

Department of Pediatrics Research Report



The PANS conference featured 4 international experts, from L to R: Dr. Susan Swedo, Dr. Jim Crowley, Dr. Tanya Murphy, and Dr. Michael Cooperstock

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Research Report!



PANS (Pediatric Acute-onset Neuropsychiatric Syndromes): Saskatchewan Conference, Oct 1-2, 2015

Dr. Alan Rosenberg and Erin Prosser-Loose

A conference titled Pediatric Acute-Onset Neuropsychiatric Syndromes (PANS): A Transdisciplinary Symposium for Development of Early Detection, Targeted Treatment, and Prevention Protocols was held October 1-2, 2015 in Saskatoon.

About PANS

PANS, which occurs in pre-pubertal children, refers to neuropsychiatric disorders that are characterized by an abrupt onset of dramatic obsessive compulsive behaviors and/or severe restriction in food intake and concurrent presence of additional severe, neuropsychiatric symptoms and signs including: severe anxiety, emotional lability and/or depression; irritability, aggression and oppositional behaviors; developmental regression; deterioration in school performance; sensory/motor abnormalities;

sleep disturbances. In some instances PANS occurs in association with an infection and when a streptococcus infection is implicated, the syndrome is referred to as PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections).

Health care professionals and systems have not been serving children with PANS and their families well. Few health care providers know about PANS and are unaware of the crucial need for prompt recognition and treatment interventions. The diagnosis of affected children is often missed or delayed.

The PANS Conference

The conference was held to: 1) heighten awareness and impart information about PANS to Saskatchewan health care providers

so that the condition is correctly recognized quickly, and 2) create a framework for a care delivery program that will serve as an easily accessible resource for primary and specialty health care providers throughout Saskatchewan.

The conference was privileged to have four international PANS experts in attendance including: **Dr. Michael Cooperstock**, MD, Chief, Division of Infectious Diseases, University of Missouri School of Medicine; **Dr. Jim Crowley**, PhD, Department of Genetics, University of North Carolina at Chapel Hill; **Dr. Tanya Murphy**, MD, Director, Rothman Centre for Pediatric Neuropsychiatry, Pediatrics and Psychiatry; **Dr. Susan Swedo**, MD, Chief, Pediatrics and Developmental Neurosciences Branch, National Institutes of Mental Health.

One hundred and twelve people registered for the conference including parents and families (11), physicians (31), nurses (11), psychologists (11), school counsellors (7),

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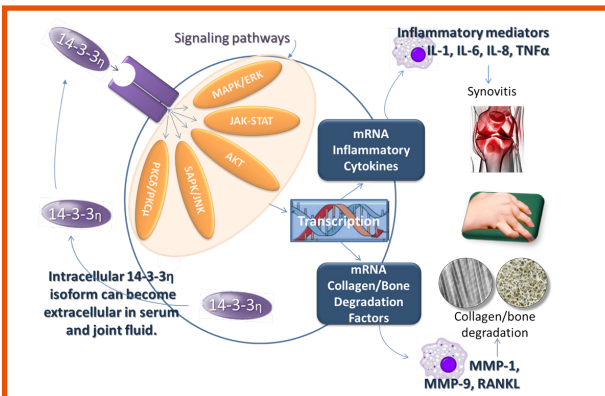


Image of Interest

14-3-3η is an intracellular chaperonin involved in protein trafficking, cell signaling, and cytoskeletal transport. Extracellular expression of 14-3-3η results from an active secretory process from inflammatory cells. Externalized 14-3-3η stimulates cells of the innate immune system to activate key signaling cascades that promote production of inflammatory cytokines (IL-1, IL-6, IL-8 and TNFα) and collagen and bone degradation factors (MMPs and RANKL). Serum 14-3-3η levels are found in adults with rheumatoid arthritis and correlate strongly with erosive disease. Elevated 14-3-3η have been described recently in children with juvenile idiopathic arthritis particularly in those with polyarthritis and rheumatoid factor positivity.

Congratulations!

Rebecca Hoiland (MedII) won Best Dean's Biomedical Project at the Regina Academic Health Science Research Day. Camille Legoux (RII) was 1 of 10 residents chosen to present at the American Academy of Pediatrics National Conference.

Metabolomic Analysis of Urine: Improved Diagnosis of Respiratory Conditions.

R Hoiland, A Ellis, L Kosteniuk, J Dietz, D Adamko

Background: Diagnosing lung diseases like asthma and predicting exacerbations is difficult for physicians in a primary care setting as they do not have the ability to measure lung function or airway inflammation accurately in clinic. A simple, non-invasive test for primary care doctors is currently not available. The purpose of this project was to determine whether the metabolomic analysis of patient urine could be used to differentiate asthma from other airway diseases like Chronic Obstructive Pulmonary Disease (COPD) or Cystic Fibrosis (CF). We also sought whether a metabolomic profile could be used to determine the severity of allergic rhinitis, a disease closely related to asthma. **Methods:** Patient clinical data for these conditions were collected and summarized. Methodology for analyzing patient urine using mass spectroscopy (MS) is currently being developed. Past metabolomic



data obtained using Nuclear Magnetic Resonance (NMR) was analyzed using PLS-DA analysis in relation to each clinical diagnosis. **Results:** Patient clinical data for each cohort was extracted from charts and presented as tables and figures. Metabolomic NMR data analyzed by PLS-DA suggests that a model can be created which differentiates patients based on the severity of allergic rhinitis. **Conclusions:** We now have the clinical data from our Saskatchewan based cohorts of asthma, COPD, and CF categorized and ready for comparison with their MS metabolomic data once these methods are in place. The NMR metabolomics created could provide a non-invasive diagnostic test for the severity of allergic rhinitis. This will be pursued in a larger patient cohort in the future.

Rebecca is a Med II student, supervised by Dr. Darryl Adamko, Dept of Pediatrics

Incontinentia Pigmenti: Vesicular Rash and Seizures in a Neonate

C Legoux, S Eliason, K Baerg

Drs. Legoux, Eliason and Baerg are authors of one of ten abstracts selected for presentation at the American Academy of Pediatrics annual meeting. The abstract reports a case of incontinentia pigmenti (IP).



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Featured Child Health Researcher

Dr. Jill Bally

Dr. Jill M. G. Bally is a registered nurse and Assistant Professor in the College of Nursing, University of Saskatchewan, and has over 20 years of experience in pediatrics. Her clinical practice has informed her research program which centres on family care for those who are affected by life limiting and life threatening illnesses (LLIs and LTIs, respectively). This area of study was the central point of her recent PhD studies that investigated the hope experiences of parents who had children in treatment for cancer, and it continues to be her focus and interest.



With funding from the Canadian Association of Nurses in Oncology, Dr. Bally completed her PhD studies in December 2012 which focused on parental caregivers of children with a life threatening illness. Through her doctoral studies, Dr. Bally identified 'Keeping Hope Possible' as an important process in parents' daily work to maintain their own health and wellbeing. Keeping hope possible

for these parents involved managing the challenging internal struggle that encompassed preparing for the worst and hoping for the best.

Using the four related subprocesses that emerged in the grounded theory study as a creative and helpful theoretical framework, Dr. Bally and an expert research team developed a theory-based hope intervention for parents who care for their children with LLIs and LTIs. Funding from the Royal Bank of Canada supported the related research including the completion of a metasynthesis, Delphi study, and focus groups. These inputs involved significant consultation with a national and international group of experts in pediatric family care, including parents, to support the development of the theory-based hope intervention. The intervention involves self-administered, focused writing activities that explore parental hope and caregiving experiences over approximately two weeks. The intervention encourages parents to reflect, express their emotions, and find personal and creative ways to keep hope possible in the unique journey through their child's illness. Important activities include priorities such as taking things day by day, surrounding self with hope and positivity, taking care of self, and understanding a new, changing

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Our Partners: Lupus SK Society

The Lupus SK Society is a vibrant group of patients and families that aims to raise awareness and share information about systemic lupus erythematosus. Through its remarkable fundraising efforts, Lupus SK has continued to make substantial contributions to the Pediatric Rheumatic Disease Research Laboratory to support ongoing autoimmune disease research at the University of Saskatchewan.



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

social workers (3), teachers (3), general public (31), students (2), resident (1), microbiologist (1), and naturopath (1).

Conference sessions included a presentation from a mother of a child with PANS, in order to give a family perspective; grand rounds presentations from our guest faculty examining PANS from the perspectives of diagnosis, care, infectious triggers, and genetic vulnerabilities; strategies for increasing awareness of PANS, considering education and professional development; framework of a PANS care program for Saskatchewan; and PANS research opportunities in Saskatchewan.

The conference was generously supported by The Saskatchewan Health Research Foundation (SHRF); Children's Health Research Trust Fund; Abbvie; ICAARE (Institute of Child and Adolescent Arthritis Research); PANS Public Advocacy Group; Haslam Pediatric Rheumatology Research Fund; The Department of Pediatrics, University of Saskatchewan; the Saskatchewan Pediatric Research and Innovation Group (SPRING).

PANS Research

The condition of PANS/PANDAS is not that new. William Osler eloquently described PANS-like manifestations associated with acute

rheumatic fever more than 100 years ago. Only recently, however, was a consensus conference convened to establish guidelines for diagnosing PANS and, as importantly, to help discern what is not PANS.

New research results are emerging showing that, in some affected children, molecular mimicry, involving anti-streptococcal antibodies cross-reacting with neuronal tissues, is fundamentally important in explaining the clinical manifestations of PANS. Changes in the caudate region of the brain correlate with the clinical manifestations.

Anti-streptococcal antibodies that cross-react with antineuronal antibodies have been identified in children with obsessive compulsive and tic disorders, Sydenham's chorea, and PANDAS. Evidence of elevated serum antibodies against human dopamine 1 receptor and lysoganglioside and higher serum activation of calcium calmodulin dependent protein kinase II activity in neuronal cells have been identified in affected children. New information is emerging to suggest that these molecular mimicry responses to streptococcus are associated with genetic vulnerability. Dr. Jim Crowley is using Genome-Wide Association Study methodology to identify common genetic variants associated with PANS/PANDAS, and Dr. Susan Swedo is utilizing whole-genome/whole-exome sequencing to detect rare association variants associated with PANS/PANDAS.

For more information and materials from the conference please contact erin.loose@usask.ca.

Coming Events

DEC THU 3	Medical Stewardship Dr. Ayisha Kurji Pediatric Grand Rounds 11am-12pm East Lecture Theatre RUH	DEC THU 10	Child Advocacy: Who Really Cares Bob Pringle, Provincial Child Advocate Pediatric Grand Rounds 11am-12pm East Lecture Theatre RUH	DEC THU 17	Holiday Rounds Dr. Robin Erickson Pediatric Grand Rounds 11am-12pm East Lecture Theatre RUH	JAN THU 7	TBA Dr. Paul Babyn Pediatric Grand Rounds 11am-12pm East Lecture Theatre RUH
JAN THU 14	Hypophosphatasia Dr. Cheryl Greenberg Pediatric Grand Rounds 11am-12pm East Lecture Theatre RUH	JAN MON 18	Royal University Hospital Foundation Research Grants Deadline http://www.ruhf.org/StaffGrants/GrantsAndScholarships	JAN THU 21	TBA Dr. Andrea Fong Pediatric Grand Rounds 11am-12pm East Lecture Theatre RUH	JAN THU 28	Child Maltreatment Dr. Juliet Soper Pediatric Grand Rounds 11am-12pm East Lecture Theatre RUH
FEB MON 29	Children's Hospital Foundation of Saskatchewan Equipment Grant Deadline Professional Development Grant Deadline https://childrenshospitalsask.ca/grants-forms/			MAR THU 24	Child Health Research Trainee Day Graduate Student Commons (Emmanuel and St. Chad, 1337 College Drive) 11am-3pm Submit Abstracts to erin.loose@usask.ca		

Recent Publications & Presentations from U of S Child Health Researchers

- Bobbitt S, Baugh L, Pei J, Cook J, Green C, Andrew G, Rasmussen C. Caregiver needs in fetal alcohol spectrum disorder. Society of Developmental and Behavioral Pediatrics Annual Meeting, Las Vegas NV, October 2-5, 2015.
- Cummings JA, Ballantyne EC, Scallion LM. Essential processes for cognitive behavioral clinical supervision: Agenda setting, problem-solving, and formative feedback. *Psychotherapy (Chic)*. 2015;52:158-63.
- DeWit Y, Pickett W, Lawson J, Dosman J, For The Saskatchewan Farm Injury Cohort Team. Farm activities and agricultural injuries in youth and young adult workers. *J Agromedicine*. 2015;20:318-26.
- Amini M, Nazemi SM, Lanovaz JL, Kontulainen S, Masri BA, Wilson DR, Szyszkowski W, Johnston JD. Individual and combined effects of OA-related subchondral bone alterations on proximal tibial surface stiffness: a parametric finite element modeling study. *Med Eng Phys*. 2015;37:783-91.
- Kent-Wilkinson A, Dietrich Leurer M, Luimes J, Ferguson L, Murray L. Studying abroad: Exploring factors influencing nursing students' decisions to apply for clinical placements in international settings. *Nurse Educ Today*. 2015;35:941-7.
- Moore SA, McKay HA, Macdonald H, Nettlefold L, Baxter-Jones AD, Cameron N, Brasher PM. Enhancing a somatic maturity prediction model. *Med Sci Sports Exerc*. 2015;47:1755-64.
- Rosenberg AM, Newkirk MM, Rezaei E, Li Z, Oen KG. Soluble low density lipoprotein receptor-related protein 1 in juvenile idiopathic arthritis. American College of Rheumatology. San Francisco. November 10th, 2015
- Rosenberg AM, Maksymowych WP, Gui Y, Marotta A. Serum 14-3-3η is present in juvenile idiopathic arthritis and is not uniquely associated with RF+ polyarthritis. American College of Rheumatology. San Francisco. November 10th, 2015
- Rosenberg AM, Rhoades G, Chapman D, Belev G, Wiebe S, Cooper D, Wong A, Eames B. Imaging growing joints by diffraction enhanced-computed tomography using a synchrotron light source. American College of Rheumatology. San Francisco. November 9th, 2015
- Shah SM, Loney T, Dhaheer SA, Vatanparast H, Elbarazi I, Agarwal M, Blair I, Ali R. Association between acculturation, obesity, and cardiovascular risk factors among male South Asian migrants in the United Arab Emirates - a cross-sectional study. *BMC Public Health*. 2015;15:204.
- Wilson-Gerwing T, Panahifar A, Cooper DML, Rosenberg AM. Age-related differences in collagen-induced arthritis: Clinical, imaging, and biological characteristics in juvenile compared to adult animals. American College of Rheumatology. San Francisco. November 10th, 2015
- Zahedi Niaki O, Clarke AE, Ramsey-Goldman R, Yeung R, Hayward K, Oen K, Duffy C, Rosenberg A, O'Neil K, von Scheven E, Schanberg L, Labrecque J, Lee J LF, Bernatsky S. Cancer Risk in 5,108 Patients with Juvenile Idiopathic Arthritis (JIA). American College of Rheumatology. San Francisco. November 8th, 2015

parental role. Several studies have recognized the benefit of writing interventions for other populations of family caregivers in relation to supporting and enhancing participant hope and, consequently, their overall health.

Currently, with funding from the Saskatchewan Health Research Foundation (SHRF), Dr. Bally and a team of researchers are set to pilot test the feasibility, acceptability, and effectiveness of the intervention by evaluating participant outcomes for parents who have children with LLIs or LTIs. Dr. Bally's research has the potential to support our pediatric palliative care program in Saskatchewan which strives to provide care that considers all aspects of child and family health. This research is a critical part of her developing program of research and it aims to enhance the care that parents of children with a variety of LLIs and LTIs receive. The completion of Dr. Bally's current research will provide the impetus to apply for additional national tri-council funding to conduct a larger, multi-site RCT study to further test the theory-based hope intervention.

Dr. Jill Bally is an Assistant Professor in the College of Nursing, University of Saskatchewan

IP is a rare X-linked dominant genodermatosis. This genetic skin condition affects ectodermal tissues (skin, eyes, teeth, hair, and central nervous system) with a 20:1 female predominance. The most common genetic defect associated with the condition is a deletion of exon 4-10 in the IKBKG gene (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase gamma). IP is often mistaken for Herpes Simplex infection due to the presence of vesicles in the neonatal period; however, the distribution along Blaschko lines is unique to IP. Lesions are shown in Figures A, B, and C.



Figure A: Vesicles in linear distribution
Figure B: Crusting of lesions
Figure C: Thick dry plaques with peeling

Mutations causing IP are de novo in 50% of cases and lead to inhibition of the NF-kB signaling pathway, impairing the regulation of cell growth and apoptosis. Classically the skin lesions are characterized by erythematous linear streaks and plaques of vesicles following Blaschko lines. Other tissues of ectodermal origin are involved in up to 80% cases. Morbidity can arise from dental anomalies (late dentition, hypodontia, and conical teeth), ocular anomalies (strabismus, neovascularizations, and retinal detachment) and central nervous system (CNS) manifestations (developmental delay, seizures, and ischemia). Prognosis and outcome worsens in the presence of CNS manifestations. White matter is particularly vulnerable to destruction, possibly involving vascular abnormalities, micro and macrovascular occlusions, and inflammation.

Incontinentia Pigmenti may be a difficult to distinguish from herpes infection in the presence of a newborn with vesicular rash and seizures. Once infection has been excluded, IP should be considered, especially if Blaschko lines, extracutaneous manifestations and eosinophilia are present, there is a family history of IP, and/or recurrent male fetus spontaneous abortions. The diagnosis of IP is important because of the high incidence of major anomalies associated with the diagnosis as well as genetic implications on further family planning.

Camille is an RII and was supervised by Dr. Krista Baerg, Dept of Pediatrics

Research Project Opportunities

“Survey of Kawasaki Disease awareness among Saskatchewan physicians”

Study format: Survey

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

“Relationship of ESR and CRP with inflammatory cytokine biomarkers”

Study format: Database analysis

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

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!

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:

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Next submission deadline is January 8, 2015!

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



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