ABSTRACTS – 2020 PEDIATRIC RESEARCH DAY – UNIVERSITY OF ALBERTA – EDMONTON, AB

ABSTRACTS

Cardiology
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HALPIN, Anne (Graduate Student)
KARWI, Qutuba (Postdoctoral Fellow)
LECLAIR, Guillaume (Subspecialty/Resident)
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Pajanen, Kiera (UofA, nonfaculty)
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Shen, Yishi (Graduate Student)
Sehn, Yishi (Graduate Student)
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Hammond, Leah (Graduate Student)
Sacre, Lori-Ann (Research Associate)

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Rajagopal, Manasi (UofA, nonfaculty)

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Hinchliffe, Tierah (Graduate Student)
Mander, Inderdeep (Undergraduate Student)
Petrova, Alexandra (UofA, nonfaculty)
Pauline, Mirielle (Graduate Student)

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Huie, Michelle (Subspecialty/Resident)
McNiven, Claire (Subspecialty/Resident)

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Walton, Jennifer (Faculty/Clinical Academic Colleague)

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Freire, Dolores (Clinical/Research Fellow)
Gates, Allison (UofA, nonfaculty)
Kimani, Emily (Undergraduate Student)
Mccreary, Megan (Undergraduate Student)
Sraje, Reshma (Graduate Student)
Wingert, Aireen (UofA, nonfaculty)

iHOPE
Aborkhees, Ghada (Graduate Student)
Brennan, Lesley (UofA, nonfaculty)
Landry, Takaaki (Graduate Student)
Wine, Osnat (Graduate Student)
Zhu, Hanjie (Undergraduate Student)

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Johnson, Peter Anto (Graduate Student)
Kim, Seung Yeon (Visiting Scholar)
Lifeso, Natasha (UofA, nonfaculty)
Mangat, Avneet (UofA, nonfaculty)
Shim, Gyu-Hong (Visiting Scholar)
Zehnder, Emily (Graduate Student)

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Mella, Allison (Undergraduate Student)
Namsechi, Risa (Subspecialty/Resident)
Narayanamurti, Rukhmani (Graduate Student)
Ng, Cheuk-Him (Andy) (Subspecialty/Resident)
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HICKS, Alex (Undergraduate Student)
TESSIER, Carmen (Graduate Student)
ZHANG, Caseng (Undergraduate Student)

Non-pediatric-Divisional Affiliation
DAMANHOURY, Samah (Childhood Obesity)
DAVILA-CERVANTES, Andrea (Office of Lifelong Learning; UofA, FOMD)
GATES, Michelle (ARCHE)
Knowledge-based 3D Reconstruction and Conventional 3D Echocardiogram Algorithms are Comparable in Measuring Pediatric Left Atrial and Ventricular Volumes

Attila Ahmad MBChB, Sachie Shigemitsu MD, Nee Khoo MD, Yozo Termachi MD, Jonathan Windram MBChB, Tim Colen MD, Luke Eckersley MBBS PhD

Introduction:
Methods used to measure cardiac chambers, including two-dimensional echo (2DE), three-dimensional echo (3DE) and cardiac magnetic resonance imaging each have limitations of accuracy, precision and availability, and commercial echocardiographic atrial measurement packages are lacking. The Ventripoint system utilized magnetic probe localization and a validated database of normal ventricular and atrial morphologies to calculate chamber volumes. This study aimed to compare left ventricular (LV) and atrial (LA) volumes obtained using Ventripoint VMS software to a conventional 3D echo software algorithm designed for the LV (Tomtec).

Methods:
Healthy controls (n=50) aged 0 to 18 years were prospectively recruited and 3D DICOM datasets focused on the LV and LA acquired. LV and LA volumes and ejection fractions were measured using TomTec Image Arena 3D LV analysis package. On the same 3D datasets, LV and LA volume, and ejection fractions were obtained using the VMS protocols. Pearson correlation coefficients and intraclass coefficients (ICC) were calculated. Results: The time to analyze volumes using VMS were less than using Tomtec (LV VMS 2.3±0.5, Tomtec 3.3±0.84 mins, p<0.001; LA: VMS 1.92±0.36, Tomtec 3.4±0.98 mins, p<0.001). There was a good correlation between VMS and Tomtec LV systolic (R2 =0.82) and diastolic (R2 =0.88) volumes, and between VMS LA diastolic (R2 =0.81) and systolic (R2 =0.87) volumes on linear regression models (Figure). The intraclass coefficients showed very good to excellent correlations between VMS and Tomtec measuring systolic and diastolic volumes: LA systolic ICC 0.91 (95% CI 0.78, 0.96), LA diastolic ICC 0.89 (95% CI 0.81, 0.93), LV diastolic ICC 0.90 (95% CI 0.77, 0.95), LV systolic ICC 0.89 (95% CI 0.81, 0.94).

Conclusion:
There was good correlation between a knowledge-based and 3D echocardiographic algorithms when measuring LA and LV volumes in pediatric patients, especially in patients with small body surface area. VMS was slightly faster than Tomtec in analyzing volumetric measurements.

Figures/graphs, next page
AHMAD, ATTILA (Cardiology, Subspecialty/Resident)
T1 mapping to assess hepatic and myocardial characteristics in children with single ventricle circulation

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Introduction:
(i) Background: Congenital heart disease consisting of a single ventricle (SV) requires the Fontan operation which results in passive flow of systemic venous blood directly to the pulmonary circulation without a ventricular pump. This leads to hepatic venous congestion which can result in hepatic fibrosis. Previous studies suggest hepatic changes occur prior to the Fontan completion. Additionally, fibrotic myocardial remodeling may lead to ventricular dysfunction, transmitting further back pressure to the pulmonary system.
(ii) Purpose: To compare quantitative T1 cardiovascular magnetic resonance (CMR) imaging of the myocardium and liver between SV patients and controls, which is a measure of fibrosis.

Methods:
Retrospective review of 16 SV patients who underwent CMR with myocardial T1 mapping with the liver also in the plane of view. SV patients were at various stages of palliation (preGlenn-6, post-Glenn-3, Fontan-7) and varying morphology, single left ventricle (SLV, n=6) vs single right ventricle (SRV, n=10). Biventricular patients who underwent CMR T1 mapping with structurally normal hearts and cardiac function were used as controls (n=21). Native T1 times were quantified using a modified Look-Locker inversion recovery (MOLLI) approach in the free-wall of the dominant ventricle at a mid-ventricular short axis level in SV and in the ventricular septum in controls. A region of interest (ROI) in the liver was measured in all patients from the same image, avoiding any vessels. Continuous variables were summarized with median and inter-quartile range and were compared between SV and controls using the Mann-Whitney U test.

Results:
SV patients were significantly younger than controls (1.6 vs 12.0 years, p=0.003). Ejection fraction (EF) was lower in SV patients (47%) than in controls (60%, p=0.012). Median myocardial T1 in SV was significantly higher than in controls (1066 vs 1014 ms, p=0.0002). Similarly, the liver T1 of SV was significantly greater than controls (705 vs 606 ms, p=0.0006). There was no difference between single LV and RV myocardial T1 (LV f 1056 vs RV 1065; p=0.43) or liver T1 (LV 678 vs RV 729; p=0.30)

Conclusion:
The increased myocardial T1 in SV suggests that myocardial fibrosis may be responsible for the ventricular dysfunction in this population. In addition, SV patients have increased liver T1 compared to controls even prior to the Fontan, suggesting that liver abnormalities occur earlier than previously thought. The findings of increased liver T1 may provide an earlier marker of liver fibrosis and warrants further study.

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<td>Liver T1</td>
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EF—ejection fraction, Y—year, SV—single ventricle, IQR—interquartile range
ABSTRACT – 2020 PEDIATRIC RESEARCH DAY, MAY 13, 2020 – EDMONTON, AB
HALPIN, ANNE (CARDIOLOGY/TRANSPLANTATION)

ABO Antibody Detection for Organ Transplantation: Time for New Technologies?

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Purpose:
ABO incompatible transplantation expands the donor pool for infants awaiting heart transplantation; this is made possible as naturally occurring ABO antibodies are not present at birth but develop by 6-12 months of age. Accurate characterization of ABO antibodies (Abs) is critical for clinical management in ABO incompatible (ABOi) transplantation. The current ABO-Ab detection method using erythrocyte agglutination is limited by lack of ABO-subtype specificity, imprecise ABO-Ab isotype differentiation, and poor reproducibility. We previously developed an ABO-glycan microarray to begin addressing these limitations. The field of histocompatibility has greatly advanced characterization of HLA Abs using bead-based tools, thus our aim here was to create a similar solid phase bead assay for ABO-Ab analysis.

Methods:
ABO A- and B-subtype antigens (I,II,III,IV,V,VI) were coupled to Luminex beads and quantified using monoclonal ABO-Abs. Bovine serum albumin was coupled as a negative control bead. IgG and IgM isotypes with specificities for ABO A and B-subtypes were measured and compared in healthy adult plasma (n=28) by mean fluorescence intensity (MFI). These samples were also tested on the glycan array and by red cell agglutination.

Results:
ABO-A and -B subtype-specific Abs were detected, with high degree of variability in MFI values amongst subjects. IgG and IgM anti-A and/or anti-B Abs were detectable in non-AB subjects, although MFIs were low in some cases as shown for anti-A in Figure 1A. Anti-A and -B IgM MFI values were similar across individuals of blood group O, as compared to B and A subjects (respectively). However, IgG MFI values were higher in O individuals than in A or B subjects. The quantity of IgM isotype antibodies did not predict IgG levels (Figure 1B). IgM Ab alone did not predict the RBC agglutination titre, as some subjects had predominantly IgG ABO Abs.

Conclusion:
Initial results of our Luminex ABO-Ab assay are promising for eventual clinical laboratory development. The specificity of this assay will allow precise assessment of ABO-Ab to antigen subtypes, known to be expressed differently in cardiac endothelium than erythrocytes (1). The ability to measure IgM and IgG ABO-Ab makes it possible to evaluate the role of each in potential allograft damage. This assay also
allows for future exploration of safe ABO incompatible donation into older children with pre-existing ABO Abs, as is done in adult renal patients using plasmapheresis and other strategies to remove Abs. IgG and IgM discrimination may be particularly relevant in the setting of plasmapheresis, which more efficiently removes IgM than IgG.


**Figure 1A.** Antibodies to ABO A (n=15) show high variability between individuals; some healthy controls had unexpectedly low anti-A for both IgG and IgM antibodies. Graph represents the 5th to 95th percentiles.

**Figure 1B.** Comparison of ABO A IgG and IgM isotype antibodies, matched for each healthy donor (n=28)
ABSTRACT – 2020 PEDIATRIC RESEARCH DAY, MAY 13, 2020 – EDMONTON, AB
KARWI, QUTUBA (CARDIOLOGY)

Selective elevation in cardiac branched-chain keto acids levels impairs cardiac insulin sensitivity by disrupting mitochondrial insulin signaling

Qutuba Karwi; Golam Mezbah Uddin; Simran Pherwani; Cory Wagg; Liyan Zhang; Gary Lopaschuk
Cardiovascular Research Centre, University of Alberta, Edmonton, Alberta, Canada

Introduction:
Insulin resistance negatively impacts cardiac energy metabolism and function. Perturbations in cardiac branched-chain amino acids (BCAAs) oxidation have been suggested to contribute to the development of cardiac insulin resistance. However, whether it is the accumulation of BCAAs or its metabolites, namely branched-chain keto acids (BCKAs), that mediate cardiac insulin resistance is not clear. It is also unknown how impaired BCAAs oxidation mediates cardiac insulin resistance.

Methods:
We specifically deleted mitochondrial branched chain aminotransferase (BCATm) in the mouse heart, which results in an increase in BCAAs and a decrease in BCKAs selectively in the heart. We also used an isolated working mouse heart model to measure cardiac insulin sensitivity and energy metabolism.

Results:
There was no difference in body weight or whole-body insulin sensitivity between BCATm−/− mice and their wildtype littermates (WTCre+/+). BCATm−/− mice also had normal contractile function compared to WTCre+/+ mice. However, there was a significant increase in insulin-stimulated cardiac glucose oxidation rates in BCATm−/− mice compared to WTCre+/+ mice, independent of any changes in glucose uptake or glycolytic rates. This enhancement in cardiac insulin sensitivity was associated with an increase in the phosphorylation of protein kinase B (Akt) and an activation of pyruvate dehydrogenase (PDH), the rate-limiting enzyme of glucose oxidation. To determine the impact of reversing these events, we investigated the impact of elevating cardiac BCKAs levels on cardiac insulin sensitivity. We perfused isolated working mice hearts with high levels of BCKAs (α-keto-isocaproate 80 μM, α-keto-β-methylvalerate 100μM, α-keto-isovalerate 70 μM), that can be seen in diabetes and obesity. The BCKAs completely abolished the stimulatory effect of insulin on glucose oxidation. We also found that these high levels of BCKAs abolished insulin-stimulated mitochondrial translocation of Akt, an effect which was associated with an inhibition of PDH.

Conclusion:
The accumulation of BCKAs, and not BCAAs, is a major contributor to cardiac insulin resistance via abrogating mitochondrial translocation of Akt.
Abstract #
Presenter: Leclair, Guillaume
Supervisor: Attallah, Joseph
Title: Neurodevelopmental outcomes after neonatal surgical intervention for cyanotic tetralogy of Fallot and other lesions with right ventricular outflow tract obstruction.
Authors: Guillaume Leclair, MDCM, Adil Digankar, MD, Charlene M. T. Robertson, MD, Gwen Y Alton, MSN, Gonzallo Guerra, MD, Joseph Atallah, MD CM.

Introduction

Neonatal cardiac surgery carries a significant risk for adverse neurodevelopmental outcomes. There is little data on right sided obstructive congenital lesions requiring repair in early infancy. We hypothesize that the neurodevelopmental outcomes in cyanotic patients undergoing neonatal repair vs. late repair in non cyanotic patients with similar lesions.

Methods

A prospective cohort of 77 consecutive cyanotic neonates underwent surgery for right outflow tract obstructive lesion (tetralogy of Fallot, Pulmonary atresia with a ventricular septal defect, or double outlet right ventricle with normally related great vessels) at a corrected gestational age of 6 weeks or less, between 2006 and 2017. Surgery include complete repair or shunt palliation. They had multisite multidisciplinary health and neurodevelopmental outcomes (Bayley Scales of Infant Development III) at 18-24 months of age. Demographic, perioperative and follow-up data was collected including data on cardiac catheterization and repeat surgical interventions. Univariate and multivariable analyses will be performed to identify factors associated with neurodevelopmental outcomes.

Results

Data analysis is ongoing. Thirteen (17%) patients underwent repair by palliative shunt. There were 6 (8%) deaths with 3 (50%) in the palliative shunt group. Seventy-one (83%) patients survived to the 18-24 month mark to assess early infancy neurodevelopmental outcome. Data on disabilities is pending.

Conclusion

We hope this study will yield insightful information on the demographic, anatomical, pre-operative, operative and post-operative variables that may affect the neurodevelopmental outcomes of neonates who undergo full repair or palliative shunt in the first 6 weeks of life for right sided obstructive congenital heart lesions. This information may be particularly useful when counseling pregnant mothers or new parents, as well as potentially identifying modifiable factors to optimize developmental outcomes.

Funded by Western Canadian Complex Pediatric Therapies Follow-up Program, Alberta Health and Wellness.
Inflammation is implicated in doxorubicin-induced cardiac and renal injury and later onset hypertension-induced cardiomyopathy and nephropathy

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¹Cardiovascular Research Centre, Department of Pediatrics and the ²Department of Oncology, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada.

Introduction:
Anthracyclines, such as doxorubicin (DOX), are very effective anticancer agents that are widely used in pediatric cancer patients. Nevertheless, anthracyclines are known to have cardiotoxic and nephrotoxic effects that may go undetected at the time of treatment but progress to cardiomyopathy and nephropathy later in life. We have developed a pre-clinical model of occult DOX-induced cardiovascular and renal toxicity in young mice and have demonstrated that juvenile exposure to DOX renders mice more susceptible to the detrimental effects of Angiotensin II (Ang II)–induced hypertension later in life. However, the molecular mechanism responsible for the pathophysiological changes of early DOX-induced cardiotoxicity and nephrotoxicity and the late-onset overt stress-induced cardiomyopathy and nephropathy remains unknown. As growing evidence suggests a central role of systemic inflammation in the development of myocardial and renal damage induced by chemotherapy, we proposed that systemic inflammation is implicated in the early and delayed DOX-induced cardiac and renal toxicity in our model.

Method:
Five-week-old male mice were administered a low dose of DOX (4 mg/kg) or saline once a week for 3 weeks and then allowed to recover for 5 weeks. Following the 5-week recovery period, mice were infused with Ang II or saline for 2 weeks. The circulating cytokines and chemokine levels were determined using multiplex assay.

Results:
One week after the last DOX administration, Interleukin-5 (IL-5), Interferon beta 1 (INFβ), CXCL9 and tumor necrosis factorα (TNFα) were increased in serum of DOX-treated mice demonstrating molecular signs of cardiac and renal stress. Furthermore, DOX-treated mice demonstrate detrimental cardiac and renal changes such as maladaptive cardiac remodeling and renal atrophy in response to Ang II–induced hypertension later in life. These detrimental observations were associated with a significant elevation of IL-1α, IL-20 and CXCL5 in the serum of DOX-treated mice exposed to Ang II.

Conclusion:
Our data suggest that inflammation may play a critical role in DOX-induced injury and later onset Ang II-induced cardiomyopathy and nephropathy. Based on this, we suggest that targeting inflammation may be a potential new therapeutic approach for the treatment of juvenile DOX-induced cardiotoxicity and nephrotoxicity.
Differences in ABO Antibody Production in Female vs. Male Mice

Bushra Anjum¹, Ibrahim Adam²,³, Jordana Fersovich¹, Maurits Sulzer¹, Jean Pearcey¹,³,⁴, Kesheng Tao¹,³,⁴, Bruce Motyka¹,³,⁴ and Lori J. West¹-⁵

¹Dept. Pediatrics; ²Dept. Medical Microbiology & Immunology; ³Alberta Transplant Institute; ⁴Canadian Donation & Transplantation Research Program; ⁵Depts. Surgery and Laboratory Medicine & Pathology; University of Alberta

Introduction:
ABO histo-blood group incompatibility is a barrier in solid organ transplant due to the presence of ‘natural’ preformed ABO antibodies. However, ABO-incompatible (ABOi) heart transplantation is successful in infants as ABO antibodies are low/absent. A better understanding of the specificity and the production of natural ABO antibodies may allow for successful ABOi transplantation at older ages. In mice, ABO antibodies develop naturally with age and can be ‘induced’ following sensitization (eg, with human A/B erythrocytes). Herein, we sought to determine the isotype (IgM/IgG) and subtype (I-VI) specificity of ABO antibodies produced naturally or induced by sensitization in mice as a function of age and sex.

Methods:
BALB/c mice were assessed for natural ABO antibody production over time (n=32/39, female/male; age 1-18 months), or challenged with human A erythrocytes (5 weekly intraperitoneal injection) beginning at 5 weeks of age to measure induced ABO antibody production (n=13/8, female/male; age 1-3 months). Blood samples from each mouse was collected in regular intervals by tail bleed and plasma ABO antibody titre and ABO antibody isotype and subtype specificity was determined by hemagglutination assay and ABH glycan microarray, respectively.

Results:
Female mice produced markedly higher natural anti-A and anti-B ABO antibodies compared with male mice. With age, natural ABO antibodies shifted from an IgM to IgG isotype in females but remained predominantly IgM in males. Most natural ABO antibodies were specific to subtypes III/IV with specificity to subtypes I and II absent or very low. In contrast, following A-antigen sensitization both female and male mice produced IgM and IgG anti-A antibodies with specificities for all subtypes (I-VI).

Conclusions:
Male and female mice show distinct differences in ABO antibody production depending on whether these antibodies are produced naturally or induced by sensitization. Future studies will explore mechanisms for these sex differences and relevance to humans.
Semi-automatic MRI tracking software reflects ventricular function and tissue characteristics in patients with myocardial dysfunction
Kiera Pajunen, Mirza Beigh, Joseph Pagano, Jennifer Conway, Simon Urschel, Michelle Noga, Chentel Cunningham, Kumaradevan Punithakumar, Edythe Tham

Introduction:
Deformation analysis (strain) of the cardiac muscle is a technique to assess cardiac function. We used a novel semi-automated MRI deformation software to explore the relationship between strain parameters, volumetric function and myocardial characteristics in pediatric myocardial diseases. We hypothesized that peak myocardial strain and strain rate would correlate with cardiac function in patients with myocardial dysfunction.

Methods:
Cardiac MRI was performed on 12 pediatric patients, 83% male, aged 11.8±3.8 years, BSA 1.46±0.49 m$^2$, on a 1.5T Siemens scanner with a diagnosis of myocarditis (n=6), Duchenne muscular dystrophy (n=4), and dilated cardiomyopathy (n=2). MRI derived LV and LA strain and strain rate (SR) were measured in the 4-chamber cine view to assess cardiac function using in-house developed software. Peak strain, being a negative value, indicates better function if values are more negative. Other metrics collected included LV end-diastolic (LVEDVi) and end-systolic (LVESVi) volumes and ejection fraction (LVEF). Myocardial tissue characteristics obtained included native T1 mapping and extracellular volume fraction (ECV), which are increased in the presence of fibrosis. Spearman correlation assessed relationships between the parameters.

Results:
Mean LVEF was 43±19%, T1 = 1042.2±56.7 and ECV = 23.5±9.7%. Improved LV peak strain, LA peak strain, and strain rate (more negative) correlated with increased LVEF (r= -0.79, r= -0.62, r= -0.76 respectively), with most correlations being strong. Decreased LV SR (less negative) showed moderate correlation with increased LV end systolic volume (r=0.58), but did not correlate with other parameters. Improved LV strain showed moderate correlation with lower T1 values (r= 0.68). Improved LA strain showed a moderate positive correlation with lower T1 values (r=0.58) and strong positive correlation with ECV (r=0.77). There were weak correlations between LV peak strain and LV volumes.

Conclusions:
The correlations between strain and SR with LVEF and myocardial tissue characteristics validates this technique as useful tool to assess cardiac function in pediatric patients with myocardial diseases. This novel MRI tracking software may be a useful tool for serial assessment of cardiac dysfunction and help predict disease progression or differences between entity of dysfunction in this population.
Administration of empagliflozin provides an extra source of fuel to the hearts of \textit{db/db} mice

\textit{Simran Pherwani}\textsuperscript{1}, Sonia Rawat\textsuperscript{1}, Kim L. Ho\textsuperscript{1}, Cory S. Wagg\textsuperscript{1}, Liyan Zhang\textsuperscript{1}, Gary D. Lopaschuk\textsuperscript{1}

Cardiovascular Research Centre, University of Alberta, Edmonton, Canada

\textbf{Introduction:}
Sodium-glucose co-transporter inhibitors (SGLT2i) are a class of anti-diabetic drugs which act to improve glycemic control by preventing glucose reabsorption in the kidneys and its re-entry into the circulation. It has been recently shown that SGLT2i, such as empagliflozin, decrease hospitalization and deaths due to cardiovascular outcomes such as heart failure in type 2 diabetic patients at high risk for cardiovascular events. However, it has not been fully established how exactly SGLT2i acts to improve cardiac function. In the failing heart, there is a decreased energy production in the heart, leading to an “energy starved” heart. SGLT2i have been shown to increase circulating ketone levels, and it has been proposed that an increase in ketone oxidation by the heart may be beneficial. We aimed to determine the effect of acute and chronic administration of empagliflozin to control or \textit{db/db} mice on cardiac energy metabolism and cardiac function.

\textbf{Methods:}
Isolated working hearts from C57BL/6J mice (8-10 wk of age) were treated with or without 100 uM empagliflozin to assess substrate oxidation rates and cardiac work. A separate set of 18-week old C57BL/6J and \textit{db/db} mice were treated with either a single oral 10 mg/kg dose of empagliflozin, or with 10 mg/kg/day of empagliflozin for 4 weeks. Echocardiography was performed to assess cardiac function.

\textbf{Results:}
Empagliflozin had no significant direct effects on cardiac work, glucose oxidation, fatty acid oxidation rates, or cardiac function in isolated working hearts. However, empagliflozin did increase plasma ketone levels in both C56BL/6J and \textit{db/db} mice following acute and chronic administration. While acute empagliflozin administration did not alter cardiac function or energy metabolism in either C56BL/6J or \textit{db/db} mice, it did improve cardiac work in chronically treated \textit{db/db} mice. This was associated with an overall increase in cardiac energy production due to an increased ketone supply to the heart, resulting in increased contribution of ketone oxidation to cardiac energy production.

\textbf{Conclusion:}
The acute administration of empagliflozin does not have direct effects on cardiac energy metabolism or function in the heart. As a result, the long-term benefit of empagliflozin on cardiac function in \textit{db/db} mouse hearts was due to indirect mechanisms, possibly by providing the heart with an extra source of fuel in the form of ketones that increased the energy supply to the heart.
Inhibition of hepatic Surf4 reduces secretion of VLDL, lowers plasma levels of cholesterol, and ameliorates the development of atherosclerosis

Bingxiang Wang#, Yishi Shen#, Lei Zhai#, Xiaodan Xia#, Hong-mei Gu*, Yongfang Zhao#, Xiaole Chang#, Adekunle Alabi, Sijie Xing, Shijun Deng, Boyan Liu#, Guqing Wang, Shucun Qin*, Da-wei Zhang*

a Institute of Atherosclerosis and College of Basic Medical Sciences in Shandong First Medical University (Shandong Academy of Medical Sciences), Taian, China. b Department of Orthopedics, The Sixth Affiliated Hospital of Guangzhou Medical University, Qingyuan People’s Hospital, Qingyuan, China. c Department of Pediatrics, Group on the Molecular and Cell Biology of Lipids, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada.

Background:
LDL is catabolized from VLDL and cleared by LDL receptor (LDLR). VLDL is assembled in the ER lumen of hepatocytes and then transported to the Golgi through VLDL transport vesicle (VTV). Surf4 is a cargo receptor that mediates protein secretion. How VLDL is recruited to VTV and the role of Surf4 in this process, however, are unclear.

Method:
We generated Surf4 liver specific knockout (Surf4LKO) mice, silenced Surf4 in hepatocytes and Ldlr knockout (Ldlr-/-) mice, and performed confocal microscope and co-immunoprecipitation.

Results:
Surf4 colocalized and co-immunoprecipitated with apoB100. Lacking hepatic Surf4 markedly reduced VLDL secretion and plasma levels of cholesterol, triglyceride, and apoB100, resulting in the retention of VLDL in the ER lumen. However, liver triglyceride and cholesterol levels, plasma alanine aminotransferase activity, liver weight, and body weight were comparable in Surf4LKO mice and their wild-type littermates. Expression of genes important for de novo lipogenesis was reduced. Furthermore, knockdown of Surf4 expression in Ldlr-/- mice drastically reduced plasma triglyceride and non-HDL cholesterol levels and the development of atherosclerosis, but did not significantly affect HDL cholesterol levels.

Conclusion:
Surf4 interacts with apoB and acts as a cargo receptor to facilitate VLDL secretion. Hepatic deficiency of Surf4 reduces VLDL secretion, but does not cause hepatic lipid accumulation or notable liver damage. Our findings indicate that inhibition of hepatic Surf4 has a potential to be a novel strategy to suppress LDL production and reduce the risk of atherosclerosis with fewer side effects for patients with hypercholesterolemia, especially homozygous familial hypercholesterolemia.
The incidence and impact of malnutrition on survival and Fontan failure

R. Sekhon, MD; R. Foshaug (research coordinator); P. Kantor, MD; G. Mansukhani, MD; S. Hollander, MD; K. Lewis, RD; J. Conway, MD

Introduction:
Patients born with functionally univentricular hearts typically undergo three stage palliation which includes the Norwood, Glenn, and the Fontan surgeries. These surgeries re-route systemic venous drainage into the pulmonary arteries, bypassing the heart. The Fontan procedure is the final stage which routes IVC flow to the pulmonary arteries. The Fontan patient is at risk of complications including chylothorax, hepatic fibrosis/cirrhosis, plastic bronchitis, and protein losing enteropathy. From a nutritional perspective, little is known about the impact of malnutrition on Fontan failure.

There are few studies documenting the incidence of malnutrition in Fontan patients. Anderson et al (2011) report a 19% incidence in their cohort of a weight-for-age Z score (WAZ) <-2 pre-Fontan; Burch et al (2016) report a lower incidence of only 5% having WAZ<-2 in the Single Ventricle Reconstruction (SVR) trial pre-Fontan. They found mean WAZ and HAZ (height-for-age Z scores) decreased from Fontan to 6 years ages. In terms of impact on survival, Burch et al (2016) report the prevalence of WAZ<-2 was similar between those who died or were transplanted versus those who survived at 6 years age. Further research will clarify the incidence of moderate-severe malnutrition in Fontans, its timing and progression post Fontan, and impact on Fontan failure.

Methods:
This is a retrospective cohort study of all patients under 18 years of age undergoing Fontan surgery at Stollery Children’s Hospital. Patients who were premature < 36 weeks gestational age or had a confirmed or suspected genetic/syndromic abnormality were excluded. The Research Ethics Office of the University of Alberta approved this study. Patients were followed up to 10 years post Fontan. Malnutrition was defined based on WAZ, HAZ, and BMIZ as per the Michigan Tool (M Tool) and was categorized as none, mild, moderate or severe based on Z scores. Fontan failure was defined as death or listing for heart transplant.

Results:
Our hypothesis is there is an underappreciated incidence of malnutrition in Fontan patients and that malnutrition negatively impacts survival or increases incidence of Fontan failure. There were 187 Fontan surgeries performed to date at our institution. Currently, we are reviewing data for these patients. Data collection is expected to be completed by April 2020.

Conclusions:
Currently, we are near-completion of the data collection phase. We anticipate completion of data analysis by mid-April 2020 with results/conclusion to follow.
Chronically elevating circulating ketones reduces cardiac inflammation and blunts the development of heart failure

Shubham Soni, Nikole Byrne, Shingo Takahara, Mourad Ferdaoussi, Rami Al Batran, Ahmed Darwesh, Jody Levasseur, Zaid Maayah, Donna Beker, Dyonne Vos, Mya Schmidt, Abrar Alam, Jon Schertzer, John Seubert, John Ussher, and Jason Dyck
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Introduction:
The failing heart has metabolic defects which impair ATP production and contractile function. Recent studies show that the failing heart upregulates ketone metabolism and may rely on ketones as a fuel. Ketones, namely β-hydroxybutyrate (βOHB), are produced in low glucose conditions, such as fasting. Furthermore, βOHB may be beneficial in heart failure (HF) as a more energy-efficient substrate, as well as a signaling molecule. However, whether chronic elevations in circulating ketones are beneficial remains unknown. Thus, regardless of the role that endogenous βOHB plays in HF development, elevating circulating βOHB levels beyond what is normally observed in HF may serve as a novel therapy to improve cardiovascular outcomes in patients with HF.

Methods:
To determine whether elevating circulating ketones may improve cardiac function in HF, we utilized an inducible skeletal muscle-specific knockout of succinyl-CoA:3-ketoacid-CoA transferase (SCOT KO), the rate limiting enzyme in ketone catabolism. We then subjected these SCOT-KO and wild-type littermate mice to transverse aortic constriction (TAC) surgery to generate pressure overload-induced HF. Levels of circulating glucose and βOHB were measured, echocardiography was used to assess heart function, and ex-vivo heart perfusions were also performed to assess signaling pathways.

Results:
SCOT expression was significantly reduced in skeletal muscle of SCOT-KO compared to wild-type mice (p<0.001) without appreciable changes in cardiac SCOT expression. Given that ketones are largely utilized in skeletal muscle, the smSCOT-KO results in a 1.6-fold increase in fasted circulating βOHB compared to wildtype mice (p<0.01). Interestingly, this rise in circulating βOHB was associated with protection from TAC-induced decline in systolic (49.8% vs 35.4% ejection fraction; p=0.0054) and diastolic (E/A: p=0.02; E/E’: p=0.0072) function in SCOT-KO compared to wildtype littermates. This was absent from any changes cardiac ketolytic enzymes, suggesting another component at play. Further analysis revealed that SCOT-KO mice had notably lower cardiac and systemic inflammation.

Conclusion:
Together, these data are the first to show that elevating circulating ketones via a skeletal muscle SCOT-KO prevents cardiac dysfunction in mice with HF via increase circulating ketones. This suggests that elevated circulating ketones in HF may be an adaptive process and that further elevating circulating ketones may be a therapeutic approach in the management and treatment of HF.
Membrane type 1 matrix metalloproteinase promotes ectodomain shedding of low-density lipoprotein receptor and accelerates the development of atherosclerosis

Xiaodan, Xia, Adekunle Alabi, Xiao-Dan Xia, Hong-mei Gu, Faqi Wang, Shi-jun Deng, Nana Yang, Ayinuer Adijiang, Donna N. Douglas, Norman M. Kneteman, Yazhuo Xue, Li Chen, Shucun Qin, Guiqing Wang, Da-wei Zhang

Low-density lipoprotein receptor (LDLR)-mediated cellular LDL uptake is the main pathway for plasma LDL cholesterol (LDL-C) clearance. It has been documented that LDLR can be proteolytically cleaved to release its soluble ectodomain (sLDLR) into extracellular milieu. Plasma sLDLR levels are positively correlated with plasma LDL-C levels. Membrane type 1- matrix metalloproteinase (MT1-MMP) is a Zn2+-dependent endopeptidase that can cleave extracellular matrix and non-matrix substrates. However, the proteinase responsible for LDLR cleavage and the contribution of MT1-MMP are unknown. We found that knockdown of MT1-MMP increased cellular LDLR abundance and reduced the levels of sLDLR in cultured hepatocytes. LDLR and MT1-MMP were co-immunoprecipitated and co-localized. Consistently, mice lacking hepatic MT1-MMP displayed an increase in liver LDLR levels and a reduction in plasma levels of sLDLR, HDL-cholesterol, and non-HDL cholesterol. Opposite effects were observed when MT1-MMP was overexpressed. Moreover, we demonstrated that overexpression of MT1-MMP in apolipoprotein E knockout (apoE-/-) mice significantly increased atherosclerotic lesion area by approximately 30%, while knockdown of hepatic MT1-MMP reduced cholesteryl ester accumulation in the aortas of apoE-/- mice by approximately 45%. In addition, we found that the majority of circulating sLDLR were associated with apoB and apoE-containing lipoproteins in both mouse and human plasma. Plasma levels of sLDLR were significantly increased in subjects with high plasma LDL-C levels. Thus, we demonstrate that MT1-MMP promotes ectodomain shedding of hepatic LDLR, thereby regulating plasma cholesterol levels and the development of atherosclerosis.
Adropin stimulates cardiac glucose oxidation by inhibiting cluster of differentiation 38 that results in activation of pyruvate dehydrogenase

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Introduction:
Although initially identified as a major regulator of liver metabolism, clinically, reduced circulating levels of adropin has been suggested to be an independent risk predictor of several cardiovascular conditions including endothelial dysfunction, heart failure, acute myocardial infarction, coronary atherosclerosis, and cardiac syndrome X. We have recently demonstrated that adropin increases glucose oxidation and suppresses fatty acid oxidation in non-obese mouse hearts. As the specific adropin receptor has not yet been identified, the question as to how adropin initiates intracellular signaling remains unclear. Nicotinamide adenine dinucleotide (NAD⁺) is involved in protein lysine acetylation. It has been demonstrated that increased lysine acetylation of PDH negatively regulates glucose oxidation. Cluster of differentiation 38 (CD38), a transmembrane protein, has been identified as an NADase in vivo. CD38 knockout mice have higher NAD⁺ levels and are protected against obesity and metabolic syndrome. Here, we investigated whether CD38 may assist adropin in initiating intracellular signaling, and if the analogs of adropin, namely A43 and A49, have similar effects on cardiac glucose oxidation in non-obese mouse hearts.

Methods:
Isolated working hearts obtained from C57BL/6J mice were perfused with stepwise increased concentration of adropin/analgos from 2 to 200 nM for 70 min with 100 μU/ml insulin present during the last 20 min to assess glucose oxidation. Differentiated H9C2 cells were treated with 10 nM adropin or 10 μM CD38 inhibitor, as well as 100 nM phenylephrine to assess molecular signaling of glucose oxidation.

Results:
Like adropin, A43 and A49 stimulated glucose oxidation in the isolated working mouse hearts starting at a dose of 20 nM. This occurred in conjunction with a deacetylation of pyruvate dehydrogenase (PDH), the rate-limiting enzyme of glucose oxidation, and a reduction in CD38 activity. In line with this, a rapid decrease in phosphorylation of PDH (decreased phosphorylation increases PDH activity) was evident in H9C2 cells treated with adropin for 15 min. These effects of adropin was replicated by pharmacological inhibition of CD38. In hypertrophied H9C2 cells induced by phenylephrine, the increase in p-PDH was also acutely prevented by adropin.

Conclusions:
Adropin and its analogs enhance cardiac glucose utilization though a mechanism that is associated with reducing CD38 activity, resulting in dephosphorylation and deacetylation of PDH.
An examination of the use and interpretation of p-values in pediatric critical care RCT’s with mortality outcomes
Sarah Farrow, Ari Joffe

Introduction:
Misinterpretation of null-hypothesis statistical testing (NHST) prevents recognition of high false positive rates (FPR), and may account for poor reproducibility of studies. We aimed to determine the implications of reported p-values and statistically significant findings in pediatric critical care randomized controlled trials (RCT’s).

Methods:
The EPICC database reports abstracts of all 444 published pediatric critical care RCT’s from 1980-2019. We searched EPICC separately for ‘mortality’ (n=135) and ‘more than 1 center’ (n=80) studies. We excluded studies with 1 or no deaths, not reporting on deaths, having pilot feasibility or short-term physiologic outcomes only, or non-obtainable publication (only n=2). This generated 120 RCT’s with a mortality outcome. Reverse Bayesian implications from the publications were obtained, including FPR (defined as a statistically significant finding that is due to chance alone).

Results:
Of 120 studies, 73 (61%) were single center, sample-size/group was median 40 [IQR 22, 80], patients often had sepsis (22%) or were ventilated (36%), and mortality was the primary outcome in 16%. Reported p-values were ≤0.005 in 1.7%, 0.0051-0.05 in 8.3%, and 0.051-0.10 in 10.8% of studies. Reverse-Bayesian analysis of the 10% of studies reporting p-value ≤0.05 found the i) prior probability of the alternative hypothesis [PrP(H1)] would need to be median 76% [IQR 54, 80] in order to have FPR 5%; ii) minimum FPR was 14.4% [IQR 5.8, 17.1] assuming a PrP(H1) 50%, and 59.9% [IQR 34.5, 64.9] assuming a more realistic PrP(H1) 10%; iii) Bayes Factor Bound (upper bound on the likelihood ratio for H1 relative to Ho) was 4.0 [IQR 3.4, 8.5]; and iv) probability that a replication study would find a p ≤0.05 was 60.9% [IQR 57.9, 73.9]. By calculating post-hoc power for medium effect sizes, and assuming PrP(H1) 50%, in the field of pediatric critical care, the PPV and NPV of studies using α≤0.05 can be expected to be 64.3% [IQR 28.6, 86.5] and 51.1% [IQR 49.2, 58.3] respectively. Assuming a more realistic PrP(H1) 10%, the PPV and NPV can be expected to be 28.6% [IQR 8.2, 55.0] and 91.2% [IQR 89.9, 95.0].

Conclusions:
Pediatric critical care RCT’s with statistically significant mortality outcomes have a high FPR, much higher than the misinterpretation that a p-value ≤0.05 implies a FPR of 5%. In this field, as in many others, most published findings can be expected to be false. We agree with recent recommendations to design RCT’s with α=0.005, and to report the FPR of study findings assuming PrP(H1) 10%. 
Novel Model for Pediatric Resuscitation

Monacelli S., Megan O’Reilly- Schmoelzer, Tze Fun Lee and Georg Schmoelzer

Introduction:
Pediatric cardiac arrest (PCA) is the result of asphyxia, in a majority of the cases, with complications and progression of respiratory failure and shock since they result from untreated progressive tissue hypoxia. PCA can occur in-hospital (IHCA) or out-of-hospital (OHCA), the incidence rate is 15201* and 2.28 to 182/100000 person-years respectively. Survival rates also vary, ranging from 60 to 97% for IHCA and 17.6 to 40.2% for OHCA. Especially for the latter only 1-4% of survival have a good neurological outcome2.

The current consensus and guidelines, on the optimal procedure for CPR in pediatric cases recommend 15:2 compression to ventilation ratio with emphasis on chest compressions (CC) because of the importance of maintaining systemic and cerebral circulation. Given these incidence and survival rates, optimizing pediatric resuscitation is an urgent issue as current extensive resuscitation practices are associated with poor survival and morbidity. The primary outcome of this study was to investigate the most effective CPR technique using a pediatric swine model, which will reduce the time needed to achieve ROSC and improve survival.

Methods:
68 pediatric piglets of age 3 weeks (approx. 6 kg) were surgically instrumented and allowed to recover to a stable baseline following surgery. They were randomly assigned to CCSI (group 1), CCaV (group 2) and Sham (group 3). Groups 1 and 2 had a sample size of 16 piglets and 8 piglets were assigned to group 3. The first randomization step was to assign piglets to intervention or sham operation. Piglets in the intervention group were exposed to 30 min of hypoxia followed by asphyxia until cardiac arrest, piglets assigned to the sham group were not. Intervention piglets were randomized to receive either CCaV at a rate of 120/min with asynchronous ventilation and continuous CC or to receive CC at a rate of 120/min with 30 sec of sustained inflation (SI), SI will be interrupted after 30 sec for 1 sec before a further 30 sec SI is delivered and CC will be delivered continuously.

Piglets that achieved ROSC were allowed to recover for 4h, after which, cerebral cortical, pulmonary and cardiac tissues were harvested for bioassays.

Conclusion:
According to previous animal studies, the mean (SD) time to achieve ROSC was 180 (60) sec. We assume that piglets resuscitated in experimental group 1 will have a faster time to ROSC. We estimate a 33% faster time to ROSC (e.g. mean (SD) time 120 (20) sec.). This 33% reduction in the time to achieve ROSC would be clinically important (i.e. 180 sec vs. 120 sec.)

*in the United States only.

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END-OF-LIFE CARE IN CANADIAN ICUS: A SURVEY OF INTENSIVISTS’ PERCEPTIONS AND PRACTICES
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Introduction:
Withdrawal of life sustaining therapies (WLST) has become common practice in the intensive care unit (ICU) at the end of life. Existing literature demonstrates significant variation between clinicians in WLST practices. Moreover, it is uncertain how end-of-life (EoL) care in Canadian ICUs may have changed with the recent introduction of Medical Assistance in Dying (MAID) legislation, which legalizes active euthanasia for defined adult populations. Our primary aims were to describe Canadian intensivists’ approach to WLST and determine if practices have changed following introduction of MAID legislation. Our secondary aim was to determine how ethical views and practices vary between provinces and based on physician demographics.

Methods:
We conducted an electronic survey of Canadian intensivists and critical care fellows (adult and pediatric) between December 2019 and February 2020. The survey was designed by a group of adult and pediatric critical care staff and fellows with input from a medical ethicist and piloted by experts in the field prior to distribution. All responses were anonymous. Quantitative data were analyzed using descriptive statistics. Free text comments were coded thematically.

Results:
Preliminary data was obtained from 142 intensivists, of whom 49% (N=70) were adult practitioners and 51% (N=72) pediatric. The majority of respondents (86%) were from academic centers. Half, 50%, have no standardized protocol for WLST in their unit and 41% have observed medications given in higher than standard doses to treat symptoms during WLST, with 14% having either ordered or personally administered such doses. Over 87% of respondents were familiar with MAID legislation, 72% in favour, 15% conflicted. 80% of respondents have experienced explicit requests from families to hasten death, with 1 in 4 being specifically for euthanasia. 47% of respondents feel it is ethically permissible to provide interventions that intentionally hasten death for patients in whom death is expected following WLST.

Conclusion:
Beliefs around WLST are varied and many Canadian ICUs lack a standardized approach. The majority of intensivists surveyed are familiar with MAID legislation but a significant minority are ethically conflicted. There is a lack of consensus amongst Canadian intensivists regarding the ethical validity of hastening death during WLST, in contradiction to major society guidelines. This study highlights a possible shift in the ethical understanding of WLST in the context of a dynamic medico-legal climate.
ABSTRACT – 2020 PEDIATRIC RESEARCH DAY, MAY 13, 2020 – EDMONTON, AB

DOSMAN, CARA (DEVELOPMENTAL PEDIATRICS)

Feasibility and Usefulness of a Novel Curriculum in Pediatric Developmental Screening

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Introduction:
There is little literature on how to train residents in developmental standardized screening instruments (SSIs). Developmental disorders are detected sooner with SSIs. Needs assessment interviews were conducted in our General Pediatrics (GenPeds) Residency Program; residents’ most common personal learning objectives on Developmental Pediatrics (DevPeds) rotations were to identify red flags in children at risk of developmental disorders (26%) and know resources for identified children (31%); the Coordinators of GenPeds Community Rotations and Continuity Clinics indicated that SSIs were not used by GenPeds clinical preceptors. Curriculum purpose, developed in response to these needs, was to offer pediatric residents hands-on screening experience to empower their future decision on screening in clinical practice.

Methods:
Longitudinal curriculum interventions were evaluated (2016-2019). Two well-researched SSIs were used (SSI-1 parent concerns, SSI-2 developmental milestones, used when positive SSI-1). During DevPeds rotations in year (R) R1 and R3 (n=63), Screening Days (SDs) provided high volume practice in two GenPeds clinics’ waiting rooms. Practice was enhanced by varied teaching methods (simulation workshop, case-based interactive tutorials, five short answer question (SAQ) exams plus feedback). Resources included publications for self-directed learning, Pocket Guide (milestones, referral resources), and SSI-1 and SSI-2 in GenPeds clinics. SSI use was added to GenPeds clinics Learning Objectives. We examined feasibility of implementation and usefulness with outcome measures resident screening volume (logs completed on SDs), attitude surveys (n=36, Likert scale 4 strongly agree, 3 agree, 2 disagree, 1 strongly disagree), and exam scores (from the five SAQs).

Results:
Devpeds rotation screening volume (mean) was SSI-1 10.65 (3-25) and SSI-2 3.18 (0-12), consistent with Canadian ratio for positive SSIs. Ninety-five % of residents gave positive feedback on DevPeds rotation SDs. All residents felt comfortable using SSI-1; 97.22% for SSI-2. Paired-t-test showed mean comfort level using both SSIs increased from baseline to end-year (2.63 to 3.63,2.54 to 3.50, p<.001). Thirty-one residents (83.11%) planned to use SSIs in future practice. Greater SSI volume on DevPeds rotation strongly correlated with exam scores (parent concerns, 0.452, p=0.016; milestones, 0.461, p=0.031). Screen volume correlated with deeming screening important (0.385, p=0.032). In GenPeds clinics, six residents screened (SSI-1 0-20, SSI-2 0-5); twelve preceptors (response rate 28/44) screened, consistent with resident comments on screening barriers.

Continued, next page
Conclusions
New curriculum on DevPeds rotation was feasible and useful. Greater use by GenPeds preceptors might yield similar success in GenPeds clinics. Future study would detect ultimate curriculum usefulness if Graduates were using SSIs in practice.
Sleep Disturbances in Adolescents with FASD: A Profile and Effects of a Self-Regulation Intervention  
Leah Hammond, Vannessa Joly, Aamena Kapasi, Gail Andrew, Jacqueline Pei & Carmen Rasmussen

Introduction:
Fetal Alcohol Spectrum Disorder (FASD) refers to a range of physical, behavioural, and neurodevelopmental deficits resulting from prenatal alcohol exposure. Children with FASD display a wide range of sleep difficulties, at elevated rates relative to healthy children. Currently, there is no consistent sleep profile for children with FASD supported by the literature. Furthermore, few studies have focused specifically on sleep disturbances in adolescents with FASD. In this study, we examined the pattern of sleep problems in adolescents with FASD. We also examined the impact of a modified self-regulation intervention (the ALERT® Program) on these sleep disturbances.

Methods:
Twenty-seven adolescents with FASD, aged 11-17, participated in this study: 17 in Edmonton and 10 in Vancouver. Participants completed a 12-week self-regulation intervention based on an adapted version of the ALERT® Program. At baseline and following completion of the intervention, participants completed the Pediatric Sleep Questionnaire (PSQ), a caregiver-reported survey which assesses sleep disturbances on three distinct subscales: sleep-related breathing disturbances (SRBD), snoring, and daytime sleepiness. On each subscale, a mean score ≥0.33 indicates that behaviour falls in the clinically abnormal range. Frequencies were calculated for scores <0.33 and ≥0.33 on each subscale. Paired t tests were performed to assess change in mean subscale scores following the self-regulation intervention.

Results:
At baseline, the proportions of adolescents with FASD with SRBD (18.5%) and daytime sleepiness (33.3%) were elevated relative to reports for the general population (SRBD: 4-7%; Sleepiness: 7-15%). Only 7.4% of adolescents with FASD experienced snoring at baseline, falling within the normal range. Interestingly, older age was significantly associated with worse SRBD (r=0.491, p=0.009) and more daytime sleepiness (r=0.382, p=0.049). No change to SRBD (t(22)= -1.149, p=0.263), snoring (t(21)= -1.172, p=0.254), or daytime sleepiness (t(23)= -0.401, p=0.692) was observed following the self-regulation intervention.

Conclusions:
Sleep impairments in childhood and adolescence have negative implications for short-term adaptive functioning and long-term cognitive development. Youth with FASD experience high rates of SRBD and daytime sleepiness, relative to the general population. It is therefore critical to understand and address these sleep disturbances. This project lays the foundation for a clear understanding of the sleep challenges experienced by adolescents with FASD. Although we did not report improvements in sleep problems over the course of the intervention, further research with more objective measures of sleep (e.g. actigraphy) is warranted.
ABSTRACT – 2020 PEDIATRIC RESEARCH DAY, MAY 13, 2020 – EDMONTON, AB
SACREY, LORI-ANN (DEVELOPMENTAL PEDIATRICS)

Dyadic Play in 12-Month-Old Infants At-Risk of Autism Spectrum Disorder
Lori-Ann R. Sacrey, Lonnie Zwaigenbaum, Vickie Armstrong, Sarah Raza, Jessica Brian, Isabel M. Smith, and Susan Bryson

Introduction:
In addition to impairments in social communication, children with autism spectrum disorder (ASD) also show unusual play with toys. Together, these atypicalities can make it difficult for caregivers to engage their child in reciprocal social play. The purpose of this study was to examine the relationships between the quality of child and caregiver play at 12 months of age and ASD symptom presentation at 24 months of age in a high-risk sibling cohort.

Methods.
Participants: Dyads of high-risk infants and caregivers (HR; have an older sibling diagnosed with ASD; n=77) and low-risk infants and caregivers (LR; no family history of ASD; n=37). Assessments: At 12 months, dyads engaged in a session of free play for three minutes. At 24 months, children completed an Autism Diagnostic Observation Schedule-2 (ADOS). Coding: Free Play was coded using Coding Infant Behaviour (Feldman, 1998), a dyadic rating scheme for infants aged 2 to 36 months with Parent Sensitivity, Parent Intrusiveness, Parent Limit-Setting, Child Involvement, Child Withdrawal, Child Compliance, Dyadic Reciprocity, and Dyadic Negative States composites. Statistical Analyses. Composites were compared by Group using Mann-Whitney U analyses. Within the HR group, children were divided and compared based on 24-month ADOS total algorithm score (‘moderate-to-high’ = score of ≥8; ‘low-risk’ = score of ≤7). The relationship between composite scores and ADOS total severity score was explored using Spearman’s Correlations.

Results:
Mann-Whitney U tests: (1) caregivers of LR infants were less intrusive and set more limits in play compared to caregivers of HR infants (p<.05), (2) LR children were more compliant to caregivers than HR children (p<.05), and (3) LR dyads displayed higher levels of reciprocity and lower levels of negative states than HR dyads (p<.05). Mann-Whitney U tests comparing HR infants who were ‘low-risk’ versus ‘moderate-high’: (1) caregivers of children who were ‘low-risk’ had greater levels of sensitivity and limit setting (p<.003), and (2) children who were ‘moderate-high’ showed less involvement, engaged in less reciprocity with caregiver, and showed higher negative states (p<.05). Correlations showed significant relationships for Parent Sensitivity (r=-.41,p<.001), Parent Limit-Setting (r=-.32,p<.01), and Child Involvement (r=-.34,p<.01) with ADOS total severity score in the HR dyads but no relationships in the LR dyads.

Conclusions:
Caregiver-child interactions in HR dyads are less synchronous and reciprocal compared to LR dyads and these differences are associated with later ASD symptom presentation. Understanding differences in dyadic play can help inform play-based interventions for infants at-risk of ASD.
Short-term use of therapeutic opioids for children and opioid use disorders: a systematic review and qualitative study of decision-maker perspectives  
Afzalzada-Ahrari, M., Hartling, L., Dyson, M., Ali, S.

Introduction:  
Despite an overall decline in opioid prescriptions in Canada, healthcare visits, hospitalizations, and deaths due to opioid-related harms continue to rise for children. Decision-makers require high quality syntheses to inform decisions regarding opioid use for children. Previous research has found that how systematic review (SR) results are presented may influence uptake by decision-makers. Evidence summaries are appealing to decision-makers as they provide key messages in a succinct manner. The objectives of this study were to conduct a SR examining the association between short-term therapeutic exposure to opioids and development of opioid use disorder, and to gain perspectives from policy decision-makers on the usability and presentation of results through the form of an evidence summary.

Methods:  
We conducted a SR following methods recommended by Cochrane. A medical librarian conducted a comprehensive search and two authors were involved in study selection, data extraction and quality assessment. Studies were eligible if they reported primary research in English or French, and study participants had therapeutic opioid exposure before age 18 years. Results were described narratively. Decision makers were recruited through purposive and snowball sampling methods, 13 participated in interviews discussing an evidence summary about the SR. Interviews were transcribed and data was analyzed using latent content analysis.

Results:  
Of 4,072 unique citations, 16 studies (634,556 participants) were included. Five studies were comparative and explored the association between therapeutic exposure to opioids and misuse, 11 studies were non-comparative and only reported on prevalence of misuse following therapeutic exposure. One comparative study showed an association between short-term therapeutic use and opioid misuse. The other four were missing information on the duration of exposure; however, all suggested an association between therapeutic exposure and misuse.

Decision makers had mixed preferences for the presentation of evidence, depending on their involvement in research versus practice. A majority shared preferences for having statistics, methods and key characteristics of studies included in the evidence summary. They generally liked key messages highlighted on the first page, but noted the summary should not be too text-heavy.

Conclusions:  
Preliminary evidence suggests a link between lifetime therapeutic opioid use and opioid misuse; however, there is insufficient evidence available to determine whether short-term therapeutic exposure...
to opioids in childhood is definitively associated with developing these disorders. While this SR contributes evidence to guide clinical practice and future research, the qualitative findings help in understanding information needs of policy decision-makers and preferred presentation formats.

PROSPERO Registration: 122681.
ABSTRACT – 2020 PEDIATRIC RESEARCH DAY, MAY 13, 2020 – EDMONTON, AB
REITER, ELISE (EMERGENCY MEDICINE)

SKIPping at the Stollery: A Year in Review and Future Directions
Elise Reiter, PhD, Christine Chambers, PhD, Doug Maynard, MBA, Katie Birnie, PhD, Samina Ali, MD

Introduction:
All children experience pain. Canada is a world leader in children’s pain research and effective treatments exist, but this research evidence is not consistently mobilized into practice due to systemic barriers and sub-optimally organized efforts. Canadian children subsequently suffer undertreated and preventable pain, leading to negative short- and long-term health outcomes for both them and their families, as well as detrimental impacts on the healthcare system.

Methods:
Solutions for Kids in Pain (SKIP) is a national knowledge mobilization network that seeks to bridge the gap between current treatment practices and available evidence-based solutions for children’s pain. SKIP’s vision is healthier Canadians through better pain management for children, with a mission to improve children’s pain management by mobilizing evidence-based solutions through coordination and collaboration. SKIP brings together Canada’s world-renowned pediatric pain research community, front-line knowledge user organizations, and end beneficiaries (patients and caregivers). The Stollery Children’s Hospital/University of Alberta lead SKIP’s Western Canadian hub.

Results:
Our hub, active for approximately one year, has undertaken knowledge mobilization initiatives to improve children’s pain management in the hospital, throughout the province, and across Canada. At the Stollery, SKIP is supporting culture change across all units by disseminating informational posters, reviewing and revising children’s pain-related resources in Connect Care and MyHealth Alberta, and discussing the ChildKind certification process with key individuals. SKIP is also currently working to spread the Commitment to Comfort program, aimed at managing procedural pain in children, to Dynalife labs across the province. SKIP is also supporting the spread of a positive immunization experience (PIE) program in public health centres across the Edmonton zone. Nationally, the Edmonton hub helped lead a national meeting on opioid prescribing for acute pain in children and holds regular, collaborative meetings for all pediatric hospitals across Western Canada.

Conclusions:
At a national level, SKIP is working to deliver: 1) a user-informed approach to knowledge mobilization that meets the needs of diverse knowledge users; 2) best evidence in children’s pain management applied in practice; 3) improved institutional commitment to pain management; and 4) increased public support for evidence-based pain management. In Edmonton, SKIP is working at local, provincial, and national levels to ensure children’s pain is adequately managed and is strengthening the Stollery’s and the University of Alberta’s leadership role in managing children’s pain in Canada.
ABSTRACT – 2020 PEDIATRIC RESEARCH DAY, MAY 13, 2020 – EDMONTON, AB
RAJAGOPAL, MANASI (EMERGENCY MEDICINE)

Pediatric injuries due to falls from windows and balconies: an eight-year prospective and retrospective review
Manasi Rajagopal, MBT, Manu Kundra, MD, Neelam Mabood, MSc, Samina Ali, MDCM, Tara Rankin, MSc, Nadia Dow, RN, and William Craig, MDCM, MSc

Introduction:
Unintentional falls from windows and balconies pose a serious health risk to children. Limited Canadian data describing such falls currently exists. This study aimed to describe the frequency, demographic characteristics, injury patterns and risk factors associated with pediatric falls from windows and balconies.

Methods:
This study employed both prospective data collection and retrospective medical record review. Prospectively, consenting families were enrolled from February 2015 to February 2017; retrospectively, charts from January 2009 to December 2014 were reviewed. Children 0-16 years of age, who presented to the Stollery Children’s Hospital (Edmonton, Alberta) emergency department due to a fall from a window or balcony were included.

Results:
A total of 102 children were included; 30 were enrolled prospectively and 72 retrospectively. Median age was 4.5 years (IQR 2.83-6.83) with 63.7% (65/102) males. 87.2% (89/102) of falls were from windows and 12.8% (13/102) from balconies. The median estimated height of fall was 4.1 meters (IQR 3.04-4.73). 58.4% (59/101) had at least one major injury (i.e. concussion, fractured skull, internal injury, fractured limb, severe laceration), 36.6% had minor injuries only (i.e. minor lacerations, abrasions, contusions, bruising and sprains), and 5.0% had no documented injuries. There were no fatalities. 30.4% (31/102) were admitted, with 48.4% of these children (15/31) requiring surgery. Among prospectively enrolled participants with falls from a window, 96.2% (25/26) had screens in place, while only 26.9% (7/26) had either guards or stops in place. Out of these seven, only one stated that they were in use at the time of the fall.

Conclusions:
Most falls from windows and balconies occurred in children under the age of five years and were associated with serious morbidity, high admission rates, and need for surgery. Installation of key safety features in windows, and legislation to mandate this may help minimize pediatric fall-related injuries.
An Incidentally-Discovered Paraganglioma

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Introduction:
Pheochromocytomas and paragangliomas are rare neuroendocrine tumors arising from chromaffin cells of the adrenal medulla and extra-adrenal cells. Functional tumors often cause clinical symptoms related to catecholamine release however, some children can be asymptomatic. We describe a patient presenting with acute appendicitis, in whom severe hypertension following appendectomy led to the discovery of an incidental paraganglioma. We highlight the clinical and imaging features of paragangliomas and discuss the importance of appropriate medical therapy with alpha blockade.

Case Presentation:
A previously healthy 17-year-old male presented with abdominal pain secondary to acute appendicitis and was treated with an uncomplicated open appendectomy. Post-operatively, he had episodic hypertension with systolic blood pressures up to 300mmHg. He was admitted to the pediatric intensive care unit and started on nitroprusside and beta blocker therapy. While on Esmolol, he had dramatic fluctuations in his blood pressure with corresponding severe bradycardia and hypotension. A clinical diagnosis of catecholamine secreting tumor was made, and he was initiated on alpha blockade with Doxazosin, resulting in rapid stabilization in both blood pressure and heart rate. Subsequent investigations revealed elevated plasma and urine catecholamines, with normetanephrine predominance. CT scan showed a 6cm posterior mediastinal mass adjacent to the descending aorta with strong uptake on MIBG-scintigraphy and limited uptake on FDOPA- PET imaging, which were both negative for metastases. Genetic investigations revealed an SDHB gene mutation.

Conclusion:
This case describes the clinical presentation of an incidentally discovered paraganglioma and highlights the factors involved in false positive and false negative findings on MIBG-scintigraphy and FDOPA-PET imaging of paragangliomas. The importance of alpha blockade prior to beta blocker therapy is highlighted for the medical management of these tumors and pitfalls of beta-blockade therapy are reviewed.
Gut microbes play an important role in preventing dietary fiber-associated inflammation and improving barrier integrity in children with IBD

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Introduction:
The etiology of inflammatory bowel diseases (IBD) remains unknown, although gut microorganisms and diet have been implicated. Interestingly, dietary fibers pass through the bowel undigested, and are fermented within the intestine by gut microbes, typically promoting gut health. However, fiber receptors on immune cells interact with fibers on the surface of fungal cells, resulting in a pro-inflammatory response. These fibers are structurally similar to dietary fibers, which many IBD patients, along with IBS patients, describe experiencing sensitivity to. As our previous work indicates an altered balance between commensal and pathobiont microbes in IBD, we hypothesize that the lack of fiber fermenting-microbes populating the IBD gut leads to dietary fibers not being efficiently broken down into their beneficial biproducts (e.g., Short Chain Fatty Acids), resulting in binding of intact fibers to host cell receptors; this ultimately drives pro-inflammatory responses and a microenvironment that promotes continued dysbiosis and increased pathogenicity of select microbes.

Methods:
Fiber receptor expression was examined using immunohistochemistry and flow cytometry of human biopsy tissues. ELISA and qPCR were utilised to evaluate cytokine secretion, in response to fiber (5mg/mL) or pre-fermented fibers, cultured with microbes of interest, in both individual cell lines in vitro and biopsy tissues cultured ex vivo. Fermentation products were evaluated by mass spectroscopy.

Results:
Expression of a number of fiber receptors was increased on specific immune cell types in IBD, suggesting an increased sensitivity to unfermented fibers. After further examination, whole-fibers induced secretion of pro-inflammatory cytokines in select cell types, and specific microbes were capable of fermenting fiber into acetate, propionate, and butyrate, thus reducing the associated inflammation. Interestingly, biopsies cultured ex vivo demonstrated patients with more severe disease respond to oligofructose in a pro-inflammatory manner; while their corresponding whole gut microbiome, collected from intestinal washes, was not able to ferment oligofructose or reduce inflammatory response the way nonIBD and remission patient samples were.
Conclusions:
Comparing *in vitro* findings to our readily available patient food frequency questionnaires (FFQs), intestinal washes (microbe abundance), and detailed patient history will allow us to define the relationship between microbes, dietary fibers, and gut inflammation in IBD.
Impact of treatment with long-acting GLP-2 analogues on small intestinal growth and adaptation in neonatal piglets with short bowel syndrome

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Introduction:
Short bowel syndrome is the leading cause of pediatric intestinal failure, resulting in dependency on long term parenteral nutrition (PN). The purpose of this study was to compare effects of two GLP-2 analogue treatments on intestinal growth and adaptation of neonatal piglets following 75% small intestinal resection, with jejunocolic anastomosis.

Methods:
Piglets were assigned to: saline control (SAL), teduglutide (0.05mg/kg) treatment twice daily (TED), or apraglutide (5mg/kg) treatment twice weekly (APRA). Subcutaneous treatments were administered in the first 7 days, with terminations on Day 7 (SAL7, APRA7, TED7) or Day 14 (SAL14, APRA14, TED14). Animals were given PN at 80% and enteral nutrition at 20% of nutritional requirements. At termination, the small intestine was measured, weighed and jejunal tissue collected for histology. Data are presented as mean (SD) with units indicated.

Results:
Piglets were not significantly different for age at surgery, weight gain by 7 or 14 days, or post-surgery remnant small bowel length. GLP-2 treatment induced mucosal adaptation, with mucosal mass maximal at one week for apraglutide treated pigs, regressing or ceasing after treatment discontinuation [SAL7: 2.0g (0.4), APRA7: 2.7g (0.6), TED7: 2.1g (0.3); SAL14: 2.3g (0.7), APRA14: 2.6g (0.4), TED14: 2.5g (0.4); p=0.112]. In contrast, linear intestinal growth was induced by both GLP-2 analogues already by Day 7, and continued through day 14 only with APRA treatment [SAL7: 4.2cm (13), APRA7: 32.1cm (14.8), TED7: 22.2cm (8.6); SAL14: 22.6cm (20.9), APRA14: 68.8cm (18.7), TED14: 41.1cm (13.5); p<0.001]. Teduglutide did not significantly increase linear growth beyond Day 7. In control, length only increased with additional time.

Conclusions:
Intestinal growth appears to be a lasting outcome of early trophic treatment. This lengthening benefit following treatment can be enhanced further over time compared to untreated. This has significant clinical implications for neonates given their potential for intestinal growth. This may enable neonates with SBS to achieve autonomy from PN after early trophic therapy without the need for continued long term treatment.
DEFINING THE RELATIONSHIP BETWEEN DIETARY FIBERS AND INFLAMMATORY RESPONSE IN PEDIATRIC INFLAMMATORY BOWEL DISEASES

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Introduction

The incidence rates of inflammatory bowel diseases (IBD), Crohn disease (CD) and ulcerative colitis (UC) are increasing in children. Although the etiology of IBD is poorly understood, factors such as urban lifestyle, diet, increased hygiene, and reduced microbial biodiversity have been implicated as risk factors. Compositional changes and reduced microbial biodiversity have been linked to therapy failure in pediatric IBD. Non-digestible dietary carbohydrates, such as fiber, must undergo fermentation by gut microbiota within the large bowel, producing short chain fatty acids (SCFAs). Animal studies have shown that dietary fibers can inhibit IBD-associated inflammation, and clinical trials have demonstrated that SCFAs can prevent intestinal atrophy and allow for tissue recovery in IBD patients. In disease settings with altered gut microbes, fermentation of dietary fibers may be greatly affected. Unfermented fibers interact with receptors on host immune cells and can induce proinflammatory immune response, production of oxygen species and inflammation, or an inhibition of proinflammatory receptors. Based on this rationale, we hypothesize that dysbiosis in the IBD gut leads to decreased fiber fermenting microbes, resulting in reduced SCFA production. This contributes to increased inflammatory responses both in in vitro cell lines, as well as ex vivo patient biopsies. Because intact fibers can bind to host cell receptors, this promotes inflammatory response and continued dysbiosis.

Methods

To assess effects of intact fiber on immune cells, macrophage and T-cell in vitro cultures were used to measure cytokine response to inulin (5mg/mL) and oligofructose (5mg/mL) through ELISAs/qPCR. These cell lines and ex vivo patient biopsies were treated with whole fibers and IL-1β secretion was measured. Fibers were also pre-fermented with microbes of interest or whole microbe patient intestinal washes and used to treat cell lines and patient biopsies.

Results:

Whole fibers induced a pro-inflammatory response in macrophage cells but not T-cells, and this pro-inflammatory response was mitigated by pre-fermenting the fibers. Intestinal washes from severe IBD patients were unable to successfully ferment oligofructose or reduce fiber-associated inflammation in macrophage cell lines, whereas washes from remission or non-IBD samples reduced IL-1β. Oligofructose was found to increase IL-1β secretion in UC and CD patient biopsies, but not in non-IBD specimens. This increase was also correlated with disease severity.
Conclusions:
These results indicate that a lack of fiber-fermenting microbes and presence of whole fibers can lead to pro-inflammatory responses, both in cell lines and patient biopsies. However, the presence of appropriate fermenting microbes can reduce fiber-associated inflammation.
Infliximab clearance during and post induction predicts clinical and endoscopic outcomes at 1 year in children with Crohn’s disease


**Introduction:**
Infliximab (IFX) clearance (CL) is varied in children with Crohn’s disease (CD), and CL is increased relative to body weight in those under 30kg at induction. Our aim was to determine if IFX CL at and post induction can predict 1 year outcomes in children.

**Methods:**
IDEal study was conducted at 3 Canadian Children Inflammatory Bowel Disease Network sites. We prospectively followed 35 pediatric CD patients who initiated IFX. Dose optimization was allowed. NONlinear Mixed Effects Modelling was used to develop a population PK model. 1 year follow-up data for 26 patients were available. Non-responders were defined as Weighted Pediatric CD Activity Index (wPCDAI)≥12.5, persistently elevated C-reactive protein (CRP)>4, intestinal surgery, discontinuation of IFX, or steroid use in the last 6 months. Fecal calprotectin (FCP), erythrocyte sedimentation rate (ESR), and Simple Endoscopic Score for CD (SES-CD) were also collected. Correlation analysis, Fisher exact test, logistic regression and ROC were used to identify predictors of clinical, endoscopic and biomarker response at 1 year and estimate cut-off points for predicting a response.

**Results:**
20 patients were responders (11 males) and 6 non-responders (2 males). Age, weight and gender had no effect on the outcomes. Of the 6 non-responders - 1 switched to a new class biologic, 1 remained on IFX, 4 required intestinal surgery (2/4 remained on IFX). 21/26 patients had a follow-up colonoscopy and 13/21 achieved mucosal healing. Dose1 CL≥0.321L/day and Dose5 CL≥0.305L/day were associated with poor clinical and endoscopic outcome: AUC[95%]=0.78[0.56;0.99] and AUC[95%]=0.85[0.66;1.00], respectively. The non-responders had higher IFX trough at Dose5 compared to the responders (10.1 [7.3;13.5] and 4.9 [3.4;7.4], respectively, p=0.028). All non-responders were dose optimized with median dose 6.0mg/kg [5.4;9.0] and frequency 4.3 weeks [4;6] at Dose5 as compared to 7.2mg/kg [6.9;7.8] and 6 weeks [4;6] in responders (p>0.1). wPCDAI<12.5 at Doses 4 and 5 predicted clinical response, with Dose5 being the better predictor (p<0.0001, r=0.697). Dose 5 FCP≤221 mcg/g was a predictor of remission and mucosal healing (AUC[95%]=0.78[0.48;1.00]).

**Conclusion:**
Increased IFX CL, high wPCDAI and FCP suggest inadequate response to IFX treatment. With dose optimization, IFX trough was no a longer predictor of better clinical or endoscopic outcome at 1 year. 1 year analysis indicates that with dose optimization at induction, the medium-term response to IFX can be predicted as early as Doses 4 and 5 and effort should be made to alter treatment earlier if inadequate response was observed.
Head to head comparison of two glucagon like peptide-2 analogues in the treatment of short bowel syndrome in neonatal piglets


Introduction:
A priority goal in treating short bowel syndrome (SBS), is autonomy from parenteral nutrition (PN). This relies upon intestinal adaptation, which may be augmented by intestinotrophic therapies, like administration of glucagon like peptide-2 (GLP-2) analogues. In neonatal piglets with SBS, we compared intestinal adaptation following treatment with two GLP-2 analogues with different pharmacokinetic profiles: teduglutide (TED) and apraglutide (APRA).

Methods:
Following 75% distal small intestinal resection, neonatal piglets receiving 20% parenteral nutrition were allocated to four treatments by subcutaneous injection: daily saline (CON: n=8), twice weekly APRA (5mg/kg/dose; n=8) and teduglutide once daily (TED, 0.05mg/kg/dose; n=8) or twice daily (TEDBID, 0.05mg/kg/dose; n=7). On Day 7, small intestinal length and weight were measured and jejunal tissue was collected to perform histology. Pharmacokinetic studies were previously conducted on animals to compare pharmacokinetic profiles and exposure following treatment with apraglutide or with teduglutide.

Results:
Pharmacokinetic studies revealed different pharmacokinetic profiles of the 2 analogues injected in neonate animals. APRA injected only twice showed superior intestinotrophic activity compared to the once-a-day clinically approved regiment of TED administered for 7 consecutive days. Teduglutide intestinotrophic activity was comparable to apraglutide only when injected twice daily (TEDBID) for 7 consecutive days. Thus, compared to saline, APRA and TEDBID significantly increased small bowel length (cm) [CON: 141, APRA: 166, TED: 153, TEDBID: 165; p=0.004] and APRA increased small bowel weight (g) [CON: 26, APRA: 33, TED: 28, TEDBID: 31; p=0.007]. APRA remained superior to both TED and TEDBID for increasing the height of the intestinal villi (µm) [CON: 0.59, APRA: 0.90, TED: 0.58, TEDBID: 0.74; p<0.001].

Conclusion:
With intestinotrophic therapies as emerging treatment for SBS, comparison at pharmacokinetic equivalent doses is essential. In SBS piglets, treatment with teduglutide and apraglutide at equivalent doses, increased intestinal length and weight. Apraglutide appeared to exhibit greater trophic effects in the mucosa, including villus hyperplasia, and as apraglutide is given at lower dose frequency, warrants further studies in the pediatric population.
Motivational Interviewing in Managing Adolescent Obesity: Preliminary Findings from a Scoping Review

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Introduction:
Motivational Interviewing (MI) is used frequently as a standalone (or part of an) intervention for managing obesity in adolescents. Despite evidence that suggests MI is efficacious, research investigating MI-based interventions in adolescent obesity management remains limited. The objective of our research was to examine the application of MI-based interventions for the management of adolescent obesity.

Methods:
Scoping review methodology for this study was adapted based on Arksey and O'Malley’s framework with recommendations by Levac et. al. The review included: (i) adolescents 13-17-year-old with a body mass index (BMI) ≥85th percentile, (ii) MI-based interventions focused on the secondary prevention and/or management of adolescent obesity, (iii) parents if they identified as the primary caregiver of the adolescent and if the adolescent was the focus of the intervention, and (iv) records published in English. We systematically searched 8 electronic databases, 3 online archives of conference proceedings and reference lists of 33 selected studies for publications from 1983 to July 2017. We conducted an updated search in October 2019. Two independent reviewers screened studies for eligibility using inclusion criteria developed before screening and data extraction. Cohen's kappa coefficient was used to determine inter-rater agreement. Descriptive approaches were used to summarize the data.

Results:
After an initial screen of 3,080 records, 1,779 records were identified after duplicates were removed. Of the 1,779 records screened for eligibility, 1,545 were titles and abstracts and 234 were full-texts. The rater agreement for the original search was 0.53 and 0.95, respectively, and 1.0 for the updated search. A total of 33 studies were included in this review. Of the 33 included studies, 23 (70%) were randomized controlled trial (RCT) designs. Fifteen (45%) of these 33 studies were published within the last 5 years and 22 (67%) were conducted in the United States. Most MI-based interventions were delivered in-person in the health care setting (session duration ranged from 15-60 minutes). Thirty-one studies (94%) reported that providers (e.g., Registered Dietitian) who delivered MI-based interventions were trained in MI (e.g., 80 hours of theoretical and practical training).

Conclusions:
Based on our initial descriptive analyses, most MI-based interventions were tested in health care settings using RCTs with intervention delivery by clinicians who were trained in MI. Next steps include the assessment of intervention fidelity as it’s an important methodologic consideration in the
effectiveness of MI-based interventions. A stakeholder consultation will also be conducted and analyzed qualitatively.
Pediatric Benign Neutropenia: Assessing Practice Preferences in Canada

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Introduction:
In children, chronic isolated neutropenia is commonly a self-limiting condition with a benign clinical course. This entity is referred to as benign neutropenia, autoimmune neutropenia (AIN), or chronic idiopathic neutropenia (CIN). Although the underlying pathophysiology is presumed to be autoimmune-mediated peripheral destruction of neutrophils, the approach to management is often the same as that of neutropenia induced by chemotherapy or malignancy. An evidence-based approach to pediatric benign neutropenia is not well-defined in the literature. Our aim was to elucidate practice preferences in the diagnosis and management of pediatric benign neutropenia in Canada.

Methods:
A case-based survey was distributed to pediatric hematology/oncology staff and trainees across Canada. The survey included multiple choice and free text questions to capture information about clinical decision-making at different time points in the presentation of benign neutropenia. Exploratory statistical analysis was performed using contingency tables to identify associations between demographic characteristics and management of neutropenia.

Results:
We received 45 completed surveys for a response rate of 64%. The survey case follows a previously healthy Caucasian toddler at first presentation with fever and severe neutropenia. At initial presentation, most respondents (67%) recommended partial septic workup, but 11% recommended no investigations. Nearly 70% would treat with empiric intravenous antibiotics, while 24% would discharge home with no antibiotics. All respondents recommended follow up with observation and repeat complete blood count (CBC).

For neutropenia lasting longer than 3 months, 53% would continue with observation only. The most frequently recommended investigation at this point was quantitative immunoglobulins (42%), but a small cohort (7%) recommended bone marrow studies. Nearly 60% of respondents do not use anti-neutrophil antibody testing in their practice. There was a significant association between level of training and use of anti-neutrophil antibody testing, with more trainees reporting that they would use this test ($P=0.049$).

The most common indications for bone marrow biopsy were initiating granulocyte colony-stimulating factor (G-CSF), recurrent/severe infection, or prolonged neutropenia. The most common indications for genetic testing were positive family history or age less than 12 months. Indications for G-CSF therapy were primarily based on severity and frequency of infection. Most respondents (84%) would not recommend prophylactic antibiotics.

Continued next page
Conclusion:
There is considerable variability in the investigation and management of benign neutropenia among pediatric hematologists in Canada. This survey highlights the need for stronger evidence and consensus guidelines to develop a more consistent approach across the country.
Impact of early surgical correction/palliation of congenital heart defects in infants with symptomatic viral respiratory tract infections

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Introduction:
The development of viral respiratory tract infections (RTI) represent a significant portion of acute care provided to the pediatric population and disproportionately affects those with congenital heart disease (CHD). Mortality and morbidity concerns related to acute surgical correction suggest waiting 4-6 weeks after a symptomatic, viral RTI to correct CHD in the pediatric population. This current study investigates the impact of timing of surgery in cardiac infants with active RTI in a contemporary Western Canadian cohort.

Methods:
This is a retrospective case-control study of infants (1 week to 6 months-old, median age: 3.4 [2.4, 4.3] months) undergoing surgical repair or palliation of CHD between 2014-2017. Cases were defined as infants with active viral RTI confirmed on nasopharyngeal aspirates (NPA) with documented, corroborating clinical symptoms pre-operatively (Group 1); whereas controls had no recent (> 4 weeks), or active symptoms of viral RTI (Group 2). Cases were matched to controls based on age, congenital heart lesion and surgery type.

Results:
20 cases were compared to matched controls in a 1:2 fashion (N = 60). No statistical differences could be found in baseline characteristics (age, sex, surgery type) between groups. There were no differences in vasoactive inotropic scores at 24 hours ($p = 0.49$), 48 hours ($p = 0.20$), maximum vasoactive inotropic score ($p = 0.56$), time to extubation ($p = 0.13$) or duration of postoperative hospitalization ($p = 0.16$). Cases had a statistically significant increase in the duration of respiratory support (including non-invasive ventilation, 3.5 vs 2 days; $p = 0.011$) and duration of postoperative intensive care unit length of stay (5.5 vs 3 days; $p = 0.009$).

Conclusion:
To our knowledge, this is the first study investigating the post-operative outcomes of infants undergoing surgical repair/palliation of congenital heart disease in the setting of active viral respiratory infections in a case-control manner. This data suggests surgical intervention in infants with active RTI is associated with longer total respiratory support and duration of PCICU stay. However, it can be performed without apparent differences in duration of invasive mechanical ventilation, hospital length of stay or mortality. This approach is an important consideration in infants in northern latitudes who may have appropriate surgical intervention delayed when a reasonable RTI free interval is not practicably achievable.
Preferred pediatric resident learning styles: from junior to senior resident
Michelle Huie & Karen Forbes

Introduction:
Medicine is a career that encompasses life-long learning. Studies in medical trainees have shown that individual learning styles (LS) change during the progression from medical school to residency (Bitran, 2012). Further, LS differ across varying sub-specialties with limited literature in non-surgical specialties such as Pediatrics (Lai, 2014; Richard, 2014). We sought to evaluate LS in our Pediatric residents, and how they may change throughout residency.

We hypothesized that Junior residents will represent an abstract and reflective LS (Assimilator) as this style is most consistent with the lecture-based formal instruction in medical school. Further, as Junior residents progress through residency and become Senior residents, they will adapt a concrete and active LS (Accomodator) as the learning in residency is less formal instruction and more experienced based.

Methods:
The Kolb Learning Style Inventory (LSI) is a well-established and validated 12-item tool used to classify learning styles. There are four classifications: 1) Diverger, 2) Assimilator, 3) Accommodator and 4) Converger. In September 2018, 22 Pediatric residents completed the Kolb LSI and in September 2019, 28 Pediatric residents completed the Kolb LSI.

Results:
In the first year of data collection, 12 Year 1 Pediatric residents and 10 Year 2 Pediatric residents participated in the study. LS ranged among the Pediatric residents and among years with each of the 4 LS represented; Convergers and Assimilators were most common (9 and 7 residents respectively) with fewer Divergers and Accommodators (3 residents each). In the second year of data collection, 8 Year 1 Pediatric residents, 10 Year 2 Pediatric residents and 10 Year 3 Pediatric residents participated in the study. Similar to the previous year, LS ranged among residents and years with 10 Convergers, 7 Assimilators and 4 Divergers and 7 Accomodators. Of the residents who participated in both years of the study, 12 residents had changed their LS while 7 residents had the same LS as the previous year.

Conclusions:
There is a variety of LS among Pediatric residents with a diversity of LS among junior and senior level of training. Further, learning styles can be dynamic. By allowing for a variety of teaching formats aligning with a diversity of preferred LS needs (e.g. didactic vs small group vs simulation), learning environments may be more conducive to the learners.
INCREASING PEDIATRIC INTENSIVE CARE ADMISSIONS AND MORTALITY DUE TO SUICIDE
Claire McNiven, Daniel Garros

Introduction:
Both the attempted and completed suicide rate in the pediatric population is increasing, with suicide being the second leading cause of death among adolescents. The objective of this study is to evaluate how Pediatric Intensive Care Unit (PICU) admissions for suicide attempts, and suicide related mortality are changing over time.

Methods:
This is a single-centre retrospective review of admissions to the PICU in a Canadian tertiary pediatric hospital. Admission data related to potential cases from 2003-2019 were collected for analysis. Inclusion criteria was age > 5 years with suicide attempt. Coded diagnoses for inclusion were ‘Suicide’, ‘Overdose’, ‘Hanging’, and ‘Self Injury’.

Results:
Overall, we identified 172 cases of PICU admission related to suicide attempt during the study period. From 2003-2017 there were 120 cases (median age 15 years, range: 8-16), with a 10.0% mortality rate. The general trend in this data showed a rising incidence rate overall. However, from 2017-2019 there was an obvious increase of suicide related admissions with 52 cases identified in a two-year period with similar mortality rate (9.62%), while the overall mortality rate for the PICU was 2.90% over the same period.

Conclusions:
The incidence of suicide attempts requiring PICU admission is increasing over time. Our centre is observing higher than expected incidence of suicide in the past two years with a sustained high mortality rate. These findings are of considerable concern and necessitate the continued development of primary prevention strategies to identify and help our patients before these events occur.
Safe to Sleep: Optimizing Infant Sleep Safety in Stollery Pediatric Medicine

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Introduction:
Recommendations for safe infant sleep practices to reduce the incidence of sudden infant death syndrome (SIDS) and other sleep-related injuries and deaths are supported by multiple pediatric and public health organizations. Alberta Health Services (AHS) released a policy, ‘Safe Infant Sleep (SIS),’ in 2014 to provide guidance to promote safe sleep practices for infants from 0-12 months of age across all care settings. Following safe infant sleep recommendations in the pediatric inpatient environment is important for patient safety and modeling of safe practices for caregivers. Adherence to safe sleep recommendations in pediatric inpatient settings is not well studied but is believed to be poor.

Methods:
A quality improvement (QI) initiative was undertaken to determine baseline adherence to the AHS SIS policy on a pediatric medicine unit at Stollery Children’s Hospital, and to improve infant sleep safety in pediatric medicine. The project occurred over 12 months (November 2018-2019). Baseline rates of SIS policy adherence were determined by infant sleep environment observations using a standardized audit form and convenience sampling. Included infants were inpatients on a single pediatric inpatient medicine unit who were less than 12 months of age, asleep at the time of data collection and did not have a medical condition precluding adherence to standard infant sleep recommendations. A multidisciplinary working group was formed to develop intervention strategies to increase SIS adherence in pediatric medicine. Plan-Do-Study-Act cycles were used to implement and assess strategies. Adherence to the SIS policy and effectiveness of interventions were tracked using statistical process control charts.

Results:
No infants (0/24) were sleeping in an environment which adhered fully to AHS SIS policy during baseline sleep observations. Sleep environments differed from recommended practice most commonly by elevation of the head of the bed without physician order, presence of items in cribs, and improper use of linens. QI interventions included staff education, identification of alternate locations in patient rooms for infant care items, provision of SIS education materials to caregivers, and Kamishibai cards (K-cards). Cumulative SIS policy adherence increased from 1.6% (1/64) to 29.3% (36/123) (p<0.001) after introducing safe sleep K-cards.

Conclusions:
Improvements in adherence to safe infant sleep recommendations on a Canadian pediatric medicine inpatient unit were demonstrated in this QI initiative. The use of a K-card for infant sleep safety significantly improved cumulative SIS policy adherence in this inpatient pediatric setting. Ongoing efforts to sustain initial successes and continue improving infant sleep safety in pediatric medicine will
be important.

References
Understanding the cohort of pediatric patients admitted to hospital with diabetic ketoacidosis in Alberta: A Physician Learning Program Collaboration

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Introduction:
Diabetic ketoacidosis (DKA) is an acute hyperglycemic emergency due to absolute or relative insulin deficiency. It is the greatest contributor to morbidity and mortality of T1DM in the pediatric population. The Physician Learning Program (PLP) partners physicians with experts in implementation science, knowledge translation, quality improvement, medical education, and human-centred design to obtain actionable clinical information and craft innovative ways to advance practice. In collaboration with the PLP, this project aims to describe the demographics and treatment pathways of pediatric patients receiving care for DKA in Alberta hospitals.

Methods:
This retrospective cohort study used Alberta Health Services administrative databases (Pharmaceutical Information Network, Laboratory Services, Discharge Abstract Database, National Ambulatory Care Reporting System, and Diagnostic Imaging) to identify patients <18 yo admitted to hospital in Alberta between January 1, 2015 and December 31, 2018 with a discharge diagnosis of DKA. Demographic and clinical characteristics were analyzed with standard descriptive statistics. Inferential statistics were used to compare results across hospitals.

Results:
There were 929 admissions (725 unique patients) for DKA during the study period. Average patient age was 11.0 years (SD 4.5), and median length of stay was 2.5 days. Most patients (62%) presented to a tertiary care pediatric hospital, with 20% to a regional hospital, 11% to a community hospital, and 4% to an adult tertiary care facility. A total of 8% of patients presenting to regional hospitals and 25% of those presenting to community hospitals were transferred to a tertiary pediatric hospital for admission. Patients admitted to tertiary pediatric hospitals were significantly younger than those admitted to community hospitals (10.4 versus 14.5 years). There were 137 admissions to an intensive care unit (15%), and 25 instances (2.7%) of head imaging for concerns of cerebral edema. No patients died during admission for DKA. The 60-day readmission rate was higher among patients admitted to regional and community hospitals than to tertiary pediatric hospitals.

Conclusions:
Pediatric patients with DKA present to and are managed at many clinical sites across Alberta. Understanding the characteristics of these patients and how they move through the hospital system is an important step towards identification of potential strategies for optimizing DKA care. Phase 2 of this project will explore how well the management of pediatric DKA in several Alberta sites aligns with established Clinical Practice Guidelines from Diabetes Canada.
Pregnancy among HIV-serodiscordant couples: case report of vertical transmission and retrospective case series.


**Introduction:**
Towards the end of 2014, while approximately 75,500 Canadians were living with HIV, women accounted for 22% of the national total. Most of these women are of reproductive age with a potential risk of vertical transmission of the virus to their offspring. The prevention of vertical transmission remains challenging for mothers who seroconvert after the antenatal screening, later in pregnancy, or while breastfeeding. Monitoring for HIV transmission during pregnancy and breastfeeding among serodiscordant heterosexual couples may yield additional opportunities to identify early HIV infection and prevent vertical transmission. Such a public health strategy could be a valuable tool toward the elimination of vertical transmission of HIV-1 infection in Canada.

Here we describe a case report of vertical HIV transmission during breastfeeding in a high-resource setting that escaped detection by the universal surveillance system for HIV in pregnancy. We also report a case series of 47 serodiscordant couples in which the female partner was pregnant and HIV-1 negative, and the male partner was HIV-1 positive. Our objective was to examine the prevalence of risk factors for HIV transmission in the pregnancy and postpartum periods in our well-resourced setting.

**Methods:**
Case report and medical records of serodiscordant pregnant couples were reviewed over an eight-year period (2008-2016) from the Northern Alberta Program (NAP), which is a publicly funded HIV treatment and surveillance program based in Edmonton, Canada. A standardized data collection tool was used to collect data by a retrospective chart review on risk factors for vertical transmission of HIV. Data gathered on partners included demographic characteristics, IV drug use, VL, CD4 T cell count, other STD testing, etc.

**Results:**
No cases of HIV transmission occurred (0/47, 95% CI 0-7.5%) among 47 HIV-serodiscordant pregnant couples. Among HIV-infected male partners, ten had a detectable viral load (VL) during their partner’s pregnancy, with median peak VL 4,700 copies/mL (IQR 200-8500), and ten males had a detectable VL during breastfeeding, with median peak VL 5,200 copies/mL (IQR 120-55,000). With respect to VL monitoring, 26/47 (55%) and 21/47 (45%) had no documented VL measurement during the pregnancy and breastfeeding periods, respectively. 45% of HIV-infected males had no VL documented, and 72% of females had no serology test documented during the postpartum period.

**Conclusion:**
Despite concerted attempts to minimize HIV transmission during pregnancy and breastfeeding in our well-resourced setting, gaps in viral load monitoring and suppression of viral replication with treatment were prevalent among HIV-serodiscordant pregnant.
Dengue fever in a tertiary pediatric hospital in Ecuador: a five year review

Freire, Dolores1,6 – Olaya, Dennise7 – Hawkes, Michael1-5

1Department of Pediatrics, University of Alberta, Edmonton, Canada; 2School of Public Health, University of Alberta, Edmonton, Canada; 3Department of Medical Microbiology and Immunology, University of Alberta, Edmonton, Canada; 4Distinguished Researcher, Stollery Science Lab; 5Member, Women and Children’s Health Research Institute. Facultad de Ciencias Medicas, Universidad de Guayaquil, Guayaquil, Ecuador. Hospital Francisco Icaza Bustamante, Guayaquil, Ecuador.

Introduction: Dengue fever (DF) is a mosquito-borne illness that causes significant morbidity and mortality in tropical climates. Prompt recognition of warning signs, adequate monitoring and support can reduce progression to shock and mortality. This study describes the clinical presentation, laboratory profile and management of fatal, severe non-fatal, and matched non-severe cases over a five year period at a pediatric hospital in Ecuador.

Methods: Retrospective case-control study of children (1 month to 15 years) admitted to Hospital Francisco Icaza Bustamante in Guayaquil, Ecuador from 2013 to 2017. Cases of fatal dengue (FD) were ascertained by screening the database of PCR-confirmed DF patients. Two control groups were chosen: (1) patients with severe dengue fever (SD) admitted during the study period; and (2) patients admitted with dengue with warning signs (DWS), matched in a 3:1 ratio for age, sex, and admission date with patients with fatal outcome. Data on demographic, clinical, laboratory and management were abstracted from the clinical record for comparison between groups.

Results: A total of 1051 patients were admitted with suspected dengue fever. Initial clinical evaluation classified 995 as DWS and 56 as SD. After serology confirmation, 518 received final diagnosis of DWS and 41 of SD, 7 patients progressed to SD. Male sex was preponderant (FD 64%, SD 56.7%, DWS 64%), most children were of school age (FD 9.6 (5.5–11.2), SD 8.1 (1.8–11.5), DWS 9.7 (5.3–11.6)) and came from Guayas province (FD 91%, SD 80%, DWS 85%). All groups had had previous evaluation before admission (FD 3 (2.5-4), SD 2 (1-3), DWS 2(1-3)), more than half were prescribed antibiotics (FD 7(64%), SD 20(66.7%), DWS 20 (58%)). Admission was within 5 days of fever (SF 3(2-5), SD 5(4-6), DWS 5(4-6)), however, fever was present in about 1/3 of patients (FD 4(36%), SD 10(33.3%), DWS 10(30.3%)). Neurological manifestations were more characteristic in the FD group: 9 (82%) patients compared to 15 (50%) in SD and 7 (21%) in DWS. Severe transaminitis accompanied FD (Aspartate aminotransferase (AST) 398 (218–1752), Alanine aminotransferase (ALT) 718.0 (133-850). Pleural effusion was the most prevalent sign of capillary leak (FD 7 (64%), SD 12 (40%) DWS 8 (24.4%).

Conclusions: Patients can present early in the course of fever and be afebrile on admission, be commonly mistaken as bacterial infection, prescribed antibiotics which may delay fluid resuscitation. Neurological symptoms were more common as the disease progressed, hepatitis and pleural effusion were also typical.
**2020 Pediatric Research Day**  
May 13, 2020

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**Figure 1 Patient population**

- **1051** admitted as dengue fever
  - **995** classified as dengue with warning signs (DWS)
    - 345 negative
    - 91 inconclusive result
    - 49 sample issues
    - 518 confirmed DWS
    - 7 progressed in hospital
  - **56** classified as Sever dengue (SD)
    - 21 negative
    - 1 sample issue
    - 41 confirmed SD

- **33 controls**
- **30 survived**
- **11 died**
### Table 1 Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Severe fatal (FD) N= (%)</th>
<th>Severe non-fatal dengue (SD) N= (%)</th>
<th>Dengue with warning signs (DWS) N= (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 11</td>
<td>n = 30</td>
<td>n = 33</td>
</tr>
<tr>
<td>Age (y)</td>
<td>9.6 (5.5-11.2)</td>
<td>8.1 (1.8-11.5)</td>
<td>9.7 (5.3-11.6)</td>
</tr>
<tr>
<td>Female</td>
<td>4 (36%)</td>
<td>13 (43.3%)</td>
<td>12 (36%)</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>42.0 (18.5 - 52.1)</td>
<td>25.5 (12-44)</td>
<td>28.0 (17-36.5)</td>
</tr>
<tr>
<td>Underweight (z score &lt;-2)</td>
<td>1 (9.1%)</td>
<td>4 (13.3%)</td>
<td>3 (9.1%)</td>
</tr>
<tr>
<td>Overweight (z score &gt;-2)</td>
<td>1 (9.1%)</td>
<td>4 (13.3%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Guayas province</td>
<td>10 (91%)</td>
<td>24 (80%)</td>
<td>28 (85%)</td>
</tr>
<tr>
<td># of previous encounters</td>
<td>3 (2.5 - 4)</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
</tr>
<tr>
<td>NSAID use</td>
<td>3 (27%)</td>
<td>4 (13.3%)</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>Prior antibiotic use</td>
<td>7 (64%)</td>
<td>20 (66.7%)</td>
<td>20 (58%)</td>
</tr>
</tbody>
</table>
Table 2 Clinical presentation

<table>
<thead>
<tr>
<th></th>
<th>Severe fatal (FD) N=11 (%)</th>
<th>Severe non-fatal dengue (SD) N=30 (%)</th>
<th>Dengue with warning signs (DWS) N=33 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days of fever</td>
<td>3 (27%)</td>
<td>5 (46%)</td>
<td>5 (46%)</td>
</tr>
<tr>
<td>Malaise</td>
<td>2 (27%)</td>
<td>11 (36.7%)</td>
<td>17 (48%)</td>
</tr>
<tr>
<td>Headache/Ocular pain</td>
<td>3 (27.3%)</td>
<td>12 (40.0%)</td>
<td>14 (42%)</td>
</tr>
<tr>
<td>CNS symptoms</td>
<td>9 (82.0%)</td>
<td>15 (50.0%)</td>
<td>7 (21%)</td>
</tr>
<tr>
<td>Muscular/joint pain</td>
<td>2 (18.0%)</td>
<td>11 (36.7%)</td>
<td>13 (39%)</td>
</tr>
<tr>
<td>Mucosal bleeding</td>
<td>5 (45.0%)</td>
<td>14 (46.7%)</td>
<td>7 (21%)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>9 (82.0%)</td>
<td>23 (76.7%)</td>
<td>23 (67%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>8 (72.7%)</td>
<td>23 (76.7%)</td>
<td>25 (73%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4 (36.4%)</td>
<td>7 (23.3%)</td>
<td>13 (36%)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (36%)</td>
<td>8 (26.7%)</td>
<td>17 (52%)</td>
</tr>
<tr>
<td><strong>Physical exam</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulse pressure</td>
<td>36.0 (27.5-46)</td>
<td>30 (26-36)</td>
<td>30.0 (30 - 40)</td>
</tr>
<tr>
<td>Fever</td>
<td>4 (36%)</td>
<td>10 (33.3%)</td>
<td>10 (30.3%)</td>
</tr>
<tr>
<td>AVPU scale (alert)</td>
<td>2 (18%)</td>
<td>25 (83.3%)</td>
<td>30 (90.9%)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>8 (73%)</td>
<td>2 (6.7%)</td>
<td>3 (9.1%)</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>5 (45%)</td>
<td>2 (6.7%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>2 (18%)</td>
<td>3 (10.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Dry mucosa</td>
<td>10 (91%)</td>
<td>21 (70.0%)</td>
<td>26 (78.8%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------------</td>
<td>--------</td>
<td>--------</td>
<td>--------</td>
</tr>
<tr>
<td></td>
<td>9(82%)</td>
<td>16(53.3%)</td>
<td>12(36.4%)</td>
</tr>
<tr>
<td>Palmar pallor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>6(55%)</td>
<td>9(30.0%)</td>
<td>15(45.5%)</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>8(73%)</td>
<td>5(16.7%)</td>
<td>8(24.4%)</td>
</tr>
<tr>
<td>Capillary refill (sec)</td>
<td>4(3-4)</td>
<td>3(2-3)</td>
<td>2(2-3)</td>
</tr>
<tr>
<td>Edema</td>
<td>1(9%)</td>
<td>7(23.3%)</td>
<td>2(6.1%)</td>
</tr>
<tr>
<td>Mucosal bleeding</td>
<td>2(18%)</td>
<td>4(13.3%)</td>
<td>1(3%)</td>
</tr>
</tbody>
</table>
**Table 3 Laboratory evaluation**

<table>
<thead>
<tr>
<th></th>
<th>Severe fatal (FD) No (%)</th>
<th>Severe non-fatal dengue (SD) No (%)</th>
<th>Dengue with warning signs (DWS) No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 11</td>
<td>n = 30</td>
<td>n = 33</td>
</tr>
<tr>
<td><strong>Laboratory</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NS1 Antigen (+)</td>
<td>3 (27.3%)</td>
<td>19 (73.7%)</td>
<td>10 (30.3%)</td>
</tr>
<tr>
<td>IgM (+)</td>
<td>6 (54.5%)</td>
<td>22 (63.6%)</td>
<td>18 (54.4%)</td>
</tr>
<tr>
<td>IgG (+)</td>
<td>5 (45.5%)</td>
<td>17 (64.7%)</td>
<td>18 (54.4%)</td>
</tr>
<tr>
<td>White blood cells x10³/ul</td>
<td>7.8 (5.3 - 17.05)</td>
<td>4.55 (3.7 - 8.6)</td>
<td>4.5 (3.6 - 7.2)</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>37.0 (34.5 - 41)</td>
<td>37 (33 - 42)</td>
<td>37.9 (34.8 - 40.7)</td>
</tr>
<tr>
<td>Platelets x10³/mm³</td>
<td>142.0 (102.5 - 156)</td>
<td>99 (71.3 - 157)</td>
<td>160.0 (90 - 184)</td>
</tr>
<tr>
<td>PT (seg)</td>
<td>16.0 (15.7 - 16)</td>
<td>13 (12.6 - 14.3)</td>
<td>12.0 (11.6 - 13.8)</td>
</tr>
<tr>
<td>PTT (seg)</td>
<td>47.0 (44 - 52)</td>
<td>42 (40.8 - 44.3)</td>
<td>36.9 (34.2 - 39.5)</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>398.0 (218 - 1752)</td>
<td>308 (168 - 818)</td>
<td>146.5 (68.5 - 296.8)</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>718.0 (133 - 850)</td>
<td>106 (73 - 510)</td>
<td>75.0 (47 - 134)</td>
</tr>
<tr>
<td>Max AST (U/L)</td>
<td>1181 (374 - 4870)</td>
<td>523 (181 - 1239)</td>
<td>171 (75.3 - 329)</td>
</tr>
<tr>
<td>Max ALT (U/L)</td>
<td>763 (216 - 2083)</td>
<td>325 (96 - 550)</td>
<td>80 (51 - 134)</td>
</tr>
<tr>
<td>Na (mEq/L)</td>
<td>134.0 (131 - 137.5)</td>
<td>133 (131 - 136)</td>
<td>136.0 (132.5 - 137.5)</td>
</tr>
<tr>
<td>PCR (mg/L)</td>
<td>2.1 (1.5 - 3.575)</td>
<td>0.9 (0.3 - 2.3)</td>
<td>0.9 (0.3 - 2.4)</td>
</tr>
<tr>
<td><strong>Ultrasound</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>7 (64%)</td>
<td>12.0 (40.0%)</td>
<td>8 (24.2%)</td>
</tr>
<tr>
<td>Ascites</td>
<td>4 (36%)</td>
<td>8.0 (26.7%)</td>
<td>12 (36.4%)</td>
</tr>
<tr>
<td>Peri vesicular edema</td>
<td>1 (9%)</td>
<td>5.0 (16.7%)</td>
<td>3 (9.1%)</td>
</tr>
</tbody>
</table>

FREIRE, DOLORES (Infectious Diseases, Clinical/Research Fellow)
Table 4 Management

<table>
<thead>
<tr>
<th></th>
<th>Severe fatal (FD) N= (%)</th>
<th>Severe non-fatal dengue (SD) N= (%)</th>
<th>Dengue with warning signs (DWS) N= (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 11</td>
<td>n = 30</td>
<td>n = 33</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>1.9(0.8 - 4.0)</td>
<td>10.4(8.7-13.8)</td>
<td>5</td>
</tr>
<tr>
<td>Required PICU</td>
<td>11(100%)</td>
<td>22(73%)</td>
<td>0(100%)</td>
</tr>
<tr>
<td>No PICU bed</td>
<td>6(55%)</td>
<td>5(23%)</td>
<td>NA</td>
</tr>
<tr>
<td>PICU days</td>
<td>2(1-2)</td>
<td>5(4-8)</td>
<td>NA</td>
</tr>
<tr>
<td>Plan (ml/m2sc)</td>
<td>2000(1650 - 2350)</td>
<td>2000.0(1275-2500)</td>
<td>2500(2000 - 3000)</td>
</tr>
<tr>
<td>[Na] mEq/L</td>
<td>154(88.5 - 154)</td>
<td>31.0(23.3-154)</td>
<td>154(24-154)</td>
</tr>
<tr>
<td>Dextrose</td>
<td>3(27%)</td>
<td>21(70.0%)</td>
<td>14(44%)</td>
</tr>
<tr>
<td>O₂</td>
<td>5(45.5%)</td>
<td>3 (10.0%)</td>
<td>1(3%)</td>
</tr>
<tr>
<td>Inotropes</td>
<td>2(18.2%)</td>
<td>0(0.0%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>Blood products</td>
<td>1(9.1%)</td>
<td>4(13.3%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>Antibiotics on</td>
<td>2(18.2%)</td>
<td>4(13.3%)</td>
<td>1(6%)</td>
</tr>
<tr>
<td>Chest tube</td>
<td>1(9%)</td>
<td>3(10%)</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Mechanical ventilation (MV)</td>
<td>11(100%)</td>
<td>9(30%)</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>MV hours</td>
<td>7.4(3.2 - 44.9)</td>
<td>124.8(102.5 - 149.3)</td>
<td>NA</td>
</tr>
</tbody>
</table>
A systematic review of the factors that influence the acceptability of childhood vaccines among Canadians
Allison Gates, Michelle Gates, Jennifer Pillay, Robin Featherstone, Sholeh Rahman, Samantha Guitard, Tara MacGregor, Lisa Hartling

Introduction:
The National Advisory Committee on Immunization (NACI) develops vaccine recommendations for Canadians. To inform considerations for acceptability when developing recommendations, we completed a systematic review of evidence for factors that influence the acceptability of vaccines among Canadians, and for the effects of interventions aimed at improving vaccine acceptability.

Methods:
We searched 4 bibliographic databases, the Theses Canada Portal, and ClinicalTrials.gov for studies published in the past 5 years in English or French. Two reviewers screened the candidate records and agreed on those included in the review. From each study, we extracted information related to the participants, intervention or exposure, comparator, and setting, and relevant outcomes. We appraised risk of bias in each study and synthesized the findings narratively. We appraised the certainty of evidence for each acceptability factor using GRADE.

Results:
We screened 3316 records and included 152 (135 unique studies). The studies investigated 13 vaccines or groups of vaccines, of which six were relevant to children: childhood vaccines (as a group) (n = 13 studies; 10,944 participants), the human papillomavirus vaccine (n = 24; 170,909), measles-containing vaccines (n = 3; 5,495), the meningococcal vaccine (n = 2; 914), the pertussis vaccine (n = 3; 4,411), and the rotavirus vaccine (n = 1; 12,525). Across vaccines, there was at least low certainty evidence for the influence of 48 factors on acceptability. Among these, 19 were common to multiple vaccines: attitudes about vaccination, number of injections, perceived alternatives to vaccination, perceived effectiveness, perceived need or importance, perceived safety, knowledge (measured), receipt of information, social support, religious or moral beliefs, trust in healthcare providers, public health authorities, and scientific evidence, vaccination history, receiving a recommendation from a doctor, perceived disease severity, costs, awareness of the vaccine, and receiving a recommendation from a family member or friend. We identified little evidence for high-risk groups, healthcare providers, and policymakers. The certainty of evidence was very low for the effectiveness of all interventions (n = 19; 1,181,194), except for reminders for parents to have their infant vaccinated and universal vaccination programs for the rotavirus vaccine. For these, we found low certainty evidence of a positive influence on vaccine uptake and coverage, respectively.

Conclusions:
Among the factors investigated across studies, we identified those that are most important to consider when developing vaccine recommendations. Future research should focus on lesser-studied vaccines and population groups (i.e., high-risk, healthcare providers, policymakers).

Funding.
The National Advisory Committee on Immunization (Public Health Agency of Canada), contract #4600001536.
Neuroprotective Agents for Cerebral Malaria  
*Emily Kimani*, Dr. Michael Hawkes, Hannah Brooks, Urvi Rai

**Introduction:**
Caused by the *Plasmodium falciparum* parasite, Cerebral malaria (CM) is one of the leading causes of malaria-related death among children in Africa. Although treatments for CM have been found and work, for the most part, an 8-20% mortality rate remains among children affected by CM. An inflammatory response is activated by immune cells in response to the sequestration of *P. falciparum* to the endothelial monolayer that lines the blood-brain barrier. As a result of this inflammatory response, the permeability of the blood-brain barrier significantly increases, leading to complications such as brain hemorrhage, cognitive defects, and death. Pathways used by immune cells to activate an inflammatory response in CM is similar to pathways used by some tumor cells to promote tumor growth, such as carcinomas. The FDA has approved some clinically studied pathway inhibitors for the suppression of tumor growth. Therefore, we hypothesize that if the inflammatory response induced by *P. falciparum* sequestration can be suppressed by inhibitors used to suppress tumor growth, the permeability of the blood-brain barrier will decrease. The FDA approved inhibitors of interest in this study are Sunitinib, Pazopanib, and Imatinib.

**Methods:**
Using a Transwell assay (TW), we can create a model of the blood-brain barrier. *P. falciparum* infected red blood cells are placed on top of the monolayer created by immortalized Human Cerebral Microvascular Endothelial Cells (hCMEC/D3), followed by one of the three FDA approved drugs and a fluorescein probe. The permeability of the monolayer is tested by measuring the resistance of the monolayer and the concentration of fluorescein present on the top and bottom chambers of the TW.

**Results:**
Pazopanib is successful in rescuing *P. falciparum* induced permeability of the monolayer in our in vitro model of the blood-brain barrier.

**Conclusions:**
If one or two FDA approved drugs result in decreased monolayer permeability, it could lead to the improvement of CM treatments and, ultimately, to the general reduction of the mortality rate.
Physician Experiences on Implementation of Antimicrobial Stewardship Rounds in Pediatric Hospital Medicine: An Exploratory, Qualitative Analysis

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2. Division of Pediatric Hospital Medicine, Department of Pediatrics, Faculty of Medicine & Dentistry, University of Alberta, Edmonton, AB
3. Division of Pediatric Infectious Disease, Department of Pediatrics, Faculty of Medicine & Dentistry, University of Alberta, Edmonton, AB

Introduction:
An antimicrobial stewardship (AS) intervention was implemented for pediatric medicine units using a bi-weekly in-person rounds-based approach to provide stewardship recommendations and education from an AS physician and pharmacist. We assessed the effects of this intervention by qualitatively exploring the experiences of pediatricians and pediatric residents one year after its implementation.

Methods:
This was an exploratory qualitative study. Purposeful sampling was used to recruit participants for individual interviews. Pediatricians and residents who attended ≥1 stewardship rounds were included. A semi-structured interview guide was created focusing on perceptions of AS, personal experiences at stewardship rounds and perceived impacts on patient care. Codes were identified using a content analysis approach and collapsed into categories then themes.

Results:
Eight pediatricians and ten residents completed interviews. Three themes were identified: Insights into Clinical Reasoning, Opportunity for Growth and Learning, and Establishing and Exploring Professional Relationships. Stewardship rounds encouraged participants to critically evaluate antimicrobial choices and review evidence to make informed decisions. The in-person approach allowed participants to explain their rationale and engage in discussion with the stewardship team. Furthermore, participants felt a sense of validation from the program and gained confidence for prescribing antimicrobials in the future. The educational aspect was an important benefit, particularly for senior residents. Stewardship rounds provided face-to-face interaction with infectious diseases (ID) physicians and some participants felt more comfortable consulting ID because of this. In contrast, others worried physicians may avoid ID consults and wait for input at stewardship rounds.

Conclusions:
Participating clinicians found AS rounds to be an effective strategy for education and development of clinical reasoning skills for optimal antimicrobial prescribing. The effects of our intervention on timing and frequency of ID consults is an interesting finding shared by participants. Further research into patient important outcomes and consultation practices are needed to explore this.
ABSTRACT – 2020 PEDIATRIC RESEARCH DAY, MAY 13, 2020 – EDMONTON, AB
SIRAJEE, RESHMA (INFECTIONOUS DISEASES)

Systematic review exploring the role of CRP biomarker as a predictor of stunting in infants under age of 5 years old
Reshma Sirajee, Michael Hawkes from University of Alberta, Edmonton AB, Canada

Background:
Human Immunodeficiency virus (HIV) poses substantial global health concerns with 37.9 million people currently living with it. The principal mode of child HIV acquisition is vertical transmission (VT) from HIV-infected mothers during pregnancy, childbirth and/or breastfeeding. Additionally, successful interventions with combination antiretroviral therapy (cART) have reduced VT of HIV to less than <1% in resource-rich areas. However, worldwide, HEU newborns significantly outnumber infected infants and represent nearly 30% of the newborn population in some HIV endemic nations. Recently, concerns have emerged about HEU infants, whose growth outcomes are not comparable with HIV unexposed uninfected (HUU) infants. HEU infants have a three-fold higher chance of growth faltering such as stunting (low height-for-age) compared to HUU. Stunting is related to health problems such as diarrhea, immune dysregulation, and systemic inflammation. The biomarker C-Reactive Protein (CRP) plays a key role in disease processes stemming from systemic inflammation. This study is in support of a master’s research project that will use measurements of biomarker CRP levels in the HEU population as a predictor of stunting.

Methods:
We conducted a scoping literature review using NCBI Pubmed Central (search terms CRP OR C-reactive protein, stunting, child or infant). The initial search returned 57 articles, which was narrowed to 25 based on the title of the article. Inclusion criteria was children’s age, CRP, and length/height measured all under 5 years of age, and both HEU and HUU children were eligible to be included. Paper were excluded if they did not include primary data and did not have quantitative measurements of CRP and stunting. A final list of 7 articles were pertinent to CRP as a predictor of stunting.

Results:
The 7 identified studies reported association between CRP and stunting and they were all examining HUU infants. Most of literature showed CRP’s association with stunting to varying degrees in HUU infants but the data was inconclusive. Lastly, there were no studies examining association between CRP and stunting in HEU infants.

Conclusion:
CRP is a general biomarker of inflammation but may serve as a predictive marker of stunting in HEU infants with more investigation. Thus, my master’s thesis will examine the role of several biomarkers and answer the question if we can use biomarkers in early infancy to predict linear growth faltering in HEU infants.

This study will be carried under the supervision and mentorship of Robert Opoka2, Sophie Namasopo4, Andrea Conroy2, Michael Hawkes1 with University of Alberta1, Makerere University in Kampala2 and Jinja Regional Referral Hospital in Jinja1.
ABSTRACT – 2020 PEDIATRIC RESEARCH DAY, MAY 13, 2020 – EDMONTON, AB
WINGERT, AIREEN (INFECTIOUS DISEASES)

Respiratory Syncytial Virus and Burden of Disease – Systematic Review

Introduction:
To systematically review evidence on the burden of respiratory syncytial virus (RSV) on infants ≤24 months with risk factors, to inform recommendations by the National Advisory Committee on Immunizations on RSV prophylaxis.

Methods:
Four databases (2014 to 2018), grey literature and reference lists were searched for studies of infants, with or without a prespecified risk factor, who did not receive RSV prophylaxis and were diagnosed or hospitalized with RSV at ≤24 months. Screening, study selection, and risk of bias assessments were independently undertaken by two reviewers, with consensus for final decisions. One reviewer extracted data, and another verified. Data were pooled when appropriate. Two reviewers assessed certainty of evidence using GRADE.

Results:
Ten of twenty-eight included cohort studies provided within-study comparators. For premature (33-36 weeks’ gestation) versus term infants, there was low-to-moderate certainty evidence for an increase in RSV-hospitalizations at or before 6 months of age (one study; n=599,535; RR 2.05 [95% CI 1.89 to 2.22]; 1.3 more per 100 [1.1 to 1.5 more]) and hospital duration (one study; n=7,597; mean difference 1.00 days [95% CI 0.88 to 1.12]). There was low-to-moderate certainty evidence of no little-to-no difference for infants born at 29-32 versus 33-36 weeks for hospitalization (one study; n=12,812; RR 1.20 [95% CI 0.92 to 1.56]). Evidence was low or very low certainty for other short-term and all long-term outcomes for premature versus term infants and for different gestational ages, and for outcomes for all other risk factors.

Conclusions:
Prematurity is probably associated with increased risk for RSV-hospitalization before 6 months of age and longer hospital length of stay. The extent of prematurity may not make a difference for RSV-hospitalization. Low to very low certainty evidence was found for other outcomes based on prematurity and for all other risk factors.
Role of leukemic cells in haemostatic abnormalities in paediatric acute lymphoblastic leukemia: a novel mechanism for risk for venous thromboembolism during chemotherapy

Ghada Aborkhees*, Kevin Dietrich, Lesley Mitchell
Paediatrics department, University of Alberta

INTRODUCTION:
Acute lymphoblastic leukemia (ALL) in children is associated with an increased risk of venous thromboembolism (VTE). While more than 80% of leukemic children survive their primary disease, over 30% experience VTE during the course of the treatment. In the literature, VTE is associated with plasma hemostatic abnormalities, which are believed to be related to abnormalities in hepatic production. To date, leukemic cell have never been investigated as a source of the hemostatic abnormalities. We hypothesized that leukemic cells have the capacity to produce hemostatic proteins and their apoptosis leads to the release of these hemostatic factors into the circulation (tumor lysis syndrome). Furthermore, we are exploring whether hemostatic protein production is a function of normal lymphocytes or a constitutive character of the immature abnormal cells.

METHODS:
Our study includes the demonstration of the capacity of protein expression in two pediatric cell lines; (CCL119-rom 4-year-old T cell ALL patient) and (CCL120-from 11-year-old B cell ALL patient). Measuring proteins by western blot with reducing sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), polyvinylidene difluoride membrane transfer and primary antibodies incubation followed by labelled secondary antibodies detection by chemiluminescence. Overall coagulation/hemostatic potential assays are optimized.

RESULTS:
We have shown protein expression of multiple hemostatic factors including Procoagulant, anticoagulant, fibrinolytic and antifibrinolytic hemostatic factors. Multiple hemostatic proteins are expressed constitutively by lymphoblasts but not normal lymphocytes and vice versa. lymphocytes but not in ALL cell lines produce plasminogen activator inhibitor (PAI-1) and Fibrinogen beta and gamma (FGB, FGG). Other proteins generated by ALL but not observed in normal lymphocytes include FV, FVII, FVIII, FXII FXIIa and TAFI. Overall coagulation and hemostatic potential assays show a difference in the fibrin generation initiation and fibrinolysis between malignant lymphoblasts and normal lymphocytes.

CONCLUSIONS:
We report, for the first time that normal lymphocytes and leukemic cells produce hemostatic factors in different capacities. A difference in the overall hemostatic capacity is demonstrated for the lymphoblasts and lymphocytes. Complete investigation of the capacity for production of hemostatic system proteins of leukemic cells will provide an insight into mechanisms of for VTE risk in children with leukemia.
Understanding Exposures in Early Life: The Children’s Environmental Health Clinic at the University of Alberta

Lesley Brennan1, Irena Buka1,2, Anne Hicks1,2, Alexander Doroshenko1,3,4,5, Abbeir Hussein1, Donald Spady1,2, Alvaro Osornio-Vargas1,2

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2 Department of Pediatrics, Faculty of Medicine and Dentistry, University of Alberta
3 Division of Preventive Medicine, Faculty of Medicine and Dentistry, University of Alberta
4 School of Public Health, University of Alberta
5 Medical Officer of Health, Alberta Health Services

Introduction:
The Children’s Environmental Health Clinic (ChEHC) is an interdisciplinary group dedicated to understanding the unique effects that interacting exposures contribute to the early-life exposome and child health. As the only Canadian program in an international network of Pediatric Environmental Health Specialty Units (PEHSU), ChEHC provides clinical service, educational resources, completes clinical research and acts as a hub for collaborative research projects. It is a WHO Collaborating Centre in Child Health and the Environment. The objective is to review exposures and health concerns presented to ChEHC and to present current research.

Methods:
Research in our program is driven by community concerns. A summary of patient chart reviews (2012-2015) was completed to highlight the most common exposures and clinical concerns presenting to ChEHC. Research studies developed based on these findings and community concerns are then highlighted.

Results:
Common clinical presentations to ChEHC include known or suspected exposures to tobacco, cannabis, mold, heavy metals, air pollution, carbon monoxide, asbestos, industrial pollutants including chemicals and byproducts of industry, and allergens. Respiratory and neurodevelopmental health effects were mostly commonly reported. Current projects include clinical cohort evaluation of home exposure to tobacco and cannabis, long-term health outcomes of children living in wildfire-impacted communities and the health impacts of air quality and environmental exposures based on health data and geotemporal mapping, with a specific focus on industrial pollutants and pregnancy outcomes.

Conclusions:
Patients are ChEHC experience a wide range of symptoms and exposures. The clinical cases and community concerns brought to ChEHC drive our research program. ChEHC started as a local clinical service for pediatric environmental health and has grown into a valuable local and global resource. ChEHC combines evidence-based clinical evaluation, with children’s unique dynamic developmental physiology to consider short- and long-term impacts of childhood environment on the exposome and health outcome.
The Fort McMurray wildfires in Alberta: Health effects in pediatric cases seen at the Children’s Health Environmental Health Clinic

Lesley Brennan1, Irena Buka1,2, Anne Hicks1,2, Alexander Doroshenko1,3,4,5, Donald Spady1, Alvaro Osornio-Vargas1,2

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5 Medical Officer of Health, Alberta Health Services

Introduction:
In May 2016, the city of Fort McMurray, located in Northeast Alberta, was struck by one of the largest and costliest wildfires in Canadian history, leading to a massive evacuation. Evidence indicates that anthropogenic activity contributing to climate change played a role in weather conditions combining high temperatures and low precipitation that lead up to the fire. The fire had a significant impact on the health on residents of Fort McMurray and surrounding areas.

Children are particularly vulnerable to the effects of wildfires as they are rapidly growing and developing. They are also susceptible to mental trauma associated with life-threatening events and personal loss. The Children’s Environmental Health Clinic (ChEHC), located in Edmonton, is dedicated to caring for children exposure to environmental hazards, including those impacted by wildfires fires.

Methods:
Following the wildfire, several children were referred to ChEHC. All ChEHC patients receive a 150 question Pediatric Environmental Health History (PEHH) to evaluate their environment in addition to a medical assessment. Here we describe two cases directly impacted by the wildfires in detail, including health effects, and outcomes to date.

Results:
Both cases described are male adolescents residing in the Fort McMurray area at the time of the fires. One is a 12-year-old boy with asthma that experienced worsening of symptoms before/during evacuation and upon returning home, the other a 16-year-old boy who experienced symptoms affecting both physical and mental health upon returning to his home after evacuation, which was damaged by the fire. Respiratory symptoms were treated with medical management, education about exposures that exacerbate symptoms, and information on how to track air quality using the Air Quality Health Index (AQHI). Other symptoms were managed by investigating all exposures potentially associated with health concerns, including those within the home, helping the family mitigate them, and identifying resources, such as fact sheets. Both families adapted their lifestyles/environments, and the children demonstrated improved health and well-being over time.

Conclusions:
Climate change is increasing the number and severity of natural disasters around the world, including in
Alberta. Children have a high risk of lifelong consequences from these disasters due to their developmental plasticity, relatively larger exposures and longevity. The health outcomes of wildfires can be devastating, especially for children who are developmentally vulnerable, have pre-existing respiratory conditions, or suffer mental health consequences as a result of the trauma.
Validation of a role for Active Beta-Catenin (ABC) in promoting Metastatic Phenotype in Osteosarcoma

Introduction:
Osteosarcoma (OS) is the most common primary bone malignancy with high incidence in children and adolescents. Approximately 20% of patients who are diagnosed with OS present with metastatic disease. Currently there are very few reliable prognostic markers for OS that could allow for a confident and confirmatory diagnosis. Better understanding of the biological mechanisms driving this malignancy is paramount for identifying prognostic markers for aggressive/metastatic disease.

The Wnt/β-catenin (β-cat) signaling pathway is one of the pathways which is shown to be deregulated in OS. However, its role in OS, especially in OS progression, remains unknown. Therefore, this study aims to investigate the role of the Wnt/β-cat pathway, especially the transcriptionally active form of β-cat, Active Beta Catenin (ABC), in OS progression and whether it can be used as a reliable prognostic marker for OS progression.

Methods:
Two sets of paired cell lines, SaOS2/SaOS2-LM7 and HOS/HOS-143B were utilized for this study. Using a pEGFP-β-cat fusion construct plasmid, we carried out site directed mutagenesis to the N-terminal S33, S37, T41 and S45 in order to mimic endogenous ABC [GeneArt, Invitrogen]. The pEGFP-ABC and pEGFP-β-cat constructs were then transfected into SaOS2 and HOS cells and subject to Western Blot analysis and immunofluorescence for protein levels/localization of GFP-ABC and GFP-β-cat. We also carried out immunohistochemical analysis (IHC) on 30 OS patient samples to determine whether nuclear ABC levels were correlated to “aggressive” disease.

Results:
Initial observations from both paired cell lines indicated that endogenous nuclear ABC levels, but not β-cat, increase with osteosarcoma progression. Immunofluorescence of SaOS2 cells transfected with pEGFP-ABC/pEGFP-β-cat showed similar localization to that of the endogenous ABC and β-cat: endogenous and pEGFP-ABC were both seen to translocate to the nucleus while both the endogenous and pEGFP-β-cat remained cytosolic/membrane bound.

We analyzed whether nuclear ABC levels were correlated to aggressive OS, as determined by metastasis at diagnosis or resection (30 patients) via IHC. We observed a significantly greater number of patients with metastatic disease at diagnosis (p=0.029, two tailed) or at the time of resection (p=0.007, two tailed) showing high nuclear levels of ABC (>25% nuclear positivity) compared to samples which did not show metastasis at diagnosis or resection.

Conclusion:
Our results suggest a strong correlation between high nuclear ABC levels and metastatic disease and encourages further work with the plasmid constructs and larger cohort of patients to determine whether ABC has potential to be used as a reliable prognostic marker.

Funded by: Women and Children’s Health Research Institute grant and WCHRI/Hair Massacure grant to SP.
Setting the stage for integrated knowledge translation in an interdisciplinary research project

Osnat Wine, Jude Spiers, Michael van Manen, Kathy Kovacs Burns, Alvaro Osornio Vargas, and on behalf of the DoMiNO Project

Introduction:
Research on health and children’s environments is complex. It requires the collaboration of diverse disciplines and knowledge users in the research process and in knowledge translation. The application of collaborative approaches, such as integrated knowledge translation (IKT), is often challenging for interdisciplinary teams. Much can be learned from an in-depth study of such processes. Based on the DoMiNO Project experience our objective is to portray what it takes to implement and shape an IKT approach.

Methods:
As part of a qualitative case study of the DoMiNO project IKT process, designed to learn about the essential components of IKT, data were collected using different methods over five years. Observation and project logbook were used to identify and describe the major IKT activities. Data evaluation informed the ongoing iKT process, and thematic analysis of surveys, project documents, interviews and focus groups with DoMiNO team members identified the contribution of these activities to the iKT process and the project success.

Results:
The operation of IKT meant that the team needs to ensure rapport, engagement, learning, reflection and the creation of an inclusive environment by utilizing different activities. The DoMiNO project iKT framework included: four annual face-to-face two-day meetings, multiple steering committee meetings, newsletters, webinars, evaluation and reflection activities, as well as ongoing emails, small group meetings, and informal and social meetings. Some of these activities were part of the original project plan, while others were developed in response to the project needs as identified by reflective activities and the ongoing evaluation of the iKT process. Some of the latter for example, included the design of specific discussions, workshops, webinars or tools that supported the project progression and productivity. Applying these activities required sufficient time, active engagement of the team, and an attentive management of the project, in order to plan and make changes as needed and set the tone for collaborative research.

Conclusion:
The findings highlight some of the aspects required for the implementation of IKT in an interdisciplinary research project. These include designated activities, on-going evaluation, responsive management, engaged team and flexibility in the iKT framework in order to foster joint knowledge creation and knowledge translation. The findings reflect the context of the DoMiNO project. However, these lessons can inform leaders, team members and knowledge users about incorporating IKT in their research practice.
Constitutive Protein Expression of Hemostatic Proteins in a Pediatric Renal Cancer Cell Line
Hanjie Zhu, Kevin Dietrich, Ghada Aborkhees, Lesley Mitchell

Introduction
In cancer, metastasis is associated with poor prognosis. By preventing spread of the tumour cells to distant sites the clinical prognosis can thus be improved. In pediatric cancer patients, one sixth of patients will develop symptomatic venous thromboemboli, signifying a pathological pro-thrombotic state. This change in hemostasis is thought to help cancer cell metastasis: metastasising cancer cells cloak themselves in a fibrin clot to avoid immune detection. As the generation of fibrin clots plays a key role in cancer metastasis, it is then important to determine how cancer cells modify the hemostatic protein balance. Specifically, the capacity of the tumor cells to produce the hemostatic proteins required for fibrin generation could directly enhance the ability of the tumor to metastasize. Thus, we set out to determine whether pediatric Wilms tumor cells could directly produce hemostatic protein. We hypothesised that pediatric Wilms tumor cells will constitutively express hemostatic proteins. Furthermore, any constitutive protein production will be affected by chemotherapy agents.

Methods:
To investigate this the CRL-1441 cell line, a pediatric renal cancer line was used. Western blotting was used to quantify hemostatic factors at a protein level. Five groups of CRL-1441 colonies were exposed to different experimental conditions, consisting of either no exposure or 24 hours incubation in standard chemotherapy drugs used in treatment of Wilms tumour: vincristine, etoposide, daunorubicin, and actinomycin. Results were compared to both normal plasma as well as depleted plasma as a control to find the band of interest. To quantitate the change in protein expression from chemotherapy exposure, amido black staining was performed to give the relative amount of total protein per lane. Each protein was assessed quantitatively using an image analysis package, with triplicate experiments performed.

Results:
The CRL-1441 cells constitutively expressed thirteen of sixteen tested for hemostatic factors. Three of the expressed proteins are fibrinolytic: von Willebrand Factor-cleaving protease, tissue plasminogen activator and urokinase; two anti-fibrinolytic protein: carboxypeptidase B2 and plasminogen activator inhibitor-1; and eight coagulative factors: Factors III, V, VII, VIII, IX, XII, XIIIa, and fibrinogen gamma. Exposure to the chemotherapy agents vincristine and etoposide were shown to significantly upregulate some hemostatic protein expression while actinomycin downregulates some hemostatic protein expression. Results are still in progress and more hemostatic factors will be tested for constitutive expression.

Conclusion:
We have shown that pediatric Wilms tumour cells can directly produce hemostatic factors to impact hemostasis. Furthermore, this production is modulated both positively and negatively using chemotherapy agents.
ABSTRACT – 2020 PEDIATRIC RESEARCH DAY, MAY 13, 2020 – EDMONTON, AB
BRUCKNER, MARLIES (NEONATAL-PERINATAL CARE-NICU)

Evaluating new methods to secure umbilical vein catheters in neonatal emergencies
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Introduction:
The current European Resuscitation Council Guidelines recommend the umbilical vein catheter (UVC) as optimal vascular access for medication administration in neonatal resuscitation. In emergency situations it may be difficult to insert and secure the UVC.

The aim of this study was to evaluate two new methods to secure UVC by using a disposable umbilical clamp. We evaluated the methods according to successful volume administration and effectiveness of fixation.

Methods:
In an experimental study, umbilical cord remnants were catheterized with commercially available intravenous cannulas using only the plastic catheter without a hollow needle. (Figure 1).

In the “Fix” secure method, the umbilical clamp was closed at the level of the transparent catheter, so it did not reach the plastic wing of the cannula. In order not to overlook relevant compression of the catheter lumen, no umbilical band was used. (Figure 2).

In the “FixPlus” secure method the umbilical clamp was closed as close as possible to the plastic wing (at the transition between the transparent plastic catheter part and the plastic wing of the cannula). An umbilical band was tightened at the level of the transparent catheter to control bleeding. (Figure 3).

In both methods, it was tested whether a predefined volume (10 ml/kg body weight of the newborn) could be infused over one minute. The force to release the fixation was measured using a spring balance, to investigate the effectiveness of the secure method.

Results:
A total of 40 umbilical cords were catheterized. By using the “FixPlus” (n=20) method, less of the predefined volume could be administrated compared to the “Fix” (n=20) method (median [IQR]: 95% [89-100] vs. 97% [0-100]; p = 0.2). Compression of the catheter prevented effective administration of the predefined volume one time in the “FixPlus” group and six times in the “Fix” group (p = 0.038). The effectiveness of the secure methods was significantly higher in the “FixPlus” than “Fix” (median [IQR]: 65.9 [56.5-68.9] Newton versus 4.6 [3.9-6.0] Newton; p <0.001).

Conclusion:
In both methods, the volume administration was possible in a high number of attempts. However, the “FixPlus” method showed less compression of the catheter lumen, compared to the “Fix” method. The effectiveness of fixation is also significantly better with “FixPlus”. Using a commercially available
intravenous cannula as a UVC and securing it with a disposable umbilical clamp might be a helpful method, especially for staff with limited experience in neonatal emergencies.

Figure 2 Experimental setup

Figure 3 "Fix" secure method

Figures continued next page
Figure 4 "FixPlus" secure method
Fostering Hope: The Comprehensive Accessible care for Infants with Neonatal abstinence (CAIN) Study
Denise Clarke, NNP; Matt Hicks, MD, Karen Foss, NNP, Natasha Lifeso, MPH

Introduction:
Neonatal Abstinence Syndrome (NAS) occurs in newborns exposed to drugs in-utero. In Canada, maternal opiate use in pregnancy has been steadily rising resulting in as many as 1850 babies born with NAS per year. Management of babies born with NAS requires supportive, interdisciplinary care. Depending on the severity of NAS, babies may be cared for with non-pharmacological interventions or some may need to be admitted to the Neonatal Intensive Care Unit for extended hospital stays to receive medication and management of ongoing complex health care needs. Hospital and community health care providers have expressed concerns around the continuity of care for these babies in their stay in hospital and their transition to home. This study examined the experiences of hospital and community-based health care providers and families regarding the management of babies with NAS. The driving force behind our inquiry related to our interest to streamline care for these babies in highly complex health and social systems.

Methods:
In total, 47 interdisciplinary participants were interviewed over a four-month period with individuals from Women’s and Child Health, Community, and family members. Interviewed transcripts were reviewed over several months and was completed in December 2019 using an inductive thematic analysis which culminated in the identification of an overarching theme linked with primary themes.

Results:
The study identified existing gaps in the management of these patients; determined how to improve communication between hospital and community networks; and provided a better understanding of the perceptions and experiences of hospital and community personnel. The overarching theme identified was hope with the primary themes being: system, mental health, mother/baby, judgement, and knowledge (see figure 1). Several gaps identified in the system included fear, stigma, and language. Certain solutions proposed for improvement included focused care in a rooming in model for the mother and baby dyad, supporting mother’s well-being, involving mothers and families, and supporting care providers in a family centered care model.

Conclusion:
This research demonstrates that programs and interventions implemented when working with mothers and babies with NAS must foster hope in mothers, families, and in the extended care provider team.
Figure 1.
ABSTRACT – 2020 PEDIATRIC RESEARCH DAY, MAY 13, 2020 – EDMONTON, AB
GHOMAN, SIMRAN (NEONATAL-PERINATAL CARE – NICU)

RETAIN digital simulation game improves short- and long-term neonatal resuscitation knowledge
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Introduction:
One million newborns worldwide die from asphyxia at birth each year. Alarmingly, 50% of this mortality is caused by deficiencies in healthcare providers’ (HCP) competence to provide care. Frequent simulation training is recommended to address this gap. However, resource constraints (e.g., time, money, personnel) limit HCPs’ training opportunities. Our objective was to examine if training with the RETAIN simulation-based digital game improves HCPs’ neonatal resuscitation knowledge.

Methods:
HCPs from the Royal Alexandra Hospital Neonatal Intensive Care Unit (Edmonton, Canada) were recruited to play the RETAIN digital game (RETAIN Labs Medical Inc., Edmonton, Canada) (Ethics Approval Pro00085274). Participants completed a i) survey, ii) pre-test, iii) two training scenarios (RETAIN digital game), iv) post-test, v) two-month post-test, and vi) five-month knowledge transfer task (low-fidelity table-top simulation).

In RETAIN, players practice stabilizing a simulated newborn baby in distress. Players must initiate appropriate interventions using the correct equipment in response to ongoing visual and cardiorespiratory feedback from the baby. Scenarios are evidence-based from real deliveries recorded at a tertiary perinatal centre.

Participants’ time-stamped keystrokes and mouse-input were recorded. Performance was scored using Neonatal Resuscitation Program 2015 guidelines and compared using paired t-test. Data is reported as mean(stdandard deviation) for normally-distributed, or median(interquartile-range) for non-normal continuous variables.

Results:
40 HCPs (nurses, nurse practitioners, respiratory therapists, fellows, and clinical associates) participated in the study (9(6.4-15.2) years of clinical experience). 16 of 40 HCPs (40%) successfully completed the pre-test (24 of 40 HCPs unsuccessful, 60%), while 31 of 40 HCPs (78%) successfully completed the post-test (9 of 40 HCPs unsuccessful, 22%) (p<0.001). 28 of 40 HCPs (70%) successfully completed the two-month post-test (12 of 40 HCPs unsuccessful, 30%). Furthermore, 29 of 40 HCPs (72%) successfully completed the five-month knowledge-transfer task (11 of 40 HCPs unsuccessful, 28%).

HCPs enjoyed playing RETAIN (4.1(0.9) on a 5-point Likert scale) and reported it would be beneficial for Neonatal Resuscitation Program training (4.2(0.8) on a 5-point Likert scale).
**Conclusions:**
Training with RETAIN improved HCPs’ short-term knowledge of neonatal resuscitation. Further, knowledge improvement was sustained long-term. HCPs also demonstrated transfer of knowledge to a novel learning environment. RETAIN may improve access to simulation training for neonatal HCPs, especially in rural, low resource, or low birth-attendance settings.
Accuracy of a novel, non-contact camera-based photoplethysmography heart rate monitoring system for infants requiring neonatal resuscitation at birth
Peter A. Johnson, BSc (Hons), Jannatul Mustofa, Kyle Mathewson, PhD, Maryna Yaskina, PhD, Georg M. Schmölzer, MD, PhD

Introduction:
Heart rate (HR) monitoring is critical for decision-making and assessing the newborn’s status during resuscitation. Electrocardiography (ECG) is the current gold standard for HR monitoring in the delivery room. However, using electrodes increase the risk of serious skin damage, injury, and pain, particularly for premature infants with delicate skin. Recently, the use of non-contact camera-based photoplethysmography (cbPPG) has been suggested as a promising alternative in the delivery room, though no study has evaluated it in the delivery room until now. The objective of this study was to evaluate the accuracy and feasibility of a novel non-contact cbPPG system for HR monitoring of early gestational newborn infants in the delivery room.

Methods:
Low birth-weight, preterm, newborn infants (n=40, <1500 g, <36 weeks gestation) were recruited from the Royal Alexandra Hospital delivery rooms. A high-resolution video camera was utilized to collect HR recordings for these infants, alongside simultaneous HR measurement by ECG. cbPPG utilizes colour changes resulting from changes in blood vessel volume during the cardiac cycle, which can be detected by the video camera, to determine HR. A Bland-Altman analysis was conducted to evaluate the accuracy of cbPPG by determining the level of agreement between cbPPG and ECG HR measurements.

Results:
Newborn infants included in this study had a mean (SD) birth weight of 1225(475) g and gestational age of 28.6(2.6) weeks. Of these, 16/40 infants were male and 37/40 received antenatal steroids. Mean (SD) HR for cbPPG and ECG HR was 146(6) and 146(8) beats/min, respectively. The Bland-Altman analysis showed a mean difference (95% levels of agreement) of 0.38 (-7.99 to 8.74) beats/minute between cbPPG HR and ECG. However, motion artefacts and frequency harmonics occasionally resulted in signal dropout and/or low signal reliability.

Conclusion:
Our study demonstrated non-contact cbPPG HR monitoring is feasible for the delivery room and had a similar accuracy to ECG for HR monitoring. However, further refinement and clinical trials are warranted to enhance and evaluate this technology before its clinical implementation.
No difference in resuscitation outcomes between males and females with different cardiopulmonary resuscitation interventions in a neonatal porcine asphyxia model

Seung Yeon Kim, Gyu-Hong Shim MD, PhD, Megan O’Reilly PhD, Po-Yin Cheung MBBS, PhD, Tze-Fun Lee PhD, Georg M Schmölzer MD, PhD

Background:
Male newborns are at greater risk of poor cardiovascular and respiratory outcomes compared to females. However, the mechanisms associated with the “male disadvantage” remains unclear. We have previously shown no difference between male and female newborn piglets during hypoxia, asphyxia, resuscitation, and post-resuscitation recovery. However, it is unknown if there are differences in resuscitation outcomes between males and females during different cardiopulmonary resuscitation techniques.

Intervention and measurements:
Secondary analysis (five previous publications and two studies currently under peer-review) of 184 term newborn mixed breed piglets (1-3 days of age, weighing 2.0 (0.2) kg), which were exposed to 30-50 min of normocapnic hypoxia followed by asphyxia until asystole. This was followed by cardiopulmonary resuscitation. For the analysis, piglets were divided into male and female groups, as well as resuscitation technique groups (sustained inflation, 3:1 compression-to-ventilation ratio, or asynchronous ventilations during chest compressions). Cardiac function, carotid blood flow, and cerebral oxygenation were continuously recorded throughout the experiment.

Main results:
Regardless of resuscitation technique, there was no significant difference between males and females in the number achieving return of spontaneous circulation (ROSC) [95/123 (77%) vs. 48/61 (79%)], the time to achieve ROSC [112 (80-185) sec vs. 110 (77-186) sec], and the 4-hour survival rate [81/95 (85%) vs. 40/48 (83%)]. Levels of the injury markers interleukin (IL) -1ß, IL-6, IL-8, and tumour necrosis factor-α in frontoparietal cortex tissue homogenates were similar between males and females.

Conclusions:
Regardless of resuscitation technique, there was no significant effect of sex on resuscitation outcome, survival, and hemodynamic recovery in asphyxiated newborn piglets.
Helping the Helpers: Peer Critical Incident Stress Management for NICU Health Care Providers to Improve Resilience, Burnout and Patient Safety

Natasha Lifeso, Matthew Hicks & Chloe Joynt

Introduction:
Health care providers in neonatal intensive care units (NICU) experience critical or distressing events that can overwhelm their usual coping skills and lead to significant stress. Ineffective support for health care providers dealing with critical incidents can lead to poor unit resilience, staff burnout and compromised patient care behaviours. A formalized peer program and process to address critical workplace incidents and support care providers, “Critical Incident Stress Management (CISM)” is used in many first responder professions. While there is growing interest in implementing peer CISM teams in critical care units, there is a lack of research describing the impact of CISM in NICU. This study examined the effect of implementing a multidisciplinary NICU health care provider peer CISM Team on resilience and burnout in a tertiary NICU.

Methods:
Multidisciplinary team members were peer selected and formally CISM trained. Change management strategies were employed to introduce CISM to the NICU. All health care providers were invited to complete an anonymous online or paper survey before and 1 year after NICU CISM Team implementation. The survey contained validated measures of resilience, burnout, and team/safety culture that were analyzed pre and post intervention.

Results:
The response rate pre-intervention was 66% (114/172 staff) and 32% post (60/186 staff). Stress recognition significantly improved as fewer staff reported being less effective at work when feeling stressed post incident (74% vs 61%, pre and post CISM respectively, p<0.05). Fewer staff reported feeling burned out from their work (41% vs 31%, p=0.4) trending towards improved resilience. Communication in the NICU significantly improved as staff indicated debriefing methods met their needs (38% vs 57%, p<0.05) and felt comfortable speaking up about safety (66% vs 79%, p=0.1). Post-intervention, despite feelings of increased workload indicated by a significant decrease in agreement that “NICU staff levels were sufficient for patient load” (54% vs 33%, p<0.001), a majority of staff reported a supportive environment in the NICU (59% vs 77%, p=0.08). Work culture significantly improved as staff felt rewarded and recognized for improving quality (13% vs 31%, p<0.05).

Conclusion:
Implementation of a peer CISM team led to improved NICU care provider resilience, stress recognition, team culture all of which can mitigate the effects of increased patient load. Findings from this research and knowledge gained from the CISM implementation process should be shared with other health care environments.
ABSTRACT – 2020 PEDIATRIC RESEARCH DAY, MAY 13, 2020 – EDMONTON, AB
MANGAT, AVNEET (NEONATAL-PERINATAL CARE – NICU)

Magnetic Acupuncture for Infant Comfort: A Multicentre Randomised Controlled Trial in Preterm Infants Requiring Eye-exam for Retinopathy of Prematurity
Avneet Mangat, Kimberly M.L Gan, Ju-Lee Oei, Im Quah-Smith Azanna A. Kamar, Alexis A.D. Lordudass, Djien Liem, Kwee Bee Lindrea, Mary Daly, Nilima Dunker, Avneet K. Mangat, Georg M. Schmölzer

Introduction:
Auricular acupuncture may decrease pain from common procedures like heel pricks in newborn infants but its effects on longer and more stressful stressors such eye examinations for retinopathy of prematurity (ROP), are uncertain. We aimed to evaluate the efficacy of magnetic auricular acupuncture (MAA) to decrease discomfort related to ROP examinations in preterm infants.

Methods:
Multicentre randomised controlled trial at three sites (Australia, Canada, and Malaysia). Infants were eligible for the study if they were >32 weeks corrected gestation, required an ROP examination and not sedated, and parental consent. A total of 132 infants were randomized to MAA (n = 64) or placebo (P, N=68). MAA stickers or placebo were placed on both ears by an unblinded investigator. Pain was assessed by blinded clinical staff with the Premature Infant Pain Profile or the Neonatal Pain Agitation Sedation Scale, which were then transformed into Z-scores for analysis.

Findings:
Infants were of similar gestation (standard deviation (SD): MAA: 28 (3) v P:27± 2 weeks), birthweight (MAA:1014 (296), P:952 (273)g) and postnatal age (MAA:7 (3) P:7 (3) weeks) at randomization. Z-scores for pain before (MAA:-0.6 (0.4), P:-0.7 (0.4)) and during (MAA:1.1 (0.8), P:1. (0.7)) ROP examinations were similar between groups but were significantly lower 1 hour post procedure in MAA infants (MAA:-0.7 (0.3, P:-0.4 (0.4)).* MAA was associated with significantly lower pain z-scores (Odds Ratio 4.03 (95% Confidence Interval, 1.05-15.54), p=0.04) after accounting for confounders (age, gestation, gender). Heart rates were also significantly lower in the MAA group during ROP examination (MAA:172 (22), P:184 (18) bpm.* No adverse events were noted.

Conclusion:
MAA may reduce physiological pain responses in infants during and after more prolonged stressful procedures such as ROP examination. Assessment of long-term effects are warranted.

*p<0.001
ABSTRACT – 2020 PEDIATRIC RESEARCH DAY, MAY 13, 2020 – EDMONTON, AB
SHIM, GYU-HONG (NEONATAL-PERINATAL CARE-NICU)

Effects of sustained inflation pressure during neonatal cardiopulmonary resuscitation of asphyxiated piglets
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Introduction:
Sustained inflation (SI) during chest compression (CC = CC+SI) significantly reduces time to return of spontaneous circulation (ROSC) compared to 3:1 compression-to-ventilation ratio in asphyxiated newborn piglets. However, the optimal peak inflation pressure (PIP) of SI during CC+SI to improve ROSC and hemodynamic recovery in severely asphyxiated piglets is unknown. To examine if different PIPs of SI during CC+SI will improve ROSC and hemodynamic recovery in severely asphyxiated piglets.

Methods:
Twenty-nine newborn piglets (1-3 days old) were anesthetized, intubated, instrumented and exposed to 30-min normocapnic hypoxia followed by asphyxia. Piglets were randomized into four groups: CC+SI with a PIP of 10 cmH2O (CC+SI_PIP_10, n=8), a PIP of 20 cmH2O (CC+SI_PIP_20, n=8), a PIP of 30 cmH2O (CC+SI_PIP_30, n=8), and a sham-operated control group (n=5). Heart rate, arterial blood pressure, carotid blood flow, cerebral oxygenation, and respiratory parameters were continuously recorded throughout the experiment.

Results:
Baseline parameters were similar between all groups. There was no difference in asphyxiation (duration and degree) between intervention groups. PIP correlated positively with tidal volume (VT) and inversely with exhaled CO2 during cardiopulmonary resuscitation. Time to ROSC and rate of ROSC were similar between piglets resuscitated with CC+SI_PIP_10, CC+SI_PIP_20, and CC+SI_PIP_30 cmH2O: median (IQR) 75 (63-193) sec, 94 (78-210) sec, and 85 (70-90) sec; 5/8 (63%), 7/8 (88%), and 3/8 (38%) (p=0.56 and p=0.12, respectively). All piglets that achieved ROSC survived to four hours post-resuscitation. Piglets resuscitated with CC+SI_PIP_30 cmH2O exhibited increased concentrations of pro-inflammatory cytokines interleukin-1β and tumour necrosis factor-α in the frontoparietal cerebral cortex (both p<0.05 vs. sham-operated controls).

Conclusions:
In asphyxiated term newborn piglets resuscitated by CC+SI, the use of different PIPs resulted in similar time to ROSC, but PIP at 30 cmH2O showed a larger VT delivery, lower exhaled CO2 and increased tissue inflammatory markers in the brain.

KEY WORDS: Newborn, Neonatal resuscitation, Chest compression, Sustained inflation, asphyxia
Does time of birth affect healthcare providers perceived workload during neonatal resuscitation?
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Background:
Adverse neonatal outcomes are more likely in infants delivered during evening and night shifts than day shifts even when adjusted for numerous potential confounds1–3. Excess workload in healthcare providers has been associated with medical errors4,5. We aim to determine if the perceived workload of healthcare providers during neonatal resuscitation is affected by the time of the day.

Methods:
Perceived workload was measured using the multi-dimensional National Aeronautics and Space Administration Task Load Index survey6. Mental demand, physical demand, temporal demand, performance, effort, and frustration are all captured with each category rated independently by participants on a scale of 0-20 (0 being lowest or best and 20 being highest or worse depending on the dimension). The Raw-TLX score is the overall workload score, which was calculated for each survey response as the mean of dimension scores multiplied by five to transform this score to a value out of 100. Over three-months, healthcare provider at the Royal Alexandra Hospital, Edmonton, AB were asked to complete a survey following their participation in a neonatal resuscitation in the delivery room. This unit is a level three center. Surveys also collected basic demographic data and information about the resuscitation including healthcare providers’ reports time of delivery. Delivery times were divided into day shift (7:00-18:59) and night shift (19:00-6:59). The 5-minute Apgar scores were divided into three groups (7-10-high Apgar score group; 4-6-medium Apgar score group; 0-3-low Apgar score group). The data are presented as mean (SD) for normally distributed continuous variables and median (IQR) when the distribution was skewed. The Raw-TLX scores were compared by time of delivery using the Wilcoxon Rank Sum test. The Raw-TLX scores were compared by time of delivery within 5-minute Apgar groups using Analysis of Variance with repeated measures and Bonferroni post-test. P-values are 2-sided and p<0.05 was considered significant.

Results:
A total of 204 surveys were completed. The overall Raw-TLX was 34(18-49). Raw-TLX was similar during day 34(18-49) vs. night 35(24-48) shifts (p=0.7561). Raw-TLX was similar between day vs. night shifts in the low (55(15) vs. 51(8), p= 0.559), medium (49(12) vs. 36(-), p=0.334) and high (30(19) vs. 32(17), p=0.624) 5-minute Apgar groups.

Conclusion
Perceived workload of neonatal healthcare providers did not differ during neonatal resuscitation when occurred either during their day or night shift. Future studies assessing the differences between day and nighttime neonatal resuscitations are warranted.

References, next page
References
Developmental Changes in Intestinal and Renal Phosphate Handling
Tate MacDonald, Megan Beggs, Todd Alexander

Introduction:
Phosphate (Pi) is a multivalent ion that is critical for a myriad of physiological phenomena. One such phenomenon is bone mineralization, where Pi and calcium form the hydroxyapatite salt that confers bone integrity. Bone mineralization occurs rapidly in the neonate relative to older children and adults. It is hypothesized that increased Pi absorption from the intestine and Pi reabsorption in the kidney occur in the neonate to ensure adequate blood [Pi] to optimize bone deposition. However, the molecular details of these alterations are incompletely understood. We therefore set out to characterize functional and molecular changes in Pi homeostasis across development.

Methods:
Mice aged 1, 7 and 14 days, as well as 1, 2, 3 and 6 months (P1-P6mo) were euthanized and their intestine, kidneys, blood and urine were collected. Real-time PCR was performed to determine mRNA abundance for genes coding for secondary active Pi transporters in the duodenum, jejunum, ileum and kidney. Immunoblotting was performed on these tissues to determine protein expression levels of Pi transporters. Blood and urine Pi and creatinine concentration were measured to calculate fractional excretion of Pi by the kidneys as a function of age. Mice aged 7-10 days and 2 months were euthanized and their duodenal, jejunal and ileal tissues isolated to measure radiolabeled phosphate (P-33) flux and paracellular Pi permeability in Ussing chambers.

Results:
Phosphate transporter expression in the small bowel (specifically NaPi2b, Pit1/2) was found to decline with age. Expression of secondary active Pi transporters in the kidney (specifically, NaPi2a/c) was found to increase between P1 and P14, followed by an age-dependent decrease in expression. Fractional Pi excretion was found to increase with age. P-33 flux and paracellular Pi permeability displayed age-dependent decreases. Expression of Claudin-4, a tight junction protein postulated to confer paracellular Pi conductance, displayed its highest expression at P7 in the duodenum and jejunum, with no developmental trend in the ileum. Claudin-12, a paracellular Pi blocker, displayed its highest expression at P7, P14 in the jejunum with no developmental trend in the duodenum or ileum.

Conclusions:
Neonates demonstrate physiological adaptations that optimize absorption and renal reabsorption of Pi so as to maintain a positive Pi balance. Maintenance of a positive Pi balance likely enables rapid bone mineralization during mammalian development.
ABSTRACT – 2020 PEDIATRIC RESEARCH DAY, MAY 13, 2020 – EDMONTON, AB
LADAK, ZEENAT (NEUROLOGY)

A Therapy to Prevent Neurodevelopmental Disabilities: Protection of Brain Cells by Sulforaphane
Zeenat Ladak1, Jenny Yoon, Elizabeth Garcia, Edward A Armstrong, Jerome Y Yager*, Sujata Persad*.
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Introduction:
Over 80% of perinatal brain injuries lead to neurodevelopmental disabilities. Therefore, preventive approaches are needed. One major factor is placental insufficiency which results in hypoxic-ischemic environment in-utero. Sulforaphane (SFA), derived from cruciferous vegetables, is a phase-II enzyme inducer that enhances anti-oxidant enzymes production. The aim of this study is to explore how SFA affects different brain cell types and the dosing range of SFA for protection/toxicity in normal and oxygen/glucose deprived (OGD) cell cultures.

Methodology:
We used primary cortical neuronal, astrocyte, and combined cell cultures (co-cultures) from newborn rodents. Cell culture characterization was determined by immunofluorescence (IF). Cultures were exposed to OGD until 50% cell death (LD50) was achieved; this was analyzed by a LiveDead Assay using IF/high-content microscopy, and also represented through Western Blots (WB) and Densitometry analysis. We exposed cultures at LD50 to varying doses of SFA. Controls were not exposed to OGD. Effect of SFA at LD50 was assessed by Live/Dead assay. Effect of SFA in control cultures was assessed by Alamar blue. One Way ANOVA and Dunette's Multiple Comparison were used for statistics.

Results:
Primary cortical neuronal, astroglial, and co-cultures have been established. Using IF for cell specific markers, we show: neuronal cultures with minimal contamination of astrocytes and microglia; astrocyte cultures with minimal contamination of neurons and microglia. The co-cultures showed markers for all cell types. We determined the LD50 to be 2 hours for neurons, 8 hours for astrocytes, and 10 hours for co-cultures. At LD50, SFA was significantly protective at 2.5uM for co-cultures (p<0.01), and a similar trend is seen in neuron and astrocyte cultures. Significant toxicity of SFA at LD50 was seen at doses ≥100uM (p<0.01) for astrocytes, and ≥25uM (p<0.01) for co-cultures. Significant toxicity of SFA in control cultures was seen at doses ≥100uM (p<0.01) for neurons, and ≥50uM (p<0.01) for both astrocytes and co-cultures.

Conclusion:
These findings suggest that SFA shows promise as a preventative agent for fetal ischemic brain injury and that dosing parameters are required for safety. Future studies will determine the safety/efficacy of SFA in a rat animal model of placental insufficiency, and work towards converting a safe/effective dose of SFA in an animal model to clinical practice.
ABSTRACT – 2020 PEDIATRIC RESEARCH DAY, MAY 13, 2020 – EDMONTON, AB
LUAN, KAILIE (NEUROLOGY)

Midline Epileptic Discharges and Seizures in Pediatric Epilepsy: Case Series and Review
Kailie Luan MD; Janani Kassiri MD, PhD; David Barry Sinclair MD

Introduction:
Pediatric medically intractable epilepsy accounts for approximately 10-30% of pediatric epilepsy. It can be a major problem, leading to recurrent seizures and severe long-term consequences of the developing brain. Epileptic discharges localized to the midline vertex are rare in pediatric epilepsy and not well understood. Previous studies have suggested that seizure onset often occurs within the first ten years of life with abnormal neuroimaging studies in 30-40% percent of patients. However, the electroclinical correlation, pathological findings underlying the epileptogenic zone, and long-term outcomes of children with midline seizures have not been adequately described. The objective of our study was to understand the etiology of midline epileptic discharges using radiological and clinical features, and to define post-surgical seizure outcomes in these patients.

Methods:
In our study we reviewed clinical charts, electroencephalography (EEG) records, and neuroimaging studies of seven pediatric patients with epileptic discharges localized to the midline vertex (Fz, Cz, Pz) on EEG at the University of Alberta's Comprehensive Epilepsy Program. The seizures were classified according to the International League Against Epilepsy criteria and semiology. Patient demographics, age, sex, seizure types, etiology of seizures, Magnetic Resonance Imaging results reported by a neuroradiologist, underlying and/or coexisting neurological diagnosis, additional presenting clinical signs and symptoms and, seizure outcomes in these patients were obtained.

Results:
Simple partial and complex partial seizures were the most prevalent seizure types experienced by six out of seven patients with midline discharges. Age of seizure onset was within the first 10 years of life in 85% of these patients. Heterogenous radiological and pathological etiologies were found in children with midline seizures with focal cortical dysplasia (FCD) type II being the most common. These patients often had normal neuroimaging studies and medically intractable epilepsy. However, seizure freedom was achieved following surgical resection of the epileptogenic zone in these patients.

Conclusions:
In this small case series we demonstrated that patients with midline epileptic discharges on EEG are associated with intractable focal seizures and early seizure onset. However, neuroimaging studies are typically reported as normal in these patients. Surgery may be beneficial for seizure control in children with midline discharges as the most common pathology found in our study was FCD. Thus these results have the potential to help localize midline epileptic discharges early on, define the epileptogenic zone for surgical resection, and achieve seizure freedom and favorable neurological outcomes in children with this electroclinical syndrome.
White Matter Alterations in the Neurolimbic Pain System in Pediatric and Young Adult Chronic Migraine
Mella A, Treit S, Linsdell M, Rajapske T, Beaulieu C, Richer L

Introduction:
Structural changes in pain processing pathways have been observed particularly within tracts of the limbic system of adult patients with migraines using diffusion tensor imaging (DTI) which examines the restricted diffusion of water. We used DTI to examine the limbic white matter tracts including the cingulum, uncinate fasciculus (UF) and inferior longitudinal fasciculus (ILF) in adolescents or young adults with chronic migraine compared with normal controls to examine if these changes are present at younger ages.

Methods:
The cohort included 15 chronic migraine patients (PCM) (17.8 ± 2.0 years, 14 female) and 25 controls (17.7 ± 2.5 years, 23 female). Deterministic tractography was used and the analyst was blinded to the group allocation. Diffusion values of fractional anisotropy (FA), mean diffusivity (MD) and tract volume in each of the three tracts in the left and right sides of the brain were determined.

Results:
No significant differences were found between the PCM and control group in comparing FA, MD or tract volume in the cingulum, UF and ILF when using Bonferroni corrected p-values of 0.001. Measures of variability (e.g. range and standard deviation) were comparable between groups indicating a relatively homogenous population. There was no significant correlation between age or migraine disability (i.e. PedMIDAS) on tract measurements. Lateralization in the tract volumes was observed in both groups. The difference in tract volumes between hemispheres was significantly greater in the cingulum tract volume of the PCM group (-0.103, 95% CI -0.149 - -0.056 vs -0.065, 95% CI -0.117 - -0.013). For the UF volume, both control and PCM groups differed significantly and in ILF the control group differed hemispherically. Similar differences were also observed in the FA and MD of the cingulum and MD of the ILF.

Conclusion:
The previously reported changes in neural tracts involved in pain processing in adult migraineurs were not observed in our younger cohort of chronic migraine patients. Age or duration of exposure to migraines may play a role in brain structural changes. We observed significant lateralization between hemispheres within the cingulum, uncinate fasciculus, and inferior longitudinal fasciculus that was more prominent in the chronic migraine cohort which has not previously been reported.
Acute Flaccid Myelitis: A Canadian Retrospective Cohort
Dr. Risa Namsechi, Dr. Colin Wilbur, and Dr. Janani Kassiri

Introduction:
Children presenting with an acute weakness or one or more limbs in the context of a recent viral illness with T2 bright signal in the grey matter of the spinal cord are diagnosed with Acute Flaccid Myelitis (AFM). It has been associated with recent outbreaks of Enterovirus D68 and A71 in North America, resulting in the Centers for Disease Control and Prevention (CDC) creating a case definition to track its prevalence.

Methods:
We reviewed the pediatric neurology inpatient and consult patient list from January 2018 to December 2019 for cases of diagnosed AFM, meeting the CDC case definition. 5 patients were identified and a retrospective chart review was performed. Their presentation, work-up, management and outcome is outlined.

Results:
We have observed 5 patients over a 2 year period with a clinical diagnosis of AFM including subacute onset of flaccid weakness of one or more limbs with characteristic imaging findings. There was varying degrees of severity of presentation among the patients. One patient had a severe course with bilateral upper extremity and cervical weakness, and progressed to respiratory and brainstem involvement, requiring a prolonged stay in ICU. Three other patients had an initial presentation of monoplegia, and one presented with asymmetric lower extremity paraplegia. Two patients were treated with pulse steroids alone, one was treated with pulse steroids and plasma exchange, and one received no treatment. All patients had some residual weakness at time of discharge. All five patients were newly diagnosed or seen in follow up at the Stollery Children’s Hospital by Pediatric Neurology within a 2 year period, although, one patient had their diagnosis made years earlier in China during an early outbreak of Enterovirus A71.

Conclusions:
AFM is a modern day polio-like paralytic illness with limited response to immunomodulatory treatments and often resulting in long term deficits in its survivors. In our cohort of pediatric patients, diagnosed and followed at the Stollery Children’s Hospital over a 2 year period, all patients had persistent weakness at time of discharge. In our cohort, the severity of initial presentation was predictive of length of hospitalization and long term disability. In addition to the risk of contagion associated with these viruses, early identification of this disease is important as management and prognosis differs compared to other inflammatory and post-infectious causes of weakness.
Nanoparticles for targeted drug delivery in neonatal hypoxic ischemic brain injury
Rukhmani Narayanamurthy, Jung-Lynn Yang, Ed Armstrong, Jerome Yager, Larry D Unsworth

Introduction:
Neonatal hypoxic ischemic (HI) injury, resulting from oxygen and nutrient deprivation due to obstructed blood flow to the brain, is most commonly associated with mortality or lifelong sensory deficits and motor disabilities. The only licensed treatment available to inhibit the extent of damage is the therapeutic cooling of the head or whole body of the infant. Although its effectiveness is limited when administered alone, it may be more beneficial in conjunction with pharmacological agents. Therefore, our objective is to design a drug delivery system using nanoparticles composed of elastin-like polypeptides which can release drugs at the site of damage in response to local changes in pH post injury (acidosis) and externally applied cooling. This would facilitate targeted and controlled drug release and prevent its non-specific distribution, thereby minimizing potential side effects.

Methods:
Elastin-like polypeptides with different amino acid compositions were expressed in E.coli using recombinant DNA technology. The purified peptides were then combined with sildenafil at varying concentrations. Self-assembly and dis-assembly of the drug encapsulated nanoparticles were analyzed at different pH and temperature values using dynamic light scattering. Basal release and pH-induced release kinetics of sildenafil was quantified in vitro. A P7 rat was placed inside a “cooling chamber” such that its head portion is cooled by circulating water at a steady state temperature of 28°C to induce hypothermia. A solution containing elastin-like polypeptides and sildenafil was injected into the rat, to assess the efficacy of the drug release by the nanoparticle, in vivo.

Outcomes:
Nanoparticle formation at the desired temperature of 37°C and pH 7.4 was observed. Sildenafil encapsulation within the nanoparticle was successful with effective drug release at low temperature and pH. External cooling was applied using the cooling chamber unit and a notable decrease in temperature of the head was observed demonstrating the induction of hypothermia.

Conclusion: The nanoparticle-sildenafil treatment is expected to improve the therapeutic effect of hypothermia by increasing blood flow to the damaged tissue in the brain, to rescue the cells that are ‘at-risk’ of dying. This would in turn prevent exacerbation of injury post HI insult and protect the affected infant from susceptibility to neurodevelopmental disorders. Thus, elastin-like polypeptides is a promising class of bio-materials for the transport and release of drugs in response to environmental cues.
The Pediatric Neuroirritability Management Protocol at the Stollery Children’s Hospital – Inspired by an Irritable Infant with GM3 Synthase Deficiency

Introduction:
We describe an infant with a diagnosis of GM3 synthase deficiency, presenting with severe neuroirritability from birth. He required multiple admissions due to extreme agitation and caregiver burnout. Multiple pharmacological agents were tried, and the effect of each medication was modest and short-lasting at best. The literature on the management of neuroirritability in children with progressive genetic and metabolic conditions is sparse, and a neuroirritability management protocol has yet to be developed at our institution.

Methods:
We searched for relevant primary research and articles on PubMed. We reviewed the evidence of each pharmacological agent and added non-pharmacological strategies. We developed management guidelines for neuroirritability at our hospital. This protocol was reviewed by several pediatric neurologists and pediatric palliative care specialists at the Stollery and SickKids Hospitals.

Results and Conclusion
We present the Pediatric Neuroirritability Management Protocol for the Stollery Children’s Hospital. Further study is required to assess whether this protocol can be adapted to treat irritability in the context of other neurological conditions such as hypoxic-ischemic encephalopathy and non-accidental injury. In addition, we will expand our guidelines to include other symptoms such as spasticity, dystonia, and autonomic dysfunction.
Managing children with acute bronchiolitis: a systematic review and network meta-analysis
Sarah Elliott, Lindsay A. Gaudet, Ricardo Fernandes, Ben Vandermeer, Lisa Hartling

Background:
In Canada over 35/1000 children under one year of age are hospitalized annually with bronchiolitis, with estimated yearly costs of over $23 million. Uncertainty exists as to which treatment is most effective, with considerable practice variation within and across healthcare sites. To address this, we conducted a systematic review and network meta-analysis (NMA) to evaluate the comparative effectiveness of the most commonly used treatments for managing bronchiolitis among children less than 2 years.

Methods:
We included a range of interventions: bronchodilators, glucocorticoid steroids, hypertonic saline solution, antibiotics, heliox therapy and high flow oxygen therapy. Search results from four primary literature databases, two clinical trial registries and relevant conference proceedings were screened based on a priori inclusion criteria. Data were extracted and independently verified. Cochrane Risk of Bias tool was used to assess risk of bias in individual studies. The primary outcomes were admission rates and hospital length of stay. Frequentist NMA estimated mean differences (MD) with 95% confidence intervals (CI) of each treatment compared to nebulised placebo. Treatment effectiveness was ranked based on the Surface Under the Cumulative Ranking curve (SUCRA).

Results:
150 studies were included; 27 studies (4656 patients) reported relevant data for admission rates while 57 studies (7605 patients) provided data for length of hospital stay. For admission rates, nebulised epinephrine (OR: 0.64, 95% CI: 0.44 to 0.93) and nebulised hypertonic saline plus salbutamol (OR: 0.44, 95% CI: 0.23 to 0.84) were both more effective than nebulised placebo (i.e., 0.9% saline); no other treatments significantly affected admission rate. Hypertonic saline plus salbutamol was ranked as the most effective treatment, and was significantly more effective than nebulised salbutamol alone (OR: 0.55, 95% CI: 0.33 to 0.91). For length of hospital stay, nebulized hypertonic saline (MD: -0.64, 95% CI: -1.01 to -0.26) and nebulized hypertonic saline plus epinephrine (MD: -0.91, 95% CI: -1.14 to -0.40) were effective compared to nebulised placebo (i.e., nebulised 0.9% saline). Nebulised hypertonic saline plus epinephrine was the first ranked treatment.

Conclusion:
The is the most comprehensive systematic review to date, examining comparative effectiveness across a wide range of commonly used interventions. Evidence shows the effectiveness and superiority of hypertonic saline with salbutamol to reduce admission rates. Nebulised hypertonic saline alone, or in combination with epinephrine seems beneficial to reduce length of hospital stay. Understanding the most appropriate management for bronchiolitis has the potential to mitigate inappropriate healthcare utilisation and reduce costs to the healthcare system.
Actually, it is easy being green: 10 years of CPS meetings viewed through a sustainability lens

P.M. Hicks, A. Hicks

Introduction:
The Canadian Pediatric Society (CPS) recently released the “Global climate change and health of Canadian Children” statement. As climate rapidly evolves from “change” to “crisis” there is increasing pressure toward sustainable conferencing. Knowing the value of meetings, the growing body of literature evaluating travel-related carbon and convention sustainability informs harm minimization. This project evaluates the past 10 CPS annual general meetings through a sustainability lens.

Methods:
Travel-related carbon cost was estimated using a round-trip calculator for most direct available flights. Attendee origins were estimated using 11 CaRMS-matched Pediatric training programs. Venues were evaluated based on current available self-reported information using sustainability criteria suggested through a literature review and public rating tools (Green Key, Quality Standards of the International Association of Convention Centres).

Results:
The last 10 CPS were held in western (3), eastern (1) and central (6) provinces; 2020 is in Vancouver. Average air travel-related carbon cost ranged from 0.479 (London) to 0.919 (Vancouver) tonnes, with Ontario and Quebec sites averaging 0.518, Charlottetown 0.654 and Edmonton 0.756 tonnes. Ground transportation, scored by public transport from airport (1), formal shared transport (1), fee deterrence for parking (1), differed by city from Montreal (3/3) to London (0/3). Venues differed between hotel with meeting facilities (H) vs standalone conference center (CC), with CC outranking H for clear, posted sustainability plans (1.6 vs 1.2/2; 2=venue-specific, 1=company chain policy, 0=no plan), sustainable community building plan (1.6 vs 1.2/2; 2=greening local communities, 1=company chain policy, 0=no plan) and waste management (1.2 vs 0/2; 2=venue-specific, 1=company chain policy, 0=no plan). Walkable accommodation was equal for all venues.

Conclusion:
Over the last 10 years the CPS selected conference venues that reflect equitable distribution across Canadian geography and training sites. Central Canada sites have the lowest air travel carbon cost per attendee. Host city ground transportation is more sustainable in larger cities. Venues were evenly split between CC and H, with CC having more sustainable practices through increased local supports and rentals to events and exhibitors and better posting of sustainability practices. Conferences can pressure venues to increase sustainability by choosing wisely and communicating their requirements to rejected sites and offer carbon offset purchase through credible companies (e.g. Gold Standard). Pediatricians should consider climate change and sustainability when attending events.
Exploring the Gut-Brain Axis: Associations Between Maternal Prenatal Depression, Infant Colonization with *C. difficile*, and Child Neurodevelopment


Introduction:
The incidence of infants colonized with *Clostridioides difficile* (*C. difficile*) is on the rise. Although testing is not recommended as infants appear to be asymptomatic, those that are colonized with this pathogen have an increased risk for allergies and atopy with a suggested mechanism through inflammation. This study aimed to examine the impact of maternal prenatal depression on the colonization of *C. difficile* in infants at 3-4 months of age. With increasing evidence of the negative impact of inflammation on the central nervous system, our secondary objective was to explore whether *C. difficile* colonization is a mediator on infant neurodevelopment at 1 year of age.

Methods:
The primary objective used a substudy of 1,500 term infants and the second objective used 550 term infants from the CHILD Cohort Study. Maternal reports were used to measure prenatal depression and feeding method. Birth mode was retrieved from hospital records. Fecal samples were collected at 3 months after home assessment. Analysis of *C. difficile* was performed using quantitative polymerase chain reaction (qPCR) with appropriate primers. Cognitive neurodevelopment scores were assessed using the Bayley Scales of Infant Development administered by education psychologists at 1 year of age. Linear and logistic regressions were used to examine the direct associations among maternal prenatal depression, infant *C. difficile* colonization, and cognitive scores. Structured equation modelling was used to conduct the mediation analysis.

Results:
In our sample, one-third (31%) of the infants were colonized with *C. difficile* at three months of age. During their third trimester of pregnancy, 24% of mothers reported clinically significant depressive symptoms. Prenatal depression significantly increased the odds of *C. difficile* colonization in the infant (Odds Ratio [OR]=1.44, 95%[CI]= 1.11, 1.85; p=0.006), adjusted for birth mode and breastfeeding status. Colonization of *C. difficile* in infants at 3-4 months of age was associated with significantly lower cognitive scores at 1 year of age (Beta= -2.31, 95%[CI]= -4.18, -0.45; p=0.015), with limited adjustments. The relationship between maternal prenatal depression on cognitive scores was not mediated by *C. difficile* (Beta=-0.22, 95%[CI]= (-0.49)-(0.047), p=0.105).

Conclusions:
At 3-4 months of age, infants of mothers who experienced prenatal depression had significantly increased risk of *C. difficile* colonization in their gut. Infants colonized with this pathogen at 3-4 months of age had significantly lower cognitive neurodevelopment scores. Our findings further suggest that maternal mood may contribute to alterations in early infant microbiome, which may have implications for the developing infant brain.
Harm Mitigation for Unintentional Tobacco Exposure in Children
Caseng Zhang, Alex Hicks, Alvaro Osornio-Vargas, Lesley Brennan, Matt Hicks, Anne Hicks

Introduction:
Despite published guidelines outlining health risks associated with tobacco smoke, young children are continually exposed to the detrimental effects of household smoking. Factors like comfort and environment can influence parents to smoke indoors, increasing exposure for children. This project compared location of reported tobacco use to detection of nicotine byproduct cotinine in child urine samples. Understanding this correlation can inform harm reduction strategies for smokers. This study’s primary objective is to determine the impact of smoking location on unintentional tobacco exposure in children. The secondary objective is to determine the impact of climate on the location of tobacco use in households.

Methods:
This prospective cross-sectional study focused on children under age ten, since 13% of Canadian children in grades 6 and up have tried a cigarette at least once. Of 286 parents approached during a pediatrician visit, 231 agreed to complete an exposure questionnaire and 132 children provided a urine sample. A standard ELISA assay was used to measure urine cotinine.

Results:
About half of the 31% of households that reported smoking had indoor smoking bans. In homes that reported smoking, the number of smokers in the household ranged from 1 to 10. Some indoor smokers isolated their activity to the garage (56%). Of the 84 children with detectable urine cotinine, 62 lived in homes that reported smoking. This suggests some children were exposed to tobacco smoke through other sources or underestimation of potential tobacco exposure. 15% of children from smoking homes had cotinine levels similar to nonsmoking homes. Children of indoor smokers were more likely to have detectable cotinine than those of outdoor smokers. There was no significant difference between the percentage of people who reported smoking indoors versus outdoors regardless of winter or summer climate. This suggests that location based smoking behaviour is not substantially affected by environmental conditions.

Conclusions:
Roughly 50% of smokers with children have an indoor smoking ban as a harm reduction strategy. In our study, children of smokers with an indoor smoking ban were less likely to have detectable urine cotinine. Although not smoking is the best strategy, limiting smoking to outside is an optimal harm mitigation strategy. For families with indoor smokers, encouraging them to isolate smoking to a single space like the garage may decrease unintentional pediatric tobacco exposure.
Prevalence and Predictors of Metabolically Healthy Obesity (MHO) in Children Enrolled in the CANadian Pediatric Weight management Registry (CANPWR): A Cross-Sectional Study

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Introduction:
In 2018, we established a consensus-based definition of MHO by surveying international experts in the field of cardiometabolic health and obesity, and the current study represents the first application of this definition. Few studies have examined the relationship of the MHO status to lifestyle behaviours (e.g., dietary intake, sleep, screen time). These variables could help to distinguish between MHO and metabolically unhealthy obesity (MUO) phenotype, which has potential utility in offering targeted treatment approaches for each group. This study aimed to determine the prevalence of MHO using the new definition, and to examine demographic, anthropometric, and lifestyle variables as independent predictors of MHO in children with obesity.

Methods:
A cross-sectional analysis was conducted using baseline data of 2–17 year-olds with a body mass index ≥85th percentile who were enrolled in the CANPWR. Those with MHO had normal levels of cardiometabolic risk factors, including triglycerides, high-density lipoprotein cholesterol, blood pressure and fasting glucose. Multivariable logistic regression was used to determine predictors of MHO using odds ratios with 95% confidence intervals.

Results:
In total, 945 children were included in the study (mean age: 12.3 +/- 3.3 years; 51% female). Overall, the prevalence of MHO was 31% (n=297), and it decreased across increasing age groups (2-5 years old [n=18; 43%], 6-11 years old [n=127; 35%], 12-17 years old [n=152; 28%]). Children with MHO were younger, shorter, lighter, and less overweight than their peers with MUO. Physical activity (OR: 1.180, 95% CI: 1.007-1.383), and intakes of skim milk (OR: 1.095, 95% CI: 1.008-1.190), and fruit (OR: 1.121, 95% CI: 1.017-1.235) were positive predictors of MHO. BMI z-score (OR: 0.689, 95% CI: 0.599-0.793), screen time (OR: 0.792, 96% CI: 0.681-0.921), and intake of fruit flavoured drinks (OR: 0.913, 95% CI: 0.837-0.996) were negatively associated with the MHO status.

Conclusions:
Thirty-one percent of children were classified as MHO by using the new MHO definition, and they were less overweight and had more favorable lifestyle characteristics than their MUO peers.
Experiences of Faculty Members Giving Negative Feedback to Medical Trainees in a Clinical Setting

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Introduction:
Imperative to medical training is the observation and provision of feedback. In this era of competency-based medical education, feedback is one of the core components of this new model. A better understanding of medical faculty’s attitudes and experiences to providing negative feedback is essential. Currently, there are no in-depth qualitative studies that have explored the attitudes and experiences of faculty members when they give negative feedback to medical trainees.

Methods:
In order to allow an in-depth exploration of this phenomenon a hermeneutics phenomenology approach was used. We conducted semi-structured interviews with ten faculty members representing 6 disciplines and used thematic analysis to create data-driven codes and identify key themes through an iterative consensus building process.

Results:
Four main themes were identified by the authors. 1) Elements of effective feedback, 2) Faculty members’ perception of giving negative feedback, 3) Challenges as it relates to the culture of giving negative feedback, and 4) Providing effective negative feedback as a mutual process focused on relationship building between learners and preceptors.

Conclusions:
By exploring faculty members’ perceptions of providing negative feedback, we identified actionable recommendations based on the study participants’ experiences, expectations and challenges that could be addressed with future faculty development focusing on modifying concepts of feedback and institutional changes that will promote an attitudinal and a cultural shift.
Coming soon - reporting guideline for overviews of reviews of healthcare interventions! Preferred Reporting Items for Overviews of Reviews (PRIOR)

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Introduction:
Overviews of reviews of healthcare interventions (overviews) compile information from multiple systematic reviews to provide a single synthesis of relevant evidence. There are currently no systematically developed reporting guidelines for overviews. As a result, published overviews are often incomplete and lacking in transparency. We are using explicit, systematic, and transparent methods to develop an evidence-based and agreement-based reporting guideline for overviews of healthcare interventions: Preferred Reporting Items for Overviews of Reviews (PRIOR).

Methods:
We are developing the PRIOR reporting guideline in four stages, using established methods. We are developing an original stand-alone guideline that will allow us to focus on the challenges that are unique to the reporting of overviews and facilitate future guideline extensions. First, in December 2018 we launched the project and established an international and multidisciplinary expert advisory board who have been overseeing the conduct of the project and providing methodological support. Second, we conducted comprehensive literature reviews (scoping review of methods guidance for overviews; descriptive review of the reporting characteristics of published overviews) that were used to inform a list of prospective checklist items. Third, we are currently using a 3-round modified Delphi exercise to achieve high level of expert agreement on the list of items to be included in the PRIOR reporting guideline. We aimed to recruit up to 100 international experts (editors, authors, peer reviewers, and end-users of published overviews such as guideline developers, policymakers, patients and consumers) to participate in the Delphi process. The first two rounds will occur via online survey. The third round will occur during a smaller (~8 to 10 participants) in-person meeting following the 2020 Cochrane Colloquium. Fourth, after reaching agreement on the included items, we will produce and disseminate the PRIOR reporting guideline.

Conclusions:
A systematically developed reporting guideline specific to overviews will help to support the high quality and clarity of reporting that is needed to substantiate overviews as a robust source of evidence related to healthcare interventions. By holding overviews to a minimum standard of reporting, we expect PRIOR to enhance the translation of otherwise overwhelming volumes of literature into accurate, complete, and transparent syntheses for use by healthcare decision-makers.