, Strother D, Lafay-Cousin L, Fryer C, Scheinemann K, Carret AS, Fleming A, Percy V, Afzal S, Wilson B, Bowes L, Zelcer S, **Mpofu C**, Silva M, Larouche V, Brossard J, Bouffet E. Incidence of medulloblastoma in Canadian children. *J Neurooncol*. 2014;120:575-9.
- Wakayo T, Belachew T, **Vatanparast H**, **Whiting SJ**. Vitamin D deficiency and its predictors in a country with thirteen months of sunshine: the case of school children in central Ethiopia. *PLoS One*. 2015;10(3):e0120963.
- Williamson LE, Lawson KL, **Downe PJ**, Pierson RA. Informed reproductive decision-making: the impact of providing fertility information on fertility knowledge and intentions to delay childbearing. *J Obstet Gynaecol Can*. 2014;36:400-5.

Coming Events

JUN

**FRI
5**

**Beware of Cognitive Biases
'Plus!' Subtle influencers of EBM,
healthcare-related organizations
and clinical evidence.**

Dr. S. Seshia
Neuroscience Grand Rounds
11:00am
Room 1130, E-Wing Health
Sciences Building

SEP

2015

TO

JUN

2016

The 2015-2016 Pediatric Grand Rounds program will include presentations by eminent local, national, and international speakers. In addition to invited speakers from the Department of Pediatrics, the Grand Rounds schedule will also include scholars from elsewhere in the College of Medicine and University of Saskatchewan, and many visiting lecturers from other institutions. Watch for further information about forthcoming presentations and visitors.

OCT

**THU
1**

&

OCT

**FRI
2**

SAVE THE DATES!

**Pediatric Scute Onset
Neuropsychiatric Syndromes:
An International Trans-
Disciplinary Conference for
Development of Early Detection,
Targeted Treatment, and
Prevention Protocols**
Saskatoon, SK

More information regarding the agenda and registration will be posted on the Department of Pediatrics webpage, and distributed in the near future.

Research Project Opportunities

SUPERVISORS LOOKING FOR TRAINEES

• **“Relationship between vitamin D levels and inflammation”**
Study format: Database analysis. Contact: Dr. Alan Rosenberg,
alan.rosenberg@usask.ca

• **“Survey of Kawasaki Disease awareness among Saskatchewan physicians”**

Study format: Survey. Contact: Dr. Alan Rosenberg,
alan.rosenberg@usask.ca

TRAINEES LOOKING FOR SUPERVISORS

- A Pediatric R2 resident is interested in examining the prevalence of e-cigarette use among youth in Saskatchewan.
- A number of undergraduate medical students are looking for summer research opportunities.
- If you are a faculty member interested and willing to supervise, please contact erin.loose@usask.ca.

Dr. Daniel MacPhee

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The lab of Dr. MacPhee has held grants from the Canadian Institutes of Health Research and has been funded by the Natural Sciences and Engineering Research Council since 2002. Dr. MacPhee also holds an Establishment Grant from the Saskatchewan Health Research Foundation to support his novel research on placental development and was recently awarded a John R Evans Leaders Fund Infrastructure Grant from the Canada Foundation for Innovation for purchase of a state of the art live-cell imaging microscope system. With advanced cell, molecular and imaging tools, Dr. MacPhee's research on small stress proteins has inspired investigation of these molecules in the human myometrium by other laboratories. Now, Dr. MacPhee and his team are working to provide additional functional evidence that small stress proteins should be considered potential targets for future tocolytic design in the myometrium during pregnancy.

Dr. Daniel MacPhee is an Associate Professor, Department of Veterinary Biomedical Sciences, Western College of Veterinary Medicine, U of S

YOUR OPINION PLEASE!

We would appreciate your opinion about the Department of Pediatrics Research Report and suggestions for future editions. Please complete a brief survey at: <https://www.surveymonkey.com/s/NQVV6SB>. Thank you!

Dr. Nathan Goluboff

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Dr. Goluboff was Chief of Pediatrics at Saskatoon City Hospital and associate staff at the University Hospital and St. Paul's Hospital. He was a strong advocate for more effective poisoning prevention and served as the Director of the Poison Control Centre for many years. Throughout his distinguished career he was a clinical professor at the University of Saskatchewan renowned for his diagnostic acumen and his scholarly approach to medical practice. He was a vibrant, inspiring and entertaining educator who served as a mentor for generations of students.

Dr. Goluboff contributed important new information to the medical literature. He published the first case of methemoglobinemia in Saskatchewan resulting from well water nitrites (Can Med Assoc

J 58:601-603, 1948) and a case of methemoglobinemia associated with tar-benzocaine ointment (J Pediatr 47:222-6, 1955). In 1961 he documented a relationship between methylene blue administration, skin discoloration and hemolytic anemia (J. Pediatrics, 58:86-89, 1961). In 1960 he reported on the clinical utility the antistreptolysin O titre in identifying children with streptococcal syndromes (Can Med Assoc J 82:77-80, 1960). In 1963 he reported on the benefits of early delivery to prevent adverse effects of RH hemolytic disease (Can Med Assoc J 28:1313-9, 1963).

Dr. Goluboff exemplified compassionate and dedicated care with a commitment to lifelong learning and inquisitiveness, attributes which benefited the many patients, families and students with whom he interacted.

contact us

For more information about The Department of Pediatrics Research, SPRING, or to contribute content to The Department of Pediatrics Research Report, please contact:

The SPRING Office
Department of Pediatrics
Royal University Hospital
103 Hospital Drive
Saskatoon, SK
Canada S7N 0W8.
Phone: 306-844-1229
Email: erin.loose@usask.ca

Online version of newsletter:
www.medicine.usask.ca/pediatrics/research/newsletter

**Deadline for submissions for the next
Research Report is September 11, 2015!**



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The Children's Health Research Trust Fund (CHRTF) was established in 1983 to help raise funds to support child health research at the University of Saskatchewan. As all donated funds are endowed, the CHRTF has continued to grow to become an important partner in helping advance research in the Department of Pediatrics.

For further information about the CHRTF:
<http://www.medicine.usask.ca/pediatrics/research/CHRTF>

To **Donate** to the CHRTF:
<http://give.usask.ca/online/chrtf.php>



Child Health Research Trainee Day

April 16th, 2015

Presentation Abstracts

ANDREA VASQUEZ, JONATHAN GAMBLE, KELLY FEDORUK, GRANT MILLER

Postoperative vomiting in children: Is dextrose an effective prophylactic anti-emetic? A non-inferiority, randomized control trial

Introduction: Post-operative vomiting (POV) in children is a frequent (8.9-42%) indication for unexpected hospital admission. Studies using Intravenous (IV) fluids containing dextrose in the perioperative period have shown improvement of POV in adults. Similar studies have not been done in paediatric patients. **Objective:** To investigate the efficacy of intraoperative IV dextrose for antiemetic prophylaxis in children undergoing ambulatory surgery. **Methods:** This was a double-blinded randomized control trial on 290 healthy children (3-9 years old) with low risk of POV undergoing ambulatory dental surgery. Patients were randomized into two groups. The control group received dexamethasone (0.15 mg/kg IV) and ondansetron (0.05 mg/kg IV); the intervention group received dexamethasone (0.15 mg/kg IV) and intravenous 5% Dextrose in 0.9% normal saline (D5NS) maintenance fluid. The primary outcome, emesis in the post anaesthetic care unit (PACU), was compared using Chi-Square. The secondary outcomes were analysed by T-test and non-parametric analysis where appropriate. Non-inferiority analysis of intraoperative IV dextrose relative to ondansetron was conducted with $\delta = 10\%$ as the non-inferiority limit. **Results:** Data from 289 patients were analyzed (intervention group 144, control group 145). Demographics and intraoperative anaesthetic management were similar. Emesis in PACU was not different between groups ($p = 0.11$). The 95% CI upper limit of the POV proportion was below the non-inferiority margin (9.94 vs 11.33), demonstrating that intraoperative IV dextrose was non-inferior compared to ondansetron. Patients who vomited in the PACU were 6.2 times more likely to vomit at 24 hours ($p=0.015$). POV within 24 hours of surgery occurred in 36 participants (12.4%). **Conclusion:** This study demonstrates that IV dextrose is not less effective than ondansetron in preventing POV. The effectiveness, different mechanism of action, and safety profile of IV dextrose may lead clinicians to consider this as an alternative, or additional therapy for POV prophylaxis.

TANYA HOLT, ERIN BINGHAM, JANLYN ROZDILSKY, KELSEY BALUTIS, ASHOK KAKADEKAR, WILLIAM BINGHAM, LAURENCE GIVELICHIAN

Myocardial dysfunction related to respiratory viral illness in the pediatric intensive care setting

Background : Viral respiratory illness (VRI) is the leading cause of pediatric hospitalizations in North America. An association between respiratory viruses with extra pulmonary manifestations has been identified. The incidence, timing and severity of myocardial dysfunction (MD) associated with VRI have not been well studied. A prospective observational study is ongoing to define criteria and examine independent predictors. The primary objective of this portion of the study is to retrospectively identify independent predictors of VRI with MD (VRI/MD). **Methods:** Retrospective chart review was performed at a pediatric intensive care unit (PICU) in a university hospital. Charts were reviewed from 2011-2013 for patients that tested positive for a VRI ($n=50$). Logistic regression analysis was performed with multiple independent predictors for MD with VRI. This study was approved by the university board of ethics. **Results:** Of all the children with confirmed VRI, 57% (95% CI 48-67%) had MD. 75% of VRI patients with congenital heart defects developed MD. 74% ($p=0.004$) of the patients with a secondary bacterial infection developed MD. VRI patients with history of extreme prematurity or younger than 6 months of age showed an increased rate of MD. Ethnicity, gender and type of virus were not independent predictors of MD/VRI. **Conclusion:** 57% of patients with VRI in the PICU developed MD. Congenital heart defects, history of prematurity, and secondary bacterial infections are important independent predictors of MD in VRI. These findings emphasize the need for further examination through the prospective component of this trial.

BONITA BODANI, XY YE, JP BODANI, L MIREA, K SANKARAN

Morbidity outcomes at discharge of premature neonates born at <30 weeks gestation in Canada over the last decade

Background: Advances in perinatal-neonatal care have significantly reduced neonatal mortality; however, morbidities in survivors are still of concern. Recent morbidity trends and the lowest gestational age (GA) for morbidity-free survival (MFS) of extremely premature neonates born in Canada are unknown.

Study Objectives: 1) Identify the lowest GA possible for survival without severe morbidities at discharge and associated maternal and neonatal characteristics. 2) Assess rates of survival free of single and multiple morbidities at discharge for each GA. 3) Compare MFS between genders. **Methods:** This retrospective observational study used data collected by the Canadian Neonatal Network/TM on neonates born at 22+0 to 29+6 weeks gestation and admitted to NICUs from 2003 to 2012. Neonates with major congenital anomalies, missing information or who were moribund on admission were excluded. Morbidities included moderate or severe bronchopulmonary dysplasia (BPD) as lung morbidity, Grade 3 or 4 intraventricular hemorrhage (IVH) or periventricular leukomalacia (PVL) as brain morbidity, Stage 2 or higher necrotizing enterocolitis (NEC), Stage 3 or higher retinopathy of prematurity (ROP), and Nosocomial Infection (NI) (culture-proven late onset sepsis). MFS rates were calculated for each GA. Survival rates without brain or lung morbidity and without multiple morbidities (brain and lung morbidity with or without NEC, ROP or NI) were estimated at each GA. At the lowest GA with MFS, associated maternal and neonatal characteristics were assessed by Chi-square or Fisher exact tests for categorical variables and t-tests for continuous measures. Similar analyses compared MFS between genders at each GA. **Results:** Study participants consisted of 16,312 neonates from across Canada. The lowest possible GA for MFS was 23 weeks (4.6%; 95% CI 2.7 - 6.5). Factors predictive of MFS at this GA were caesarean delivery, maternal antibiotics and maternal hypertension ($p=0.03$). Antenatal steroids ($p=0.07$) and female gender ($p=0.08$) may impact MFS. Females had higher MFS rates at 25 and 27 - 29 weeks. **Conclusions:** The lowest GA possible for MFS in Canada is 23 weeks. Females have higher MFS rates after 24 weeks GA. Survivors had lower rates of multiple morbidities than single morbidities. Further studies are needed to identify specific targets in the management that will lower morbidity rates at younger GAs. Future studies should also explore the relative burden of single or multiple morbidities on long-term neurodevelopmental outcomes on a national scale. This may identify future research opportunities to improve outcomes and overall quality of life for survivors.

SARAH FINCH, ANTHONY KUSALIK, MICHAEL SZAFRON, SUSAN WHITING, HASSAN VATANPARAST, ALAN ROSENBERG

The impact of vitamin D on disease activity in children with Juvenile Idiopathic Arthritis

Juvenile idiopathic arthritis (JIA) is one of the most common chronic diseases in children affecting 1 in 1000 or approximately 7000 Canadian children and adolescents. The pathogenesis and progression of JIA are poorly understood and may include both genetic and environmental components. One nutritional factor that may play a role at both the environmental and genetic levels is vitamin D. Recent studies suggest that, physiologically, vitamin D plays a role by enhancing macrophage production of antimicrobial peptides, and suppressing inflammation and immune responses. Genetically, specific polymorphisms of the VDR gene may be associated with different biologic responses to vitamin D. The overarching goal of the proposed study is to understand how vitamin D affects disease activity in children who are suffering from JIA. The specific objectives of this research are: (1) To evaluate and compare vitamin D status and anthropometric characteristics between healthy children/adolescents and patients with JIA. (2) To determine vitamin D status and its association with disease activity in children with JIA. (3) To identify potential association of the vitamin D receptor (VDR) gene polymorphisms and JIA. The data to be analyzed are derived from the Biologically-based Outcome Predictors (BBOP) study, a prospective longitudinal study. One hundred and eighty-six patients with newly diagnosed JIA were recruited from multiple centres across Canada as part of the (BBOP) in JIA cohort study (December 2007- December 2012). Environmental and clinical data were collected and blood samples were obtained. Follow up took place every 6 months for 2 years. Surveys, physical examination and anthropometric measurements occurred every 6 months for 2 years, blood samples were collected at baseline and 6 months and saliva sample for DNA extraction were collected at enrollment. Age-matched children from the Canadian Health Measures survey (Cycles 1 and 2) will serve as a comparison group for our study. Analysis will focus on characterising the relationship between vitamin D status to disease outcome over time in children with JIA This is the first comprehensive Canadian study to i) assess vitamin D status in a population of children newly diagnosed with JIA and follows the outcome of the disease; ii) investigate both the genetic and environmental role that vitamin D plays in the prevention and control of JIA. The result of this study would help to recommend guidelines for vitamin D status as a potential adjunct therapy in the management of JIA.

MONA M. KHAMIS, HANAN AWAD, KEVIN ALLEN, DARRYL ADAMKO, ANAS EL-ANEED

Investigation of the urine metabolome using targeted mass spectrometry for improving the diagnosis of asthma in children

Background: Asthma is the most diagnosed chronic childhood disease affecting over 13% of Canadian children. Asthma causes frequent hospital visits and impaired quality of life. The guidelines for asthma treatment recommend the adjustment of therapy based on the inflammation of the airway. However, this cannot be easily achieved in a typical outpatient clinic. Metabolomics is the comprehensive identification and quantification of small molecules created by the cellular metabolism. Out of the “omics” family, metabolomics is characterized by its high dynamic flux, where changes in metabolite concentrations, in response to a stimulus, occur within seconds. Urine is an attractive option for metabolome biomarker discovery. It can be readily obtained in large quantities non-invasively with expected high participant compliance. It also poses low risk of infection to researchers. Our group showed that 1H-NMR urine metabolomic analysis of asthmatic children contains a unique pattern of 50 differentially expressed metabolites compared with those without asthma. It is crucial to accurately quantify and validate these metabolites with respect to their sensitivity and specificity as potential biomarkers using a more sensitive analytical platform such as mass spectrometry (MS). Therefore, the objective of this research is to develop liquid chromatography-tandem mass spectrometric (LC-MS/MS) methods to confirm the accuracy of the metabolites measured by 1H-NMR. A comprehensive list of differentially expressed endogenous urinary metabolites would serve as validated diagnostic or prognostic biomarkers for asthma. Methods: The 50 targeted metabolites are classified into 4 groups based on their chemical structures. Groups 1 and 2 contain 37 metabolites and are quantified based on the differential isotope labeling (DIL) approach using C12/C13 labeled dansyl chloride and dimethylaminophenacyl bromide derivatizing reagents, respectively. Results: The experimental parameters affecting the derivatization reactions were optimized. The MS/MS fragmentation pathway for each derivatized metabolite was studied for the selection of the proper quantitative diagnostic fragment. The LC binary gradient mobile phase systems were optimized allowing for the adequate separation of each metabolite group within 40 min. Conclusion and Future Work: Our previous 1H-NMR work suggested a list of 50 metabolites as candidate biomarkers for the diagnosis/prognosis of asthma in children. The developed LC-MS/MS methods can be used for the measurement of 37 endogenous urinary metabolites with higher sensitivity and selectivity in comparison with 1H-NMR. Future work includes the complete validation of the LC-MS/MS methods, quantification of the metabolites in asthma patients’ urine samples and finally identification of the statistically significant diagnostic or prognostic biomarkers.

VIRGINIA LANE, HASSAN VATANPARAST

Unpacking the nutrition and health risks of newcomer children

Background: Newcomers, particularly children, are usually healthy when they arrive in Canada, but subsequently experience health declines shortly thereafter. It is important to understand the health and nutrition issues of newcomer children as dietary patterns are established early in childhood and impact the development of chronic disease. Objective: To characterize health and nutritional concerns among immigrant and refugee children. Methodology: This study evaluates the health/nutritional status of newcomer children through a cross-sectional analysis of 299 participants aged three to thirteen years who have been in Canada for less than five years. Questionnaires evaluate socio-demographics, food security, and physical activity. Participants’ diets are assessed through 24 hour recalls. Physical measurements include total body bone mineral content (TBBMC), blood pressure, serum vitamin D, total cholesterol, and glucose. Results: Half of refugees (43%) and one quarter of immigrants (26%) were low income. Forty percent of refugees and 24% of immigrants experienced food insecurity, which is higher than the prevalence of food insecurity previously observed among immigrants (13%) in the Canadian Community Health Survey 2008. There was a higher rate of overweight/obesity among immigrants (32%) compared to Canadian-born children (26%), while refugee children were at reduced risk (22%). Dietary assessments revealed that newcomers do not consume sufficient servings of milk/alternatives, and have low intakes of vitamin D (92%) and calcium (81%). Inadequate zinc intake was common among participants (38% girls versus 22% boys). Newcomer children’s TBBMC was similar to the Canadian-born; however, 44% of refugees and 38% of immigrants had low TBBMC. Seventy-two percent of refugee and 53% of immigrant children were vitamin D deficient or had inadequate levels to support optimal development, which is greater than the Canadian-born. In addition,

28% of refugees and 8% of immigrants had high blood cholesterol. Conclusion: Overall the study results indicate that newcomer children are at risk for food insecurity, vitamin D deficiency and poor dietary practices; while immigrants are at increased risk of obesity and refugees are at risk for high cholesterol, which puts both groups at risk for the development of chronic disease.

AMANDA HALL, GORDON ZELLO, CHRIS ARNOLD, JANE ALCORN, ROBERT BERTOLO, JANET BRUNTON, GRANT MILLER

Aluminum content in parenteral nutrition negatively effects bile acid transporters

Background/Purpose: Parenteral nutrition (PN) is an essential therapy available to hospitalized infants, but it is also hepatotoxic. The pathophysiology of parenteral nutrition associated liver disease (PNALD) is unclear, although aluminum (Al) may be one of the contributing factors. We are assessing the impact of Al contamination in PN to determine which bile acids transporters are effected and the extent of damage, thereby gaining a better understanding of the disease pathophysiology. Methods: A randomized control trial using a newborn Yucatan miniature pig parenteral nutrition model. Fourteen piglets were placed into 2 groups of 7 animals each. The control group received standard PN, (Al 38µg/kg/day). The treatment group received PN with a lower aluminum contamination (<2µg/kg/day). After 3 weeks, the piglet livers were collected for analysis. We chose four bile acid transporters (Mrp2, Bsep, Ntcp and Oatp), a stabilizer protein (radixin) and a nuclear receptor (FXR) as indicators of developing cholestasis. These targets are examined by real time polymerase chain reaction (qPCR) to evaluate mRNA expression, immunofluorescence confocal microscopy to evaluate the co-localization of the bile acid transporters and radixin and Western blot to determine final protein presence. Serum was collected to determine bile acid levels. Results: Initial qPCR for Mrp2 and Bsep has shown a fold difference of 1.8 (SD 0.8) and 4.3 (SD 2.7) respectively, in favour of the low aluminum vs the high aluminum group. qPCR for radixin has not shown any significant difference between the groups, with a fold difference of 0.75 (SD 0.20). Serum bile acid levels between the two groups were not significant different (p=0.07). Immunohistochemistry, Western blot and qPCR for the remaining bile acid transporters are ongoing. Conclusions: Aluminum has a negative effect on the bile acid transporters Mrp2 and Bsep. As our analysis continues, we will further characterize the contribution of Al to PNALD.

JOELLE SCHAEFER, RACHEL ENGLER-STRINGER

Investigation of the dietary intake and food security status of high-risk pregnant women

The Healthy Mother Healthy Baby Program (HMHB) is part of Primary Health Care within the Saskatoon Health Region (SHR). Its primary purpose is supporting vulnerable pregnant women within the SHR to have the healthiest pregnancies and babies possible. Women in the HMHB program face many barriers to a healthy pregnancy, one of which is poor nutritional status. A significant research gap exists regarding the nutritional status, including fruit and vegetable consumption, and food security status of high-risk pregnant women in the Canadian context. HMHB has partnered with the Public Health Observatory and the University of Saskatchewan to evaluate components of nutritional support within the program. Nutritional supports that women receive from HMHB include education and counselling, prenatal multivitamins, milk vouchers, as well as vouchers for fruit and vegetables. This collaborative partnership has allowed for a unique opportunity to investigate the nutritional status of pregnant women who live in conditions at risk. Furthermore, there is limited available research regarding efficacy of voucher interventions and the present study provides an opportunity to examine the effectiveness of a fruit and vegetable voucher on improving fruit and vegetable consumption and food security status of this population. This is important knowledge for the continuation of effective community-based programming to improve the health of women and children within the Saskatoon Health Region. Public health nurses (PHNs) and prenatal outreach workers (POWs) within the HMHB program will recruit participants into the study at intake to the program. PHNs and POWs will collect data using surveys that include demographic questions, the adapted versions of the Household Food Security Survey Module (HFSSM) and Behavioural Risk Factor Surveillance System (BRFSS) six-item fruit and vegetable module, and 24 hour recalls. Data will be collected at two time points, prior to participation in the program and at the end of participation, allowing this study to examine the success of the nutritional support voucher intervention. This research study provides an opportunity to investigate nutrition during pregnancy, an important time during the healthy development of a child. This investigation will add needed research to the body of Canadian literature.

WHITNEY DUFF, KELSEY BJÖRKMANN, CHANTAL KAWALILAK, SAIJA KONTULAINEN
Precision of pQCT measurements of total, trabecular, and cortical bone area, content, density, and strength in children

Introduction: Peripheral quantitative computed tomography [pQCT] imaging has been increasingly used in pediatric research to monitor skeletal development in both arm and lower leg bones. However, it is unknown how precise bone measurements with pQCT are in children. **Objective:** To characterize pQCT precision errors in bone area, volumetric density, and estimated strength measurements in children. **Methods:** We recruited 34 (14 boys, 20 girls) healthy children (mean age: 10.5 ± 1.7 yrs) for duplicate measurements of the distal radius, radial shaft, distal tibia, and tibial shaft using pQCT (Stratec XCT2000). Scans were performed a minimum of 24 hours apart. Images were analysed using the ImageJ software (Rantalainen et al. 2011). **Outcomes for the distal sites included:** Total area (ToA; mm²), content (ToC; mg/mm), and density (ToD; mg/cm³); trabecular area (TrA; mm²), content (TrC; mg/mm), and density (TrD; mg/cm³); and bone strength indices during compressions (BSIc; mg²/mm⁴). **Outcomes for shaft sites included:** Total area (ToA; mm²) and content (ToC; mg/mm); cortical area (CoA; mm²), content (CoC; mg/mm), and density (CoD; mg/cm³); and stress-strain indices during torsion (SSIp; mm³). Precision was assessed by calculating root-mean-square CV% (%) for each outcome (Gluer, 1995). **Results:** Distal radius precision errors were: ToA (7.9%), ToC (6.7%), ToD (4.6%), TrA (11.5%), TrC (14.4%), TrD (4.6%), and BSIc (8.2%). Radial shaft precision errors were: ToA (13.1%), ToC (10.4%), CoA (9.7%), CoC (10.1%), CoD (5.1%), and SSIp (17.9%). Distal tibia precision errors were: ToA (10.3%), ToC (7.8%), ToD (3.7%), TrA (13.4), TrC (16.0%), TrD (3.1%), and BSIc (6.5%). Tibial shaft precision errors were: ToA (2.5%), ToC (1.1%), CoA (1.4%), CoC (1.5%), CoD (1.7%), and SSIp (2.1%). **Conclusion:** Bone properties can be imaged in children with precision errors comparable to those reported in older adults in our lab (Duckham et al. 2013). Reported precision errors will assist in selection and interpretation of pQCT outcomes in studies monitoring bone development in children.

KELSEY BJÖRKMANN, JOEL LANOVAZ, CHANTAL KAWALILAK, WHITNEY DUFF, JD JOHNSTON, SAIJA KONTULAINEN

Role of muscle area, grip strength, and neuromuscular performance in predicting radius bone properties and strength at the wrist

Objective: To assess if forearm muscle area, grip strength, number of push-ups or peak force from a push-up test would independently predict variance in bone properties and estimated strength at the wrist and forearm in children after controlling for confounders of sex, maturation, and body size. **Methods:** We obtained wrist and forearm scans from 39 boys and 41 girls (mean age 10.5; SD 1.6y) with both high resolution and conventional peripheral quantitative computed tomography (pQCT). We assessed total, cortical and trabecular bone properties, including bone micro-architecture and estimated compressive strength at the distal radius and torsional strength at the radius shaft. Muscle area was determined from the forearm pQCT scan and grip strength measured via a hand held dynamometer. We calculated peak push-up force from a single maximum push-up performed on force platforms and recorded the number of standard push-ups completed in a single attempt. We controlled for sex, maturation (age from peak height velocity), and body size (weight) in the hierarchical linear regression models, and assessed the independent effect of forearm muscle area, grip strength, number of push-ups, or peak push-up force by entering them separately into the models. We report (adjusted) partial R² for significant ($p < 0.05$) predictors of bone properties and strength at the distal radius and radius shaft in children. **Results:** At the radius shaft, muscle area predicted 41-47% of the variance in total area, cortical area and torsional strength as well as 30% of the variance in cortical density while grip strength accounted for 23-28% of the variance in total area, cortical area and torsional strength. At the distal radius, muscle area independently predicted 35-38% of the variance in trabecular area and compressive bone strength while grip strength accounted for 39-43% of the variance in total area and trabecular area. Variance in trabecular number at the distal radius was predicted only by peak push-up force (28%). The number of push-ups was not a predictor of any bone measures. **Conclusion:** Findings suggest that muscle size, grip strength, and peak push-up force are associated with total, trabecular and cortical bone properties and bone strength in children. These findings will help to design exercise interventions aiming to optimize bone strength development in the fracture-prone wrist and forearm in children.

ELHAM REZAEI, BRETT TROST, CHANDIMA KARUNANAYAKE, ALAN ROSENBERG
Predictors of disease outcome in juvenile idiopathic arthritis

Background: Childhood arthritis is a group of heterogeneous conditions denoted by the juvenile idiopathic arthritis (JIA). In clinic, heterogeneity among patients regarding disease course, response to therapy and outcome is evident. There are no evidence-based guidelines for starting or stopping different medications. There are few publications suggesting predictors of disease course, and response to therapy. Thus, there is a need to develop a tool to predict JIA outcome. Moreover, to provide guidance for the duration of the treatment required to improve outcomes, limit risks, and minimize socioeconomic burdens. **Hypothesis:** A profile comprised of clinical findings, and biomarker characteristics can propose disease outcome predictors. **Method:** Data for this study were derived from data collected in a prospective longitudinal cohort design known as the Biologically-Based Outcome Predictors in JIA (BBOP Study). The clinical manifestations and biomarker elements were used as outcome predictors. Data collected from 186 children who were newly diagnosed with JIA. The patients were evaluated at enrolment and every 6 months up to two years. The endpoint was set as visit number 4 (18 months after enrolment). Outcome variables were defined as: active joints, effused joints, joints with limited range of motion, and joints which were active and effused, at visit number 4. Seven different selection methods were applied to determine the variables that best predict the outcome variable. Each method produced a ranked list of variables. The top 50 variables were selected from each method. The variables that were predicted by at least 5 of the 7 methods were retained for classification. A Bayesian Network was constructed using these variables and was used to predict the outcome variable. **Results:** Approximately 30 variables were selected out of 898 from visit number 1 (enrolment) and 2 (6-months) using Bayesian Network classification method. The predictive accuracy rates for class variables were: 1) 77.67% for active joints; 2) 85.84% for effused joints; 3) 78.57% for joints with limited range of motion; and 4) 80.35% for active and effused joints. Ethnicity, cervical joints, ankle, and wrist involvement in the first and second visits can predict JIA outcome 18 months after diagnosis. **Conclusion:** BBOP data can be useful for identifying outcome predictors of JIA. The best classification algorithm for BBOP data is Bayesian Network. Among a vast number of variables few of them identified as the disease outcome predictor including: ethnicity, cervical joints, ankle, and wrist involvement at the beginning of the disease.

CHRISTINA WIST, HASSAN VATANPARAST, ANNE LEIS, MATHIEU BÉLANGER, AMANDA FROELICH CHOW, RACHEL ENGLER-STRINGER, AMIN TAVASSOLIAN, NATHANIEL OSGOOD

The Impact of Healthy Start/Depart Sante intervention on improving dietary intake of 3-5 year-old children attending childcare centres in Saskatchewan and New Brunswick

Background: Early childhood obesity rates continue to rise in Canada and we know that obesity in children increases the risk of obesity in adulthood. Early childhood is thus a critical time for prevention. Like parents, educators have a significant role in shaping children's dietary behaviours – an important determinant of overweight and obesity. Healthy Start-Départ Santé is a population health intervention program designed to encourage and enable families and educators to integrate daily physical activity and healthy eating in the lives of children ages 3 to 5 years. In a pilot study, the program was shown to be effective in helping educators increase physical activity and healthy eating opportunities. However, the impact of the program on young children's healthy eating, total food intake, and physical activity has yet to be determined. The Healthy Start program is now being expanded to childcare centres in Saskatchewan and New Brunswick, as these two provinces have the highest prevalence of overweight and obesity among children ages 0-5 years in Canada. **Purpose:** To assess the effectiveness of the Healthy Start Program in improving the diet of children ages 3 to 5 years in licensed childcare centers throughout Saskatchewan and New Brunswick. **Methods:** A population health randomized controlled intervention study with gradual implementation within 44 weeks is being conducted. This 3-year study has involved 40 francophone and anglophone centers in Saskatchewan and New Brunswick, 20 with a Healthy Start program, 20 routine practice. Sites will be compared over 10 months and one-year follow up. Healthy Start interventions will be evaluated in terms of health information dissemination, menu planning, eating behaviours, and actual food intake. Methods will include a weighted plate waste study enhanced with smart-phone iEpi technology; a nutrition risk assessment questionnaire for preschoolers (NutriSTEP); and menu analyses before, during and after the intervention. We will also assess the self-efficacy of educators and changes to the

food environment and practices using a RCT-tested nutrition self-assessment questionnaire for childcare providers. Significance: In Saskatchewan and New Brunswick, no studies have evaluated the implementation and impact of a targeted intervention on increasing healthy behaviours among early years children and their educators. The proposed study will generate detailed information about the efficacy and impact of the Healthy Start program on healthy eating. Findings will address the needs and barriers to healthy eating in the childcare center environment to assist children, parents, and educators and better inform policies shaping early childhood nutrition.

TRACY WILSON-GERWING, ALAN ROSENBERG

The effects of omega fatty acid supplements on systemic levels of cytokines and chemokines associated with arthritis inflammation

Background/Purpose: Arthritis is among the most common chronic conditions in Canada in both children and adults. Arthritis is a potentially disabling disease causing joint inflammation and pain. Increasingly, people suffering from arthritis are using alternative therapies including nutraceuticals. This research aims to create new knowledge about the effectiveness of omega fatty acid supplements to improve arthritis outcomes, and how their effectiveness differs between children and adults with arthritis. Our research, by studying the mechanisms and key factors that produce pain associated with inflammation in arthritis and its effects, will provide scientific evidence that omega fatty acid supplementation will improve care and outcomes in childhood and adult arthritis. Methods: Juvenile (5 wks old) and young adult (13 wks old) male Wistar rats were immunized with an emulsion of bovine type II collagen and incomplete Freund's adjuvant. At the onset of arthritis, rats were randomly divided into four groups: 1) no treatment; 2) treatment A [γ -linoleic acid (GLA), eicosapentanoic acid (EPA) and docosahexanoic acid (DHA)]; 3) treatment B (GLA, EPA, DHA and boswellia serrate extract); and 4) treatment C (boswellia serrate extract). After two weeks of treatment, animals were euthanized and blood samples were collected via cardiac puncture. Samples were processed and serum collected and stored at -80°C . Serum was assayed at Eve Technologies using a rat 27-plex cytokine/chemokine array. Data were subsequently processed and analyzed using Microsoft Excel and Prism GraphPad. Results: Of 27 cytokines/chemokines reported, 13 were selected for initial review based on their known relationship to inflammation and arthritis. Preliminary findings indicate that the effectiveness of the effects on systemic cytokines and chemokines of the three omega fatty acid supplements differ between juveniles and adults with experimental arthritis. Most notably, Treatment B was found to increase levels of many pro-inflammatory mediators in adult but not juvenile arthritis. Treatment C most noticeably decreased levels of the proinflammatory interferon- γ and interleukin-4 in juvenile arthritis but not in adult arthritis. Treatment A decreased systemic levels of the anti-inflammatory cytokine interleukin-10 in adult arthritis but enhanced it in juvenile arthritis. Conclusion: This research provides preliminary evidence that the efficacy of omega fatty acid supplements may not be universally effective in treating inflammation associated with arthritis. The results of this discovery assay will need to be correlated with other indices such as the Arthritis Score, paw thickness measurements and micro-CT imaging to determine the ultimate usefulness of these supplements in treating arthritis inflammation.

JESSICA NICOLETTI, BRYAN WHITE, EWA MISKIEWICZ, DANIEL MACPHEE

HSPB5 is highly expressed in myometrium during late pregnancy and labour and induced by uterine distension

The underlying cellular and molecular mechanisms controlling uterine smooth muscle (myometrium) cell contraction are not well understood. Resolving this knowledge deficit must be a priority if clinicians and scientists are to reduce the incidence of preterm deliveries in Canada that comprise ~8% of all births and account for 75% of all deaths in the perinatal period. The myometrium completes phases of differentiation throughout pregnancy to become a powerful contractile tissue at term. Small Heat Shock proteins (sHSPs) are a family of ten (B1-B10) small molecular weight proteins that are induced by many physiological stressors such as oxidative stress and uterine distension. sHSPs act as chaperones, but also assist in cell death regulation, cytoskeleton rearrangements, and immune system activation, particularly when they are phosphorylated proteins. Therefore, we examined the spatio-temporal expression of HSPB5 protein throughout gestation via immunoblot and immunofluorescence analysis, as well as the effect of uterine distension on myometrial HSPB5 protein expression using unilaterally pregnant rat models. HSPB5 protein expression significantly increased on day (d) 17 of pregnancy ($P < 0.05$; vs all other timepoints) and levels steadily decreased thereafter through

to postpartum (PP). In contrast, serine 59-phosphorylated (pSer59) HSPB5 protein expression was significantly increased from d19 through to labour and PP ($P < 0.05$). Both HSPB5 and pSer59-HSPB5 were detected in the cytoplasm of myocytes within both uterine muscle layers mid- to late-pregnancy. In unilaterally pregnant rats, HSPB5 protein and pSer59-HSPB5 protein expression were significantly elevated in gravid uterine horns at both d19 and d23 (labour) of gestation compared to non-gravid horns. Therefore, uterine distension during mid to late pregnancy plays a major role in the stimulation of myometrial HSPB5 expression. Recent research has indicated sHSPs can be released into the extracellular fluid; thus, this protein should be investigated as a potential biomarker to predict impending human pre-term or term labour. Funded by the Natural Sciences and Engineering Research Council of Canada.

STEFAN SLOMP, TRACY WILSON-GERWING, JOAN DIETZ, TANYA HOLT, ALAN ROSENBERG

High mobility group box 1 protein in pediatric sepsis and Kawasaki disease

HMGB1 is a pro-inflammatory, nuclear protein and known to be elevated in adult sepsis and other inflammatory conditions. There is little evidence outlining levels in pediatric sepsis and kawasaki disease. Our study aims to identify high levels of HMGB1 early in the course of severe sepsis and predict poor prognosis in pediatric sepsis. Because of its elevation in other inflammatory conditions, we are also identifying levels of HMGB1 in Kawasaki disease and Juvenile Idiopathic Arthritis as our comparative, inflammatory control. Our early results indicate a non-statistically significant trends between KD and sepsis but significant differences between both KD vs non-KD subsets and between KD and JIA inflammatory control groups. These results support further enrollment in our study and further analysis including HMGB1 relation to clinical subtypes of JIA and their outcomes.

TARA LESON, MEGAN WEBER, LEE MURRAY

Healthy Relationships

Dr. Lee Murray from the College of Nursing, in partnership with the Red Cross RespectED, Greater Saskatoon Catholic Schools (GSCS) and Saskatoon Sexual Abuse and Information Centre (SSAIC), for over 10 years, has developed and implemented a safe environments and healthy relationships program for adolescents with developmental disabilities attending GSC High Schools. This program entails the provision of educational resources to increase personal safety by: promoting knowledge in relation to safe environments, body ownership, personal boundaries, and preventative skills. Additionally, this project provides education and supports to parents and teachers, enabling them to further educate and support adolescents in healthy relationships and healthy sexuality. Parents and teachers learn about the myths surrounding sexuality and adolescents with developmental disabilities, and develop skills to proactively promote healthy sexuality, prevent abuse, and help adolescents develop risk-management strategies. The current project utilizes a peer-to-peer training model to teach typical high school and university students to deliver the program to youth with developmental disabilities. This was accomplished through continued consultation and collaboration with Red Cross RespectED, GSCS, and SSAIC. Approximately 3-4 high school students from each of the five GCS high schools in Saskatoon and 8-10 interprofessional university students involved in their senior practica on the interprofessional clinical team will receive the education the deliver this program. This will include understanding of the content, methods of engagement and delivery, and techniques of puppeteering. This proposal demonstrates best practices in Community-Engaged Scholarship, contributes to the potential for ongoing collaboration in providing experiential learning opportunities for students, and contributes to the sustainability of the project developed over the course of the 10-year partnership.

This project is designed to assist students to understand the link between enhanced self-awareness and communication theory, skills, and techniques. This understanding is utilized as a basis for students to learn to create both personal and therapeutic interpersonal relationships, communicate effectively with people with developmental disabilities, interact with families, and work effectively as a contributing member of an interprofessional team.

Experiential learning and integration of critical thinking contributes to the discovery and creation of knowledge and a deeper understanding and comprehension of the subject matter as students are fully engaged in an active learning process. This community-engaged learning experience provides the foundation for interprofessional student understanding of inter-personal communication as an essential skill for professional practice and also reflects the competencies for effective praxis.