

Department of Pediatrics Research Report



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Alert Community, Prepared Hospital Decreasing maternal and newborn mortality in rural Mozambique Dr. Ron Siemens

The Alert Community Prepared Hospital project is а shared 4.5-year venture between the University Saskatchewan of and Universidade Lurio in Marrere Mozambique.

It is an implementation research study of a system-wide approach to decreasing maternal and newborn mortality in rural northern Mozambique.

Understanding context and building relationships is vital to the success of any venture. Our team of Mozambican and Canadian researchers first reviewed the literature to determine the most common issues that led to increased rates of maternal and newborn mortality. We developed an interviewer-directed questionnaire to determine what were the main issues in our catchment area, Natikiri District, Nampula province, Mozambique. We interviewed 300 people representing all ages of the local community and health professionals. We then held 11 focus groups with representative segments of the local community and health professionals. From this we learned that the main issues as seen by the community were:

1) Limited knowledge about maternal health and family planning (FP) needs; 2) Lack of transportation to access maternal newborn health care; 3) Poor quality of maternal health care; 4) Lack of attendance at antenatal care visits and follow up of maternal care needs; 5) Continued need for government support and funding for maternal newborn care.

The focus group data supported the above findings: "The question of pregnancy too early is worrisome and those responsible (community) don't know how to overcome this problem. But they worry a lot." (Community Leader). "The long distances make it so the pregnant women don't go to the hospital or if they arrive to the hospital, they arrive very tired or they deliver on the road. And when the delivery is complicated, they end up dying." (Traditional Healer). "One of the mothers said that when she was pregnant, at the time of delivery, after being admitted, the maternity nurse asked if she had any money. She asked how much, but the maternity nurse did not answer but left her alone during labor and she gave birth alone." (Community Leader). "There are mothers that do not allow their daughters to continue with their family planning because they want grandchildren and they claim that these contraceptives spoil the reproductive system of the girls." (Nurse).

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Image of Interest

ALL ABOARD! Research in Dr. MacPhee's lab focuses on the smooth muscle of the uterus, particularly near the time of labour and delivery. Currently we are investigating a molecular chaperone called Heat-Shock Protein (HSP) A1A. This fluorescence image is a close-up view of HSPA1A expression within the longitudinal layer of the uterine muscle. We have found HSPA1A appearing to be packaged as cargo in many small structures that appear to be leaving the cells right near the time we would expect the fetus to be preparing to leave the womb at labour. The little packages of HSPA1A form these lovely little bright dots that start lining the edges of cells as they appear to make their exit from their "stations". We used an Andor Zylos cMOS camera, epifluorescence optics, and Olympus CellSens software to produce the image.

Image submitted by Mckenzie Russell, Masters Student, supervised by Dr. Daniel MacPhee, Veterinary Biomedical Sciences.

Diagnosing Respiratory Diseases via Metabolomic Profiling of Urine

Kevin Durr

Asthma is the most common chronic illness affecting children. Diagnosis is currently based on patient history, physical examination, and pulmonary function tests (PFT). Common symptoms of asthma include coughing, wheezing, and shortness of breath. However, these symptoms are also present in many other respiratory diseases, making diagnosis difficult in a typical doctor's office. In addition, children younger



increasing the difficulty of making an accurate diagnosis. Currently, A variety of patient data was collected for a characteristics table there is an absence of objective and available diagnostic tests in a including age, sex, body mass index (BMI), pulmonary function, typical doctor's office when managing asthmatic patients.

cellular metabolic activity. Dr. Adamko's lab has shown that metabolomic profile for the asthma and COPD patients was done measuring urine samples of asthmatic patients generates a unique using urine samples collected from the subjects on two separate metabolomic profile. The urine samples are analyzed using Mass Spectrometry (MS). Our study had two principal objectives. The first

was to see if metabolomic profiling could be used to differentiate asthma from another airway disease called COPD. We hypothesized that adults with asthma would have different metabolomic profiles than those with COPD. Our second objective was to determine if asthma severity in children could be determined via metabolomics. We hypothesized that the metabolic activity of more severe asthmatic children would be different than the metabolomic activity of asymptomatic well controlled asthmatic children. This work was approved by the University of Saskatchewan Health Research Ethics Board.

Subjects were recruited from the Respirology Clinic at the Royal than six years old cannot perform lung function testing, further University Hospital outpatient clinic (Drs. Cockroft and Marciniuk). and medications. Compared to the COPD subjects, the asthma Metabolomics is the study of small molecules generated from group was a bit younger, and had worse lung function. Creating the outpatient visits, then analyzed by liquid-chromatography mass-

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Featured Child Health Researcher

Dr. Tracy Wilson-Gerwing

Dr. Tracy Wilson-Gerwing is currently a Research Associate working with the Pediatric Rheumatic Disease Research Group within the Department of Pediatrics. Dr. Wilson-Gerwing began her undergraduate studies with an eye towards entering medical school. However, in the final year of her Bachelor of Science degree majoring in Anatomy and Cell Biology, she took part in an advanced independent research



course where her passion for research was ignited. Eager to pursue the research path, she went on to complete both a Master of Science and a Doctor of Philosophy degree in the area of Neuroscience with a specific focus on the neurobiology of neuropathic pain. Eventually, Dr. Wilson-Gerwing joined the Pediatric Rheumatic Disease Research Group working with Dr. Alan Rosenberg as a Post-doctoral Fellow with a new research focus on inflammatory pain and arthritis.

"Research is to see what everybody else has seen, and to think what nobody else has thought." Albert Szent-Gyorgyi

Inflammatory pain is a particularly important component of chronic childhood and adult arthritis, debilitating conditions that affect more than 4 million Canadians. To date, there is only rudimentary understanding of the mechanisms that generate

Our Partners: Hub City Optimist Club

The Saskatoon Hub City Optimist Club continues to be a strong supporter of child health research in the Department of Pediatrics. Optimist Clubs in Saskatchewan, led by Saskatoon's Hub City Optimist Club, established the Optimist Children's

Research Fund in 2010 and since that time have contributed approximately \$25,000 in support of pediatric research. The contributed funds are endowed and administered under the auspices of the Children's Health Research Trust Fund. As the funds accumulate we anticipate the Optimist Club donations will help to translate research discoveries into disease preventative strategies for Saskatchewan children.



arthritis-related inflammatory pain or how the body innately attempts to mitigate this pain. Understanding interrelationships between inflammation and pain pathways in general, and their differences across sex and age in particular, are paramount to guiding future development of targeted approaches to treatment and will generate more effective tools to assess the effectiveness of arthritis treatment interventions at the tissue, cellular and molecular levels.

The project titled Novel Pain and Inflammation Networks in Juvenile Idiopathic Arthritis (NoPAIN in JIA) discovered, using an animal model, that age is an important factor in time to onset of arthritis, the severity of arthritis, the expression of overt pain behaviors, and the degree to which bone and joint health are affected. Specifically, the younger age group is able to innately control the inflammation and associated pathologies. Based on these initial findings, Dr. Wilson-Gerwing has demonstrated that as age advances, the natural balance between pro-inflammation and the innate resolution of inflammation shifts to favor the promotion of inflammation. This research has now expanded to include both sex and age as variables in arthritis outcomes. Results indicate that both age and sex factor into in arthritis incidence, severity and associated inflammatory biomarker profiling in the CIA model. Maturity of the immune system, rates of bone growth and changing hormonal levels are likely to contribute to these observed differences.

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Clinical Investigator Program (CIP) for Residents

The CIP at the University of Saskatchewan is available to residents enrolled in a Royal College accredited residency program who have interest and potential for a career as a clinician investigator or clinician scientist. CIP offers two streams: A Graduate stream for participants enrolled in a graduate (M.Sc. or Ph.D.) program, and a Postdoctoral Stream for residents who already hold a Ph.D. and are interested in undertaking a structured research program. For further information about CIP, please contact Dr. Alan Rosenberg, alan. rosenberg@usask.ca.

Mozambique

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In partnership with community members, traditional medical practitioners, traditional birth attendants, local health care workers, representatives from the district hospital, provincial/national health system, health professional organizations, the World Bank, USAID, we developed the culturally safe, feasible, appropriate interventions as follows: 1) Expanding family planning especially with adolescents; 2) Community based transport system for pregnant women; 3) Strengthening maternal and child health services by training birthing center personnel in Obstetrical Emergency care (EmOC) and neonatal resuscitation (Helping Babies Breath)l; 4) Providing four quality prenatal visits; 5) Providing quality cesarean deliveries; 6) Supporting the Mozambican government's campaign against bribery.

Over the next 3.5 years these interventions will be put into place and regular implementation research will be done every 6 months to give real time opportunities to make effective changes throughout the course of the research period. Our intention is to scale up to the rest of the province of Nampula and hopefully Mozambique.

This study is part of the Innovating for Maternal Child Health in Africa funded by IDRC, Canada.

Dr. Ron Siemens is a Clinical Assistant Professor in

Tracy Wilson-Gerwing

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Dr. Wilson-Gerwing has also used these models to examine the effects of omega fatty acid supplements on arthritis. Post-doctoral funding from Mitacs Elevate facilitated a partnership with Bioriginal Food & Science Corp to undertake this study.

Chronic, nongranulomatous anterior uveitis is among the most common and potentially debilitating extra-articular manifestations of JIA. Research is currently underway to generate a panel of biomarkers that will serve as a tool to portend uveitis occurrence, inform new treatment targets, predict treatment response and help in exploring etiologic triggers for JIA-uveitis.

Dr. Wilson-Gerwing's research is leading towards the creation of more individualized pain treatments based on age, sex, and the duration of the pain syndrome. These innate mechanisms may be exploited to optimize arthritis and pain interventions and help guide evidence-based, age, and sex appropriate treatment strategies for pain.

Research Project Opportunities

"Relationship of ESR & CRP with inflammatory cytokine biomarkers"

Dr. Tracy Wilson-Gerwing is a Research Associate in the Department of Pediatrics, University of Saskatchewan

the Department of Pediatrics, Division of Emergency Study format: Database analysis Medicine, University of Saskatchewan. Contact: Dr. Alan Rosenberg, alan.rosenberg@usask.ca **Coming Events** Cannabinoid Research Speech & Language Social Pediatrics Organ Donation APR **APR APR** APR Initiative of Saskatchewan Disorders Dr. Maryam Mehtar Dr. Matt Weiss Dr. Richard Huntsman, Dr. Ruth Neufeld Pediatric Grand Rounds THU THU Pediatric Grand Rounds THU THU Pediatric Grand Rounds et al 11am-12pm 11am-12pm 13 20 27 6 Pediatric Grand Rounds 11am-12pm East Lecture Theatre RUH East Lecture Theatre RUH 11am-12pm East Lecture Theatre RUH East Lecture Theatre RUH Pain and Palliative Care Technology-Enhanced TBA Critical Thinking Dr. Stefan Friedrichsdorf Learning Dr. Lonnie Zwaigenbaum Dr. Pat Crosskerry THU Dr. Brent Thoma Pediatric Grand Rounds THU THU THU Pediatric Grand Rounds Pediatric Grand Rounds 11am-12pm Pediatric Grand Rounds 4 11am-12pm 11am-12pm 11 18 25 East Lecture Theatre RUH 11am-12pm East Lecture Theatre RUH East Lecture Theatre RUH East Lecture Theatre RUH

Recent Publications & Presentations from U of S Child Health Researchers

• Bradley TJ, Bowdin SC. Multidisciplinary aortopathy clinics should now be the standard of care in Canada. Can J Cardiol. 2016;32:8-12.

· Dart AB, Zappitelli M, Sood MM, Alexander RT, Arora S, Erickson RL, Kroeker K, Soo A, Manns BJ, Samuel SM. Variation in estimated glomerular filtration rate at dialysis initiation in children. Pediatr Nephrol. 2017;32:331-340.

• Hansen G, Beer D, Vallance JK. The impact of critically ill pediatric transports on Manitoba's rural emergency departments. Can J Rural Med. 2017;22:8-12.

· Khattab A, Haider S, Kumar A, Dhawan S, Alam D, Romero R, Burns J, Li D, Estatico J, Rahi S, Fatima S, Alzahrani A, Hafez M, Musa N, Razzghy Azar M, Khaloul N, Gribaa M, Saad A, Charfeddine IB, Bilharinho de Mendonca B, Belgorosky A, Dumic K, Dumic M, Aisenberg J, Kandemir N, Alikasifoglu A, Ozon A, Gonc N, Cheng T, Kuhnle-Krahl U, Cappa M, Holterhus P-M, Nour MA, et al. Clinical, genetic, and structural basis of congenital adrenal hyperplasia due to 11β-hydroxylase deficiency. Proc Natl Acad Sci. USA. 2017;114:E1933-E1940.

• Pockett C, Moore J, El-Said H. 3D rotational angiography for assessment of coronary arteries during melody valve implantation: introducing a technique that may improve outcomes. Neth Heart J. 2017;25:82-90.

• Rozenblyum E, Spiegel L. The transition from pediatric-centered to adult-oriented care in rheumatology. Can Rheum Assoc J. 2016;26:10-12.

· Pires P, Siemens R, Joao D, Mireheira E, Baptista A, Jemussene C, Bethe S. Women's perceptions about antenatal care access, Marrere hospital, Nampula Mozambique, 2014. 2016;3. https://edupediapublications.org/journals/.

· Baerg K, Lee C, Smith-Fehr J, Lim H. Reliability testing of JM-103 and JM-105 transcutaneous jaundice meters for a hospital and community based newborn screening program, a look behind the scene. 4th World Congress on Controversies in Pediatrics (CoPedia). 2017, Mar30-Apr1, Amsterdam.

· Kurji A. Nourishing connections: using an interdisciplinary approach to providing care to youth. Body Image and Self Esteem Conference, NEDIC (National Eating Disorders Information Centre). May11-12, 2017, Toronto.

• Hares S, Nour MA, Inman M. Pseudoacromegaly in the pediatric population. Canadian Pediatric Endocrine Group Annual Meeting. 2017, Hamilton, ON.

· Luca N, Rozenblyum E, Elliot A, Spiegel LR, Johnson N, Ahola KS, Brandelli Y, Johns C, Luca S, Mosher D, Soon G, Toupin-April K, Uifalusi G, Stinson JN. Perspectives of young people with juvenile idiopathic arthritis, their caregivers, and health care providers on transition to adult care: Informing development of a transition tool-kit. Pediatric Rheumatology Symposium (PRYSM). May 17-20, 2017, Houston TX.

Metabolomics

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spectrometry (LC-MS). 38 metabolites were quantified. The values were assessed statistically by PLS-DA (SIMCA), from which 11 metabolites were determined to be significant in separating the two groups. We have gone on to study subjects from the University of Alberta, and the preliminary metabolomic model appears to have good diagnostic accuracy.

In order to determine the difference between the metabolomic profile of severe and well controlled asthmatic children, 18 patients ranging from 6-16 years old were recruited for the study from Dr. Adamko's asthma clinic. Urine samples and clinical data were collected during each visit. Clinical data included age, sex, spirometry, three questionnaires, and a calendar indicating the subject's daily symptoms. The calendar helped to assess the child's level of asthma control. The questionnaires included the Asthma Control Questionnaire, the Mini Paediatric Asthma Quality of Life Questionnaire, and the Asthma Control Test. The first two rated asthma control during the past week, whereas the latter rated asthma control over the past month. The patients were responsible for keeping track of their daily symptoms on their personal calendar by placing a coloured sticker on each day. This provided a subjective view of the patient's asthma control. The calendar consisted of four different coloured stickers: green - when the patient felt well, blue when the patient experienced allergy symptoms, yellow - when the patient experienced asthmatic symptoms, and red - when the patient had an asthma exacerbation and required medical attention. We met with the subjects on a monthly basis over a six-month period of time, from the summer until fall. During each visit, a urine sample was collected for MS analysis, but this has not yet been completed.

Our study has shown that using urine samples, we can create metabolomic profiles that differentiate adults with asthma from adults with COPD. Dr. Adamko's lab will be conducting further research with a larger cohort to confirm these findings. Our second objective, aimed at differentiating asthma severity in children based on symptomatic control and metabolomic profiling, is still ongoing; therefore, we have not yet been able to make any conclusions.

I would like to that this time to thank Joan Dietz for her role in our project. I would also like to thank the Office of the Vice-Dean Research and the Children's Hospital Foundation for the funding that they provided, as well as the Saskatchewan Health Research Foundation and the Lung Association for their support.

> Kevin Durr was the recipient of a 2016 Dean's Summer Research Project funding through The College of Medicine, supervised by Dr. Darryl Adamko. The program is intended to foster a spark and ignite a passion for research in our medical students, facilitating an understanding of the vital role research plays in today's health care.



Progress from the Past

Wiltold Zaleski was born in Pyzdry, Western Poland in 1920. He had just finished his first year of Medicine in Warsaw when the Second World War broke out, and by the third day of the war was on the German front as a corporal in a field ambulance drawn by horses. Following escape from an internment camp to France, he joined the Polish Army in exile, and found himself defending Paris. When France fell, Witold rejoined the Polish Army in the UK, and two years later, continued his medical studies at



the University of Edinburgh. He graduated with his MB BCh in 1946. While in Edinburgh he met Anne, who was a medical student; they were married in 1948.

Wiltold subspecialized in psychiatry following a work assignment in an institution for those with intellectual disabilities. He and his family emigrated to Canada and in 1958 Wiltold became the Clinical Director of the Saskatchewan Training School in Moose Jaw (later renamed Valley View Centre) where he taught medical students and residents, and was made an Associate member of the Department of Psychiatry, and a Clinical Assistant Professor.

In 1967 he was appointed as the first Director of the Alvin Buckwold Centre (ABC), which he remained for 20 years, and Associate Professor of Pediatrics and Psychiatry. In his work at the ABC, Wiltold aimed to develop a comprehensive and holistic approach to the care of the intellectually disabled child through services that spanned the lifespan of the affected individual, and educational programs for parents, medical students, and residents. He stressed the importance of early detection and prevention, and established travelling clinics across the province, providing diagnostic assessments and counselling. He also established a biochemistry laboratory for the investigation and treatment of children with inborn errors of metabolism.

During Wiltold's directorship, the ABC became well known for the provision of innovative services and for conducting biological and behavioural studies in the field of those with developmental disabilities. When he was appointed director of the ABC in 1967, his staff consisted of only one part time psychologist, a part time secretary, one service worker, and a biochemist. With the help of Senator Sidney Buckwold, John Dolan, and the Saskatchewan Association for the Mentally Retarded (now the Saskatchewan Association for Community Living), he gained the support of the provincial government, the University Hospital (now Royal University Hospital), and the local Kinsmen Club, the latter which provided \$1.4 million towards the present Kinsmen Children's Centre.

Wiltold loved his work, and loved to travel. His lectures took him to the USA, the UK, to his native Poland, and as far as Sri Lanka, New Zealand, India, and Australia. He hiked among the Himalayas and twice paid his respects to Mount Everest. He and Anne had 4 children.

The information and photograph presented are on display at the Kinsmen Children's Centre.

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