PEDIATRIC RESEARCH DAY

2019 ORAL AND POSTER ABSTRACTS

UNIVERSITY OF ALBERTA
FACULTY OF MEDICINE & DENTISTRY
Department of Pediatrics
2019 Pediatric Research Day May 15, 2019 – Edmonton, AB

Oral Session No. 1 - ABSTRACT

SKIP: Solutions for Kids in Pain
Ali S.

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 barriers and disjointed efforts. Canadian children subsequently suffer undertreated and preventable pain, leading to negative short- and long-term health outcomes for children and families and detrimental impacts on the healthcare system.

Methods: Solutions for Kids in Pain (SKIP) is a knowledge mobilization network, based at Dalhousie University (Dr. Christine Chambers, Halifax) and co-led by Children’s Healthcare Canada (formerly CAPHC), that seeks to bridge the gap between current treatment practices and available evidence-based solutions for children’s pain in Canadian health institutions. 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).

Results: Guided by a diverse and experienced governing Board, SKIP capitalizes on the engagement of: 48 Children’s Healthcare Canada member organizations, over 75 partners, 4 regional hubs, and patients and caregivers (using a “Patients Included” approach) to collaborate and co-produce interconnected knowledge mobilization activities. Pain clinicians, researchers, champions, and experts have joined forces to support this National Centres of Excellent (NCE)-funded initiative. The Stollery Children’s Hospital/ University of Alberta’s Department of Pediatrics will be the Western Canadian hub.

Expected Outcomes: SKIP will 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 and expectation for evidence-based pain management. SKIP’s long-term outcome is to improve children’s pain management in Canadian health institutions. Progress will be evaluated using a performance measurement system supervised by the Board. With the support of Canadian and international partners, SKIP will significantly impact pain management practices and position Canada as a global leader in knowledge mobilization for children’s pain.
Oral Session No. 1 - ABSTRACT

The IBDo’s and IBDon’t of dietary fibers in IBD: defining how microbes shape the path to diet-associated inflammation, and guide diet-based therapies.

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. ELISAs 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. These results were recapitulated in a cohort of pediatric IBD biopsy tissues cultured ex vivo, more so in more severe patients.

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.
Oral Session No. 1 - ABSTRACT

*Clostridioides difficile* colonization is differentially associated with gut microbiota composition in breastfed versus formula fed infants.


**Introduction:** Colonization with *Clostridioides difficile* occurs in up to half of infants under the age of 3 months and is strongly predicted by formula feeding. Although this microbe does not appear to pose any immediate risks for infants (colonization is largely asymptomatic), its presence has been associated with susceptibility to chronic disease later in childhood, perhaps by promoting changes in the gut microbiome including increased opportunity for colonization with pathogenic bacteria. We have explored these compositional changes in exclusively breastfed, partially breastfed and exclusively formula fed infants in order to examine the microbial community and *C. difficile* colonization in infants with distinct diets.

**Methods:** This descriptive study includes a sub-set of 1562 infants enrolled in the Canadian Healthy Infant Longitudinal Development (CHILD) general population birth cohort. Infants provided a fecal sample at 3-4 months of age (Mean: 3.56, SD: 1.00) which was analyzed using 16S rRNA sequencing and targeted qPCR for *C. difficile*. Mode of feeding was recorded by mothers in a questionnaire at a 3-month follow-up visit. *C. difficile* colonization was defined as positive detection (CD+) in the fecal sample (reference: *C. difficile* not present, CD-). Multivariate association with linear models (MaAslin) was used to determine changes in microbiota composition and FDR correction for multiple comparisons.

**Results:** The prevalence of *C. difficile* colonization among all infants was 30.9% (482/1562). These colonization rates differed between feeding groups: 22.6% of exclusively breastfed infants, 35.0% of partially breastfed infants and 49.6% of formula fed infants (p<0.001). Microbes of the genus *Bifidobacterium* were decreased in CD+ exclusively breastfed infants compared to non-carriers of the same diet (q=0.02). Additionally, *Blautia* and *Coprococcus* and *Clostridium* spp., of the Lachnospiraceae family, were of higher relative abundance (all q<0.01) in breastfed CD+ infants (both mixed and exclusive). In formula fed infants, *C. difficile* colonization was only associated with a lower relative abundance of Streptococcaceae and Gemellaceae (q<0.05).

**Conclusions:** *C. difficile* colonization may be associated with a dysbiotic gut microbiota composition in breastfed infants and these changes have previously been associated with childhood atopy and obesity.
Facilitating communication and health behaviour change among adolescents with obesity.

*Kebbe M, Perez A, Buchholz A, McHugh TLF, Scott SD, Richard C, Dyson MP, Ball GDC*

**Introduction:** Health care providers (HCPs) report barriers to communicate effectively with and support adolescents in weight management. They may benefit from clinical tools to complement their consultations. Since most adolescents with obesity do not meet minimum lifestyle recommendations, we developed *Conversation Cards for Adolescents* (CCAs), a clinical, bilingual tool to facilitate adolescent-HCP communication and help adolescents with lifestyle behaviour change. The purpose of this research is to describe the conceptualization, development, refinement, and production of CCAs.

**Methods:** Our research was completed between May 2016 and August 2018. It included three interrelated phases: (1) Conceptualization, (2) Development, and (3) Production and Knowledge Translation. Phase 1 included designing our study using cross-language and patient-oriented research principles (i.e., engaging Anglophone and Francophone adolescents as partners in research). Phase 2 comprised several sequential steps, including a scoping review, an in-person patient engagement panel, 1-on-1 interviews, focus groups, an online prioritization activity, and a telephone-based, data validation consultation with adolescents with obesity and HCPs from pediatric weight management clinics in Edmonton and Ottawa. Phase 3 included designing, refining, and producing CCAs in collaboration with Obesity Canada.

**Results:** We identified and prioritized 153 factors that help, may help, or deter adolescents with obesity from adopting healthy lifestyle behaviours. The top 15 priorities in each of these three categories were included in our tool (a hard-copy deck of cards) and were organized into the following suits: nutrition, physical activity, sedentariness, sleep, mental well-being, relationships, and clinical factors. Each card contains an individual statement pertaining to a barrier or enabler that adolescents encounter in making and maintaining healthy lifestyle changes (e.g., I have a hard time falling asleep because of my anxiety or nonstop thinking).

**Conclusions:** Our research generated a practical, evidence-based, bilingual tool for adolescents with obesity and HCPs to use during clinical consultations. Future steps include empirically evaluating CCAs’ feasibility and user experience in health care settings.
Oral Session No. 1 - ABSTRACT

Skeletal muscle-specific knock-out of succinyl-CoA:3-ketoacid-CoA transferase (SCOT) prevents the decline in cardiac function during heart failure.
Soni S, Byrne N, Levasseur J, Paramor J, Takahara S, Dyck J.

Introduction: The failing heart has defects in metabolic processes that normally allow for proper ATP production which is necessary to maintain contractile function. Recent studies have shown that the failing heart upregulates ketone metabolism and relies on ketones, namely β-hydroxybutyrate (βOHB), as a fuel, presumably to increase overall energy production. Ketones, also referred to as ketone bodies, and comprised of βOHB and acetoacetate, are most notably produced by the liver in conditions of low glucose, such as fasting. Furthermore, the oxygen sparing effects of βOHB are thought to be beneficial for the failing heart, alongside other beneficial signaling effects. Thus, regardless of the role that endogenous βOHB plays in heart failure (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 in HF.

Methods: To determine whether elevating circulating ketones may improve cardiac function in HF, we utilized a tamoxifen-inducible skeletal muscle-specific knockout of succinyl-CoA:3-ketoacid-CoA transferase (smSCOT-KO), the rate limiting enzyme in ketone catabolism. We then subjected these smSCOT-KO and wild-type littermate mice to transverse aortic constriction (TAC) surgery to generate pressure overload-induced HF. Echocardiography was used to assess heart function, and levels of circulating glucose and βOHB were also measured. Lastly, protein expression of SCOT was confirmed by immunoblot analysis.

Results: SCOT expression was significantly reduced in skeletal muscle of smSCOT-KO compared to wild-type mice to 5% and 4% in gastrocnemius and soleus, respectively (p<0.001); there were no appreciable changes in cardiac SCOT expression. Given that ketones are largely utilized in skeletal muscle, the smSCOT-KO results in a 1.5-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 (47% vs 32% ejection fraction; p=0.0042) and diastolic (E/E'; p=0.002) function in smSCOT-KO compared to wildtype littermates.

Conclusions: Together, these data are the first to show that smSCOT-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.
A team-based learning approach to promote clinical reasoning in a pediatric clerkship.
Forbes K, Foulds J.

Introduction: Clinical reasoning (CR) is the process clinicians use to arrive at an initial diagnosis and management plan, based on gathering and processing pertinent information obtained from a patient’s history, physical examination and investigations. Given the nature of cognitive processing, CR is inherently challenging to teach and assess in junior learners with limited clinical experiences. The key-feature question format (KFQs) is an approach to assessment that focuses on CR and decision making aspects of medical problems rather than knowledge recall. KFQs have been found to be valid and reliable means of testing CR in high-stakes medical licensing examinations including the Medical Council of Canada Qualifying Examination Part I.

Methods: Using KFQs in a team-based approach we developed a six-case, formative learning experience to assess CR of pediatric clerkship students. A team of pediatric educators developed six case scenarios and corresponding KFQs, with varied pediatric presentations, ages and clinical settings. KFQs included write-in (WI) and short menu (SM) formats. Students first completed the assessment individually (IRAT) using an online platform. Next, students repeated the assessment in small groups (GRAT), with opportunity to discuss and debate responses. Following GRAT completion, two faculty reviewed each scenario en masse, providing verbal feedback for submitted responses. Following the session students received emails with their individual and group scores.

Results: One hundred, forty-two (142) students participated in the formative assessment over a one-year period. Individual scores were not statistically different across the year. Group scores were higher than individual scores (paired t-test, p<0.001). Individual scores correlated with performance on end of rotation MCQ (Pearson’s r = 0.29, p<0.001) and OSCE (r= 0.51, p<0.00001). Internal reliability of the 20-item assessment was calculated with a Cronbach’s alpha of 0.503.

Conclusions: Assessment of clinical reasoning of pediatric cases was correlated with student overall performance on objective summative clerkship assessments. The low-stakes, team-based approach was valuable in providing students with discussion opportunity, evident by improvement in GRAT scores. Student feedback on the session was overwhelmingly positive, with students reporting value in the case content, the question structure and the opportunity to practice the format of KFQs in preparation for high-stakes assessments. Although time intensive to develop KFQs, the correlation with summative assessment is promising. This methodology is a strategy that could be used in any clerkship.
2019 Pediatric Research Day May 15, 2019 – Edmonton, AB

Oral Session No. 2 - ABSTRACT

Novel technologies for heart rate assessment during asphyxia in a swine model of neonatal resuscitation: the digital stethoscope and a tap-based smartphone app.


Introduction: Heart rate (HR) is the most important parameter to assess a newborn’s clinical status at birth. HR assessment guides decision-making about which interventions should be performed and determines its effectiveness during resuscitation. Current neonatal resuscitation guidelines recommend auscultation and palpation along with pulse oximetry and electrocardiography. Most recently, digital stethoscopes and smartphone apps have been proposed as novel technologies to measure HR during neonatal resuscitation. The objective of our study was to evaluate the accuracy and speed of digital stethoscopes and a smartphone app to assess accuracy and speed of HR assessment using a porcine model of asphyxia-induced neonatal resuscitation.

Methods: Newborn piglets (n=20, 1-3 days, 1.7-2.4kg) were anesthetized, intubated, mechanically ventilated, and subjected to 30 min of hypoxia, followed by asphyxia. Asphyxia was induced by clamping the endotracheal tube and disconnecting the ventilator until asystole was confirmed via carotid blood flow. During asphyxia, HR assessments were performed using a digital stethoscope (Thinklabs Medical LLC, Centennial, CO) and the NeoTapLS app (Tap4Life, Stockholm, Sweden). HR obtained with the digital stethoscope was derived by counting the number of beats over 6 sec and multiplying by 10 (DS6sec), and by counting for 10 sec and multiplying by 6 (DS10sec). The HR obtained with the NeoTapLS app was derived by tapping a minimum of 3 beats corresponding to the heartbeats heard. The time needed to obtain HR was also recorded. HRs were compared to carotid blood flow, which was simultaneously recorded.

Results: Carotid blood flow recordings provided a median (IQR) HR of 72(56-81) beats per minute (bpm) during asphyxia compared to 60(60-80), 60(56-74), and 69(56-76) bpm for the DS6sec, DS10sec and NeoTapLS groups, respectively. There was no significant difference between HR obtained using the DS6sec, DS10sec and NeoTapLS groups when compared to carotid blood flow HR (Bland-Altman). The median (IQR) time required to obtain a HR using the NeoTapLS was 3(2-4) sec. NeoTapLS required a lower mean time to assess HR>30 bpm and HR>18 bpm compared to the minimal time required for DS6sec and DS10sec groups, respectively.

Conclusions: Our data suggests auscultation using either DS6sec, DS10sec or app-based auscultation methods with the digital stethoscope are comparable to carotid blood flow and feasible. Clinical trials using digital stethoscope and tap-based application are needed to confirm our findings.
A cardiac-specific branched chain aminotransferase deletion increases insulin-stimulated glucose oxidation in the mouse heart.


Introduction: Impaired branched chain amino acid (BCAA) oxidation at the level of downstream BCAA catabolic enzymes cause cardiac insulin resistance and dysfunction. However, it is not known whether it is the accumulation of BCAAs or branched chain keto acids (BCKAs) due to impaired cardiac BCAA oxidation that result in these cardiac metabolic detrimental effects. Our objective was to inhibit cardiac branched chain aminotransferase (BCATm), the first enzyme in the BCAA oxidative pathway, which functions to produce BCKAs. We anticipate deletion of upstream BCAA catabolic enzyme will result in reduced cardiac BCAA oxidation and increase BCAAs but decrease BCKAs.

Methods: Ten-week-old BCATm cardiac specific knockout (BCATm−/−) male mice and their α-MHC-Cre expressing wildtype littermates (WT-Cre+/+) received 6 intraperitoneal injections of tamoxifen (50 mg/kg). All mice were allowed a 6-week washout post-tamoxifen, following which 16-week-old mice were used to assess cardiac energy metabolism. Isolated working hearts were perfused with oxygenated Krebs–Henseleit solution, consisting of either 5mM [5−3H/U-14C] glucose, 0.8mM palmitate, 3%BSA, 0.5mM BCAA for glycolysis and glucose oxidation measurements, or 0.5mM glucose, 0.8mM [9,10−3H] palmitate, 3%BSA and 0.5mM [U-13C] BCAA from combination of 0.15mM leucine/isoleucine and 0.2mM valine for fatty acid oxidation and BCAA oxidation measurements respectively.

Results: There was no body weight, glucose tolerance or cardiac function differences observed in BCATm−/− mice compared to WT-Cre+/+ mice (control). As expected, cardiac BCAA oxidation was significantly reduced in BCATm−/− mice compared to control, however, adding insulin after 30 min of perfusion did not change BCAA oxidation rates. Interestingly, glucose oxidation was significantly higher in BCATm−/− mice. Adding insulin further increased glucose oxidation in BCATm−/− mice. Additionally, the contribution of glucose oxidation to ATP production was significantly higher in the BCATm−/− mice compared to control.

Conclusions: We conclude that impaired BCAA oxidation due to the upstream catabolic enzyme deletion increases cardiac insulin sensitivity. This also indicates that accumulation of BCKAs, not BCAAs, may be primarily contributing to cardiac insulin resistance.
2019 Pediatric Research Day May 15, 2019 – Edmonton, AB

Oral Session No. 2 - ABSTRACT

Neonatal Intubation Through the Eyes of the Experts.
Zehnder E, Law B, Schmölder GM.

Introduction: Neonatal endotracheal intubation is a difficult task as several dynamic pieces of information must be considered simultaneously and decisions must be made efficiently. Therefore, novices healthcare professionals (HCPs) struggle with this procedure and have success rates of 20-50% which contrasts with content expert HCP who’s success rates is between 60-90%\(^1\,^2\). Due to changes in intubation practices and treatment guidelines over the last decade, pediatric residents have fewer opportunities to perform intubations, which results in lower proficiency\(^1\). Therefore, optimization of teaching and training methods is prudent to improve success rates of endotracheal intubation. Our project aims to understand the cognitive strategies, which are used by expert HCPs during intubations. We are using cognitive task analysis (CTA) methods including the Think Aloud and Knowledge Audit in combination with eye-tracking technology to understand these cognitive processes employed during successful intubation. CTA is a group of methods used to obtain information about the observable physical and underlying cognitive processes (i.e., perception, predictions, judgment, and decision making) required to complete a task. When describing medical protocols to students, expert HCPs typically fail to articulate approximately 70% of the analytical and critical decisions required to complete the task successfully\(^3\). CTA forces experts to consider the implicit knowledge used during a task, in turn making this information available to a learner\(^4\).

Methods: We are having expert HCPs wear eye-tracking glasses while performing neonatal endotracheal intubation. The eye-tracking glasses record the procedure from the point of view of the wearer and record where the HPC is looking by analyzing pupillary movements. Following the intubation, we ask the individual who wore the eye-tracking glasses to watch the recorded video of the intubation procedure. While watching the video, HPCs will be asked to “think aloud,” verbalizing their thought process throughout the intubation and their rationale for each action. The video will be paused at a-priori defined periods during the intubation sequence and HCPs will be questioned about each of these periods. These questions aim to assess various aspects of clinical expertise.

Conclusions: Our approach will potentially identify information used by expert HCPs. An understanding of the cognitive processes, which drives critical decisions during neonatal intubations might guide the development and improvement of training interventions to improve success rates of neonatal intubations and ultimately decrease human errors and improve patient safety.
Early psychosocial contact for adolescents and young adults (AYA) with cancer: The impact of the AYA Oncology Navigator.

McKillop S, Kirk J, Jespersen J, Turner J, Hartford R.

Introduction: Adolescents and Young Adults diagnosed with cancer face unique challenges including a risk of poorer psychosocial well-being and increased distress. To support the unique development needs of the AYAs, the Cross Cancer Institute (CCI) introduced an AYA Oncology Nurse Navigator in May of 2017. The Navigator role is designed to help guide patients through the complex adult cancer system by providing developmentally appropriate resources and sources of support. One recognized support for this population is early contact with psychosocial services.

The purpose of this study is to identify changes in early first contact with psychosocial services following the introduction of the AYA Oncology Navigator. It was hypothesized that the introduction of the Navigator role would both increase the incidence of psychosocial team contact and decrease the time to the first contact with the psychosocial team for AYAs newly diagnosed with cancer.

Methods: Following ethics approval, a list was requested from the Alberta Cancer Registry for all patients diagnosed and treated at the CCI, ages 17 to 29 years (at time of diagnosis), between 2016 and 2018. Patients were excluded if they were never seen for consultation at the CCI or were deceased less than 1 month from the diagnosis of cancer. A retrospective chart review using ARIA electronic medical records was completed. Data was collected regarding AYA navigator contact, first psychosocial contact, the diagnosis, and patient demographics. Descriptive statistics were used for analysis.

Results: A total of 235 AYAs newly diagnosed with cancer were available for analysis. Patient contact with the AYA Oncology Navigator was associated with an increase in initial contact with psychosocial services (60% vs 27% for those without AYA navigator contact p<0.001). There is a statistically significant decrease in the median time from first consultation at the CCI to first contact with oncology psychosocial services from 39 days, prior to the introduction of the Navigator, to 13 days once the Navigator was in place (p=0.029).

Conclusions: The introduction of the AYA oncology nurse navigator is associated with an increase in access to psychosocial care and a decrease in the time to first contact for these services for AYA’s newly diagnosed with cancer. Further study is needed to examine the impact of both the increased incidence and earlier time to inclusion of psychosocial support for this population.
Oral Session No. 3 - ABSTRACT

Equilibrative nucleobase transporter 1 mediates 6-mercaptopurine uptake and cytotoxicity in leukemia cell lines.
Ruel NM, Nguyen KH, Hammond JR.

Introduction: 6-Mercaptopurine (6-MP) is a nucleobase analog drug used in inflammatory bowel diseases and acute lymphoblastic leukemia (ALL). Its most common use is in the maintenance treatment of ALL. Our lab has established that transfection of cells with SLC43A3, which encodes for equilibrative nucleobase transporter 1 (ENBT1), increases both 6-MP influx and its cytotoxicity in a heterologous transfection model. SLC43A3 is known to be expressed in leukemia cells, but its role or impact on 6-MP cytotoxicity has not been evaluated. We hypothesize that the level of SLC43A3 expression in leukemia cells impacts 6-MP uptake and cytotoxicity.

Methods: A panel of leukemia cell lines were assessed for their expression of SLC43A3 and ENBT1 function, as well as for their sensitivity to 6-MP. SLC43A3 transcript was determined using RT-qPCR. 6-MP cytotoxicity was determined by incubating cells in a range of concentrations of 6-MP (78nM – 1.28mM) for 48 hr in a humidified incubator (95% air, 5% CO2) followed by evaluation of cell viability by the MTT assay. We assessed ENBT1 function by measuring the 2 sec uptake of [14C] 6-MP in each cell line. We also developed a resistant leukemia cell line (ALL-1R) by incubating cells with 640 µM 6-MP for 48 hr, removing the 6-MP, then culturing the resistant cells in regular media.

Results: Expression, cytotoxicity, and function of SLC43A3/ENBT1 varied widely across the cell lines tested. There was a significant positive correlation between the level of SLC43A3 transcript and the uptake of [14C] 6-MP (Spearman r = 0.9524). There was also a correlation between SLC43A3 expression and the cytotoxic EC50 of 6-MP obtained in these cell lines. ALL-1R cells that were 1.7-fold more resistant to 6-MP than the parent cell line, also displayed a significant decrease in the uptake of 6-MP and expression of SLC43A3.

Conclusions: Leukemia cell lines express SLC43A3/ENBT1, and expression level correlates with both the rate of 6-MP uptake and cell sensitivity to the cytotoxic effect of 6-MP. These data suggest that the level of expression of SLC43A3 in leukemia cells may impact the therapeutic efficacy of 6-MP in the treatment of ALL.
A Comparison of Two Models of Follow-Up Care for Adult Survivors of Childhood Cancer.


Introduction: Few studies have compared follow-up care models for adult survivors of childhood cancer (ASCCs), though choice of model could impact medical adherence, survival, and health-related quality of life (QOL). This study compared two follow-up care models, cancer-center-based versus community-based, for ASCCs in Alberta, Canada. Researchers examined the differences between cancer-center- and community-based ASCC adherence to recommended Children’s Oncology Group (COG) exposure-based medical screening for late effects, QOL, self-reported physical symptoms, and adherence to yearly follow-up.

Methods: ASCC participants included everyone discharged from the Alberta Children’s Hospital (ACH) Late Effects Clinic to a community model since its inception (over 15 years) and those with comparable birth years (1973-1993) currently followed in a cancer-center model at the Stollery Children’s Hospital (SCH). Researchers recruited ASCCs directly and through a multimedia campaign. Clinicians, through chart review, identified chemotherapeutic and radiation exposures, and required guideline-recommended survivorship screening. ASCCs also completed questionnaires assessing QOL, physical symptoms, and follow-up behavior.

Results: One-hundred-fifty-six survivors participated (community (n=86); cancer-center (n=70)). Primary analysis indicated that cancer-center ASCC’s guideline-recommended total test adherence percentage (Mdn=85.4%) was significantly higher than the community model (Mdn=29.2%, U=3996.50, p < 0.0001). In secondary analysis, researchers could not demonstrate significantly higher QOL for cancer-center ASCCs (M=83.85, SD=20.55 versus M=77.50, SD=23.94; t(154)=1.77, p=0.078); though they endorsed from 0.4-7.1% fewer physical-symptom clusters, and higher adherence to follow-up behavior in comparisons using effect-sizes without p values.

Conclusions: This study highlights the cancer-center model’s superiority for COG guideline adherence and completion of screening for medical and symptom-based QOL late effects in childhood cancer survivors.
Oral Session No. 3 - ABSTRACT

Homozygosity for a Novel CARD11 Mutation Causes Severe Combined Immunodeficiency (SCID), Inflammatory Gastrointestinal Disease, and Complete Abrogation of MALT1 Activity.
Suressh S, Lu HY, McGonigle L, Luider J, Turvey SE.

Introduction/Background: The caspase recruitment domain family member 11 (CARD11)B cell CLL/lymphoma 10 (BCL10)MALT1 paracaspase (MALT1) [CBM] complex is a critical signalling adaptor that regulates lymphocyte activation, proliferation, survival, and metabolism. Primary immunodeficiencies affecting each component (termed CBMopathies) result in broad clinical manifestations ranging from severe combined immunodeficiency (SCID) to lymphoproliferation. We present the laboratory and clinical findings of two Canadian First Nations patients found to be homozygous for the same novel CARD11 mutation (c.2509C>T; p.R837*).

Results: We have identified an 8-month-old boy who presented with a severe case of entero/rhinovirus bronchiolitis with interstitial lung disease and a 17-year-old boy with a history of severe pulmonary infections (including PJP), chronic sinusitis, candidiasis, invasive bacteremia, and severe ileo-colitis and oral ulceration requiring total colectomy. Both patients possessed absent Tregs, absent memory B cells, and hypogammaglobulinemia. However, only the 8-month-old had poor T cell proliferation to PHA, ConA, and CD3. Both patients were found to be homozygous for the same novel variant of CARD11 (c.2509C>T; p.R837*). The mutation rendered CARD11 protein expression unstable and it was undetectable by immunoblot. To confirm CARD11 deficiency, we stimulated patient B cells with phorbol 12-myristate 13 acetate (PMA) and ionomycin across a time-course and immunoblotted for various signaling proteins in both the NF-κB (IKK/, IκB, p65) and MAPK (MEK1/2, MKK4, JNK1/2, ERK1/2) pathways as well as various cleavage substrates of the MALT1 paracaspase (RelB, CYLD, BCL10, HOIL1). NFB and JNK activation were completely absent and MALT paracaspase activity was lost, but surprisingly, MKK4 (which acts upstream of JNK) was intact. Furthermore, co-immunoprecipitation experiments revealed that CARD11 was required for optimal MALT1 association with BCL10 in response to stimulation.

Conclusions: These two cases highlight the crucial role of CARD11 in regulating lymphocyte development, function, and humoral responses. In addition, we have identified the oldest known living individual with CARD11 deficiency and he presented uniquely with inflammatory gastrointestinal disease in addition to SCID, further adding to the spectrum of phenotypes associated with CARD11-related primary immunodeficiencies.
Exploring the key role of Tlr4 in cisplatin-induced ototoxicity.
Babolmorad G, Domingo IK, Bhavsar AP.

Introduction: Cisplatin is a chemotherapeutic used in childhood cancer patients to treat solid tumors. However, cisplatin usage is limited due to possible irreversible adverse drug reactions, including ototoxicity which manifests as permanent hearing loss in children. A genome wide association study (GWAS) in patients treated for childhood cancer identified associations of cisplatin ototoxicity with genetic variations in the innate immune receptor, TLR4, which protected carriers against the development of cisplatin induced hearing loss. We were trying to understand the role of TLR4 signaling pathways in cisplatin ototoxicity in a murine Organ of Corti cell-based model. The specific objectives of this study were to: 1) create a Tlr4 deletion in an in vitro hair cell model; 2) confirm the loss of Tlr4 through genetic, and functional analyses; and 3) examine the impact of Tlr4 deletion on cisplatin “ototoxicity” in vitro.

Methods: The murine embryonic inner ear cell line HEI-OC1, was used as an in vitro model to study cisplatin “ototoxicity”. To meet objective 1, CRISPR/Cas9 genome-editing was used to disrupt the Tlr4 gene in HEI-OC1 cells. To meet objective 2, CRISPR-targeted HEI-OC1 clones that lack Tlr4 activity were Sanger sequenced at the Tlr4 locus to identify the nature of the genome edit. Selected CRISPR targeted cells were assessed for LPS binding/internalization (using Alexa Fluor-488 LPS) or LPS-induced cytokine secretion with and without a complementing copy of Tlr4. Finally, to meet objective 3, cisplatin ototoxic responses were compared between Tlr4-deleted or control HEI-OC1 cells.

Results: Sequencing results confirmed frame-shift mutations in exon 1 of Tlr4. CRISPR-targeted cells internalized less LPS and released less IL-6 after LPS stimulation compared to control cells. IL-6 secretion was restored upon expression of a complementing copy of Tlr4. Similar results were observed for reactive oxygen species generation and IL-6 secretion after cisplatin stimulation. Furthermore, cell viability analyses indicated that Tlr4-deleted HEI-OC1 cells are more resistant to cisplatin cytotoxicity compared to control cells.

Conclusions: 1) Identification of a new pathway (TLR4) that contributes to the development of cisplatin ototoxicity. 2) Cisplatin ototoxicity was reduced by abrogating Tlr4 activity.
Oral Session No. 4 - ABSTRACT

Supplanting Cytomorphology with Flow Cytometric Immunophenotyping for Identifying Leukemia in Cerebrospinal Fluid in Pediatric Patients

Black K, Perry S, Szkotak A, Wong B.

Methods: We retrospectively reviewed data for all pediatric patients at Stollery Children’s Hospital with CSF involvement identified by cytomorphology and/or FCI from 2017-2019. In collaboration with the iHOPE program at Stollery Children’s Hospital, all CSF samples from pediatric leukemia patients are submitted in tissue transport media to allow for FCI. Hematopathologists requested CSF FCI for acute lymphoblastic leukemia/lymphoma (ALL) if: 1) any morphology with white blood cell (WBC) count >5x10^6/L, 2) suspicious cells with WBC count ≤5x10^6/L, 3) previously positive CSF result with any WBC result until negative result in optimal sample, and 4) no peripheral blood involvement by leukemia if it is a traumatic tap. CSF FCI for non-ALL cases was ordered at the pathologist’s discretion. Reliability of the two methods was assessed with the Cohen kappa statistic.

Results: We identified 28 CSF samples from 6 Pediatric Oncology patients with CSF involvement. Five patients had B-ALL, and one patient had myeloid sarcoma with monoblastic differentiation (functionally equivalent to Acute Myeloid Leukemia). There was substantial agreement between cytomorphology and FCI (k=0.70). Both methods were positive for hematologic malignancy in 5/28 samples (18%) and both negative in 20/28 samples (71%). All positive cases identified by FCI occurred when the WBC count was <5x10^6/L. In 3/28 (11%) samples, morphologically suspicious or equivocal cells were identified but FCI was negative. Two of these morphologically suspicious samples were from the same B-ALL patient, and one sample was from the myeloid sarcoma patient.

Conclusions: In our pilot study, cytomorphology and FCI show substantial concordance in CSF assessment. FCI did not identify any positive cases that were morphologically negative. A small subset of cases were morphologically suspicious or equivocal, but negative by FCI; long-term follow-up is necessary to determine the clinical significance. Further data is needed to fully assess the CSF testing algorithm.
Oral Session No. 4 - ABSTRACT

The outdoor environment of being born too small or too soon in Canada.
Nielsen C, Amrhein C, Serrano-Lomelin J, Osornio-Vargas A.

Introduction: Adverse birth outcomes (ABO) are increasing in Canada, contribute to infant mortality and morbidity, and are linked to the maternal exposome, including exposure to environmental hazards. To better understand the contribution of ambient health hazards to ABOs, we assessed which Canadian provinces and territories had more outdoor environmental hazards spatially associated with babies born too small or too soon, and whether they differ among land hazards and industrial chemicals.

Methods: Using Statistics Canada’s Vital Statistics-Births Database for the years 2006-2012, we selected birth events meeting our criteria and classified as small for gestational age (SGA: birth weight below 10th percentile), low birth weight at term (LBWT: birth weight below 2,500 g at 37 or more weeks gestation), and preterm birth (PTB: born before 37 completed weeks gestation). To assess province-level associations of with prenatal exposures, we accessed publicly available spatial databases on 228 industrial air pollutants (National Pollutant Release Inventory) and eight land activities (gas stations, dumps, mine sites, transformer stations, electrical power lines, oil/gas well pads, aboriginal lands, cultivated lands). We used a geographical information system (GIS) to spatially and temporally assign variables to the maternal residences at birth. We used logistic regression, with covariates on sex, number of births, low SES, and road density, to identify which industrial chemical emissions or land hazards had associations for thirteen provinces/territories.

Results: From a total of 2,525,645 births, 8.55% were SGA, 1.54% were LBWT, and 6.17% were PTB. Of the 52 chemicals occurring in the same locations as AB, there were twenty four – including ammonia, benzene, carbon monoxide, methyl ethyl ketone, and particulate matter – that had statistically significant (p<0.05) positive associations with ABO. For the land-based environment, gas stations (n=18), powerlines (n=11), and dumps (n=11) had the most associations of any hazard with any ABO. The provinces having statistically significant associations with: only chemical exposures were Ontario, Nunavut, and Yukon; only land hazards were Manitoba, New Brunswick, Nova Scotia, Prince Edward Island, and Saskatchewan; primarily chemicals were Alberta, Newfoundland, and Québec; and mostly land hazards was British Columbia.

Conclusions: To support the biological plausibility of our findings, fifteen of the associated chemicals are known or suspected developmental toxicants that may affect SGA, LBWT, or PTB. There were geographical differences in exposures and associations: pollutants released to the air or land-based hazards may be more important depending on where one lives.
Ketones Can Become the Major Fuel for the Heart
Ho K, Wagg c, Zhang L, Vo K, Ussher J, Lopaschuk G.

Introduction: The heart is metabolically versatile and can dynamically adapt to various physiological conditions by altering its reliance on different fuels, namely fatty acids and carbohydrates. However, during times of starvation, consumption of a ketogenic diet, or in poorly controlled diabetics, ketone levels in the blood significantly increase, yet whether the heart orchestrates a metabolic adaptation to an increased ketogenic milieu remains understudied. Therefore, our goal was to investigate how high levels of β-hydroxybutyrate (βOHB - the main circulating ketone in our body) affect the heart’s function, efficiency and metabolic profile. We hypothesized that increased delivery of ketones to the heart would negatively impact cardiac energetics.

Methods: Isolated working hearts from C57BL/6J male mice were perfused aerobically in the working mode for 60-minutes, with radiolabeled palmitate (0.8mM), glucose (5mM) and increasing concentrations of βOHB (0, 0.6, 2.0mM). Subsequently, oxidation of these substrates was quantified, and cardiac function was also assessed.

Results: Increasing βOHB concentrations markedly increased myocardial ketone oxidation rates, but interestingly had no effect on either glucose or fatty acid oxidation rates. Notably, increasing βOHB concentrations resulted in a three-fold increase in cardiac energy production, and at 2.0mM βOHB, ketones became the major fuel source for the heart, contributing to 66% of the heart’s total energy production. Conversely, glucose and palmitate oxidation contributed to 27% and 7% of the heart’s total energy production, respectively. However, this unregulated increase in reliance on ketones for energy did not translate into improvements in cardiac work (function) and thus, cardiac efficiency decreased as the heart was exposed to higher ketone levels.

Conclusions: Here we present novel observations demonstrating that ketones can become the major fuel source for the heart. Furthermore, increasing cardiac ketone metabolism did not improve cardiac function and as such, resulted in decreased cardiac efficiency. Our findings not only indicate that ketotic environments (as with a ketogenic diet) may negatively impact cardiac energetics but also underscore the importance of recognizing ketones as a major fuel source for the heart in times of starvation, consumption of a ketogenic diet or poorly controlled diabetes.

Mian Q, Huang Y, Conroy A, Opoka R, Namasopo S, Hawkes M.

Introduction: Pneumonia is the leading cause of paediatric mortality globally with over 900 000 deaths annually. Access to oxygen is essential for the treatment of hypoxaemia in pneumonia, but such access remains limited in low-resource settings. Current methods of oxygen delivery are often unsustainable in low-income and middle-income countries (LMICs), since oxygen cylinders require a robust supply chain and operator training, and concentrators rely on consistent access to the power grid. Therefore, gaps remain in oxygen delivery in low-resource settings despite the potential to reduce pneumonia mortality by up to 35%. Through an initial proof-of-concept study, a randomised controlled trial, and further cost-effectiveness analysis, our team has compared outcomes for solar-powered oxygen delivery to standard oxygen cylinders for paediatric patients with pneumonia.

Methods: Our team has developed, installed and monitored two solar oxygen systems in Jinja and Kambuga, Uganda, to provide off-grid access to oxygen. These systems consist of solar panels, batteries, and an oxygen concentrator, and cost USD$15,420 and $17,328, respectively. A randomized-controlled trial of 130 patients with pneumonia compared outcomes between solar oxygen and cylinder therapy, based on hospital length-of-stay. Further cost-effectiveness analysis was performed using WHO-CHOICE guidelines, and qualitative assessment of these systems was provided by health care workers.

Results: Median length of stay for the solar group was 4.1 days, 0.41 days less than the cylinder group (95% CI, -1.2 to 0.43), meeting the prespecified criterion for noninferiority. There was no difference in mortality or time to discharge between solar oxygen and cylinder groups. Solar oxygen has a cost per disability-adjusted life year (DALY) saved of $27/DALY, significantly less than reported values for oxygen cylinders ($50/DALY) and other pneumonia interventions such as the pneumococcal and HiB vaccines. Maintenance costs are projected at $90 per month (including battery replacements) over the life of the system. Health-care workers reported that solar oxygen systems are easier to use than cylinders.

Conclusions: Solar oxygen is a reliable and cost-effective option to provide oxygen therapy for children with pneumonia in low-resource settings. An expansion to twenty more sites in Uganda is being planned, with a stepped-wedge randomized controlled trial to assess mortality benefit. There will also be a focus on developing best practices for training staff to use and maintain these systems. Our team has engaged with local implementing partners, including health authorities, to ensure effective uptake of solar oxygen. Further reductions in cost and experience with maintenance are required to ensure effective widespread implementation.
Oral Session No. 5 - ABSTRACT


Perrin S, Thomas J, Murdoch F, Caulfield S, Urschel S.

Introduction: Teenagers have the highest rate of rejection and organ failure among all transplant recipients. They have the hardest time adhering to post-transplant therapies and restrictions. To date no improvement strategies have been proven successful. This project’s aim was to develop a new tool to educate and motivate teenage heart transplant patients to take increased interest in and ownership of their long-term health. We hypothesized that a graphic novel—an age-appropriate narrative medium—could accomplish this purpose.

Methods: Conducting semi-standard interviews, we asked teenage transplant patients, their parents, and health care providers (n=3 each) which aspects of post-transplant life they felt the graphic novel should address. The responses directed the novel’s style and content. A script was developed and the pages were drawn using realistic pen-and-ink techniques. Standardized questionnaires were developed for evaluation of the novel and its emotional impact on 30 teenage patients after print.

Results: Interviews revealed that parents and health care providers were concerned about teenagers' lifestyle/health choices and lack of perspective. Surprisingly, the teenagers' primary concerns were not necessarily related to the post-transplant lifestyle, but rather conflict with nagging parents. Consequently we determined that subtly addressing transplant guidelines would be most effective to avoid teenage mental blocks against instructional texts and conversations. We developed an adventurous and humorous story—invoking mutant worms, chickens, and the future—while simultaneously slipping in messages addressing the key transplant concerns brought up in the interviews.

Conclusions: This is the first graphic novel developed to specifically reach and motivate transplanted teenagers. Including the target audience in the planning stage was key, since it revealed a large discrepancy between the teenagers’ and care-providers’ concerns, which could easily have resulted in an ineffective tool. Feedback from peers and assessors of the project has been extremely positive, however, a final validation of the printed novel for its quality, appeal, and motivational efficacy by 30 teenage patients will reveal if this approach is really a meaningful strategy for teenage health education.
Hemostatic factor gene expression by Wilms’ tumor and Neuroblastoma cells: Investigating a potential novel mechanism augmenting metastasis.

Abdullahi I, Dietrich K, Eisenstat DD, Mitchell LG.

Introduction: Neuroblastoma and Wilms tumor are two of the most common types of solid tumors in pediatric patients. The survival rate of both tumors is <50% when they are metastatic. During haematogenous dissemination cancer cells form a fibrin rich microemboli cloak, which protects circulating tumor cells from shear forces and allows the cancer cells to travel undetected by cytotoxic natural killer cells. We hypothesized that hemostatic factors involved in fibrin formation are expressed by cancer cells themselves, which enhances the tumor ability to form these microemboli cloaks. We also hypothesized that chemotherapy will impact gene expression of coagulation factors in pediatric cancers.

Methods: We used tissue culture methods and RT-qPCR to screen constitutive expression of 24 hemostatic system genes. Two pediatric cancer cell lines were tested; Neuroblastoma (CCL-127) and Wilms tumor (CRL-1441). To show that gene expression changes observed were not cell line specific, two more neuroblastoma cell lines were tested; CRL-2271 and CRL-2266. Changes in protein expression for hemostatic system factors were done on CCL-127 and CRL-1441 cells by western blot analysis. All experiments were done in triplicate.

Results: In all 4 cell lines, analysis showed gene expression of the following; Prothrombin, Thrombin receptor, TF, Factor VIII, Factor XII, von Willebrand factor, Tissue Factor Pathway Inhibitor, Antithrombin, Protein C Receptor, Tissue plasminogen activator, Alpha 2-antiplasmin, Plasminogen activator inhibitor-1. Expression of Factor V, Fibrinogen beta chain and Fibrinogen gamma chain was observed in CRL-1441 only. All 15 genes showed protein expression in CCL-127 and CRL-1441 cancer cells lines. GAPDH was used as control. Changes in gene and protein expression were also seen in CCL-127 and CRL-1441 cell lines when treated with chemotherapy drugs.
Conclusions: We report a novel observation of expression of hemostatic factors, in neuroblastoma and Wilms tumour cancer cell lines. This supports a direct role of the cancer cells in the formation of fibrin. We also observed a significant change of expression of hemostatic factor genes and proteins when these cancer cells were treated with chemotherapy drugs. Determining the role of coagulation factors in metastasis will assist in developing new treatment methods and ultimately a reduction in mortality rates.
No. 2 - ABSTRACT – POSTER PRESENTATION

Role of leukemic cells in haemostatic abnormalities in a paediatric acute lymphoblastic leukemia: a novel mechanism for risk for venous thromboembolism during chemotherapy.

Aborkhees G, Dietrich K, Mitchell L.

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 gene and protein expression in two pediatric cell lines; (CCL119 - from 4-year-old T cell ALL patient) and cell line (CCL120 – from 11-year-old B cell ALL patient). RNA is isolated, DNase I treated and cDNA produced to be analyzed with quantitative reverse transcription polymerase chain reaction (RT-qPCR). Measuring proteins by western blot with reducing sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), polyvinylidenedifluoride membrane transfer and primary antibodies incubation followed by labelled secondary antibodies detection by chemiluminescence.

Results: We have shown gene expression of multiple hemostatic factors including Factor VIII, Factor XIIIa, ADAMTS13 and PLAU. Protein expression presented novel observations of some proteins being produced by normal lymphocytes but not in ALL cell lines such as plasminogen activator inhibitor (PAI-1) and Fibrinogen gamma (FGG). Other proteins generated by ALL but not observed in normal lymphocytes include FVIII and VWF. Normal lymphocytes and leukemic produce FV, FVII, FIX, FX and TAFI. Enzyme linked immunosorbent assays will be used to quantify the differences in protein production in both normal and leukemic cells.

Conclusions: We report, for the first time that normal lymphocytes and leukemic cells produce hemostatic factors. There are quantitative differences in hemostatic factors production in normal lymphocytes and leukemic cells. 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.
Regulation of p53 and its E3/E4 Ubiquitin Ligases by WIP1
Abuetabh Y, Leng R.

Introduction: UBE4B is a potential oncogene implicating the outcomes of several cancers, including brain, breast and liver cancers. Recently, our lab demonstrated that UBE4B promotes degradation of phosphorylated p53 (S15 and S392) in response to ionizing radiation (IR), suggesting UBE4B plays a role in regulating p53 after DNA damage. However, UBE4B regulation is still largely unknown. Wild-type p53-induced protein 1 phosphatase (Wip1) is an essential main known phosphatase that targets phosphorylated p53. Moreover, Wip1 is found to target most of the negative and positive regulators of p53, including ATM, ATR, Hdm2 and Chk1/2. Thus, we wondered if Wip1 could also target UBE4B.

Methods: We investigated the endogenous UBE4B protein levels in response to Wip1 over-expression or silencing in different cancer cell lines with or without IR exposure.

Results: Our data showed that UBE4B and Wip1 were induced mainly in wild-type p53 expressing cell lines in response to IR. Moreover, Wip1 overexpression increased the level of UBE4B protein, while a reduction in Wip1 via Wip1-siRNA resulted in decreased UBE4B protein level. Our preliminary data demonstrated that Wip1 co-immunoprecipitated with UBE4B.

Conclusions: Our preliminary data demonstrated that Wip1 could directly or indirectly impact the expression of UBE4B. Our aim is to explore this potential relationship between Wip1 and UBE4B. Consequently, revealing the possible regulators of UBE4B may lead to development of novel therapeutic strategies to battle cancer.
No 4 - ABSTRACT – POSTER PRESENTATION

Resveratrol attenuates doxorubicin-induced injury and later onset hypertension-induced cardiomyopathy through the inhibition of NLRP3 inflammasome signaling.
Al-Maayah ZH, Alam A, Eisenstat DD, Dyck JR.

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 adverse effects that may go undetected but progress to cardiac dysfunction and eventually cardiomyopathy later in life. We have developed a new pre-clinical model of occult DOX-induced cardiovascular toxicity in young mice and have demonstrated that juvenile exposure to DOX makes mice more susceptible to the detrimental effects of Angiotensin II–induced hypertension later in life. Utilizing this model, we have also shown that co-administration of resveratrol with DOX in young mice attenuates detrimental late-occurring cardiovascular changes. However, the molecular mechanism responsible for the pathophysiological changes of early DOX-induced cardiotoxicity and the late-onset overt stress-induced cardiomyopathy remains unknown. As growing evidence suggests a central role of the nucleotide-binding domain-like receptor protein-3 (NLRP3) inflammasome in the development of myocardial damage induced by chemotherapy, we proposed that NLRP3 inflammasome is implicated in the early and delayed DOX-induced cardiac dysfunction in our model.

Methods: 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. In another cohort, mice were fed chow containing 0.4% resveratrol 1 week before, during, and 1 week after the DOX administrations. The gene expression level of NLRP3 pathway members was determined using quantitative real-time polymerase chain reaction (qRT-PCR).

Results: One week after the last DOX administration, NLRP-3, Interleukin-18 (IL-18), and tumor necrosis factorα (TNFα) were induced in hearts of DOX-treated mice demonstrating molecular signs of cardiac stress as indexed by the induction of β-myosin heavy chain (β-MHC). In contrast, mice receiving DOX with resveratrol co-administration displayed low expression level of IL-18, NLRP-3 and TNFα and in response to Angiotensin II-induced hypertension. Notably, the inhibitory effect of resevertrol on the NLRP3 pathway seems to be independent of known down-stream molecular pathways such as induction of autophagy and appeared to attenuate the NLRP-3 inflammasome through the supression of cellular redox regulator, thioredoxin interacting protein (TXNIP).

Conclusions: Our data provide supports that resveratrol attenuates DOX-induced injury and later onset hypertension-induced cardiomyopathy through the inhibition of NLRP3 inflammasome signaling. Based on this, we suggest that targeting NLRP3 inflammasome may be a potential new therapeutic approach for the treatment of juvenile DOX-induced cardiotoxicity.
No, 5 - ABSTRACT – POSTER PRESENTATION

Role of Dlx2 in regulation of cell fate determination in the developing forebrain.
Gallego J, Nevin M, Eisenstat DD.

Introduction: The Distal-less homeobox 2 gene (Dlx2) encodes a transcription factor that is present in the ganglionic eminences (GE) of the developing forebrain and regulates the development of GABAergic interneurons in the ventral subpallium. GABAergic interneurons and oligodendrocytes are predicted to share a common progenitor cell supporting that Dlx2 mediates the differentiation of GABAergic interneurons from these progenitor cells through transcriptional repression of oligodendrocyte differentiation. We hypothesize that Dlx2 represses genes that are present and required throughout oligodendrocyte differentiation and maturation, but only in cells destined to be GABAergic interneurons, and as such will directly repress Plp1 and other genes required for oligodendrocyte precursor cell differentiation and oligodendrocyte maturation. The overall aim of the project was to illustrate that Dlx2 can suppress required oligodendrocyte genes through varying time points in oligodendrocyte development.

Methods: A comparison of gene expression of Olig2, PDGFRα, Sox10, Nkx2.2, Olig1, MBP, Myt1, and Plp1 in the embryonic day (E) 13 GE of wild type (WT) and double knock-out (DKO) mice (knock-out of Dlx2 and its redundant pair, Dlx1) was completed. Immunofluorescence assays were completed to show increased PLP1 expression in E13.5 DKO, E13.5 WT and E18.5 WT. Specifically, the proteolipid protein 1 (Plp1) gene was analyzed for the presence of ATTA or TAAT candidate homeobox binding sites upstream of the promoter region and subsequently for direct binding of DLX2 by chromatin immunoprecipitation and gel shift assays, respectively to show direct regulation of this late oligodendrocyte gene.

Results: qPCR determined that all genes increased in expression in the DKO. PLP1 appeared to have early protein translation in the DKO compared to WT as per the antibody immunofluorescence assay. Chromatin immunoprecipitation determined that 4 out of the 9 regions were occupied by DLX2 in vivo and R8 was repressed by Dlx2 co-expression in vitro.

Conclusions: Results from this project supported the hypothesis that DLX2 represses genes throughout oligodendrocyte development and occupied sites upstream of Plp1 to regulate it directly or indirectly. Electrophoretic mobility shift assay and Luciferase reporter gene assays currently in progress will determine if Dlx2 binds directly to Plp1 binding sites and represses Plp1 expression in vitro, respectively. This project provides insight for GABAergic interneuron development which has several implications in brain tumours, autism and epilepsy as well as further characterize PLP1 protein to provide insight into the mechanism of Pelizaeus-Merzbacher disease.
No. 6 - ABSTRACT – POSTER PRESENTATION

DLX1/DLX2 represses oligodendrogliogenesis by direct-binding and transcriptional inhibition of Olig2 expression in the developing forebrain.
Jiang Q, Zagozewski J, Japoni S, Godbout R, Eisenstat D.

Introduction: A common pool of neural progenitors within the basal forebrain gives rise to inhibitory GABAergic interneurons and oligodendrocytes. Generation of these different cell types in proper ratios and in a correct temporal and spatial manner is essential for normal telencephalon development. The Dlx family of homeobox transcription factors, in particular DLX1/DLX2, are necessary for differentiation and migration of interneurons, while the basic helix-loop-helix (bHLH) transcription factor Olig2 is required for oligodendrocyte development throughout the central nervous system (CNS). Our hypothesis is that DLX1/DLX2 negatively regulates oligodendrogliogenesis by direct-binding and repression of Olig2 expression in the developing forebrain.

Methods: The expression pattern of endogenous DLX1/DLX2 and Olig2 was explored using in situ hybridization (ISH) or immunofluorescence (IF) assays. Chromatin immunoprecipitation assays (ChIP) were performed on E13.5 mouse ganglionic eminences to investigate the in vivo DLX2 occupancy of the Olig2 gene locus. The specificity of the binding was examined in vitro by electrophoretic mobility shift assays (EMSA). The functional significance of the binding was further analyzed through luciferase reporter gene assays. The loss-of-function effects of DLX1/DLX2 genes on the Olig2 gene expression were tested in DLX1/DLX2 knockout mice using IF and RT-qPCR. Finally, the gain-of-function studies of chicken Dlx1 gene were carried out by means of in ovo electroporation.

Results: In both chicken and mouse, Dlx1/Dlx2 and Olig2 genes are temporarily coexpressed in a common group of progenitors within the ventral embryonic forebrain, but they tend to be expressed reciprocally as cells exit the progenitor zone. ChIP assays demonstrated the in vivo binding of DLX2 protein to the mouse Olig2 gene locus. The binding of chicken Dlx1 and mouse DLX2 to Olig2 gene domains was confirmed in vitro by EMSA. Luciferase reporter gene assays further established the transcriptional repression effects of the binding of mouse DLX2 to Olig2 gene. IF and RT-qPCR data indicated that Olig2 expression is expanded in the forebrain of DLX1/DLX2 knockout mouse embryos. Furthermore, chicken Dlx1 is sufficient to repress OLG2 expression in ovo, while the mutation leading to loss of its DNA binding capability results in abrogation of this repression.

Conclusions: Dlx genes regulate progenitor cell fate decisions in the developing telencephalon by promoting interneuron differentiation, and concurrently inhibiting the generation of oligodendrocytes through direct-binding and transcriptional repression of Olig2 expression.
Sulforaphane Exhibits Anti-Cancerous Effects on U251 Glioblastoma Cells in Culture.

Khairy M, Garcia E, Eisenstat D, Yager J, Persad S.

Introduction: Sulforaphane is a natural compound that occurs in broccoli sprouts. Several reports describe that sulforaphane induces apoptosis specifically in cancer cells but not in normal cells at the same dose. In vivo, sulforaphane is metabolized to sulforaphane N- acetyl cysteine which has the ability to cross the blood brain barrier. Our research aims to test sulforaphane anti-cancer activity in glioblastoma cell lines, determine the dosage boundaries for toxicity to glioblastoma cells compared to normal cells, and identify the mechanisms that lead to the induction of cell death in glioblastoma cell lines.

Methods: U251 were cultured DMEM media, 10% Fetal Bovine Serum and 1% penicillin/streptomycin at 37°C, 5% CO₂. Cells were seeded on a 96 well plate at a density of 4 x 10⁴ cells per well for 24 hours. sulforaphane was prepared in media, and placed with the cell cultures at concentrations ranging from 5-200 μM. Each concentration of Sulforaphane was represented in three wells in two plates and incubated with cells for 24 hours. Cell viability was determined using Alamar Blue Assay using a microplate reader to detect fluorescence as indication for viable cells. For cell invasion assay, we used a Transwell® unit (8 μM) coated with BD Matrigel Basement Matrix. cells were counted (50,000) and seeded in the upper compartment of the chamber (0.1% FBS DMEM) incubated for 24 hours at 37°C and 5% CO₂), and DMEM supplemented with 10% FBS was added to the lower compartment of the well to act as a chemoattractant. Then fixed with 100% methanol and stained with 0.5% crystal violet for 10 min. The chamber was analyzed by taking images of the wells and analyzing them using image and MetaExpress software.

Results: Sulforaphane had a cytotoxicity effect beginning at a concentration 50 μM, with an LD50 of 75μM. A dose-response effect was observed. Furthermore, we observed significantly higher numbers of invading cells for untreated U251 cells compared to U251 treated with different concentrations of SFN: 25μM, 50 μM, 100 μM, respectively. Each group of data is representative of 3 experiments. ***p<0.01. Stats were done using One Way Analysis & Dunnett’s Multiple Comparison Test.

Conclusions: Sulforaphane (SFN) exhibited significant anti-cancer effects in the established U251glioblastoma cell line in vitro. SFN at these concentrations also exhibits significant interference with cell invasion. SFN is therefore an excellent candidate for further exploration in this uniformly fatal brain cancer.
Active-Beta-Catenin (ABC) as a Prognostic Marker for Osteosarcoma Progression.

Introduction: Osteosarcoma (OS) is an aggressive primary bone malignancy having peak incidence in children/young adults. Outcome remains poor for most patients with metastatic disease which develops in 1/5 cases. Presently, no reliable baseline prognostic markers for aggressive OS, other than extent and site of disease involvement, have been established. We investigated the role of the Wnt/β-catenin pathway, specifically the transcriptionally Active-Beta-Catenin (ABC), in OS progression.

Methods: We used two pairs of cell lines that simulate OS progression: Saos2/Saos2-LM7 and HOS/HOS-143B. The greater invasive potential of Saos2-LM7 & HOS-143B compared to Saos2 and HOS were confirmed using invasion assays. Total cellular/nuclear levels/localization of ABC/β-catenin were evaluated/quantified by Western blot, immunofluorescence and High Content analysis. Transcriptional activity of ABC/β-catenin was evaluated by qRT-PCR of target genes (MMP2/MMP9/Cyclin D1/VEGFA). For immunohistochemical analysis (IHC) of nuclear ABC levels in OS tissue samples, we used pre-treatment biopsies with matched resection specimens from thirty patients (15 males: average age 11.6 years & 15 females: average age 13.4 years). Colon cancer tissue used as positive control and spleen as negative control. ABC immunoreactivity was calculated by quantifying the number of ABC positive nuclei over a given section. ABC score was assigned as low (<25% nuclear positivity) and high (>25% nuclear positivity).

Results: ABC levels were significantly higher in the nuclear fraction of Saos2-LM7 and HOS-143B cell lines compared to respective parent cell lines (Saos2 & HOS). No significant differences in cytoplasmic ABC levels or cellular/nuclear levels/localization of β-catenin were observed. In correlation, Saos2-LM7/HOS-143B exhibited significantly greater transcriptional activity compared to Saos2/HOS cells. Since there was no significant difference in β-catenin levels in the two cell lines, the higher TF activity in LM7 likely corresponds to higher nuclear ABC levels. IHC analysis of of tumor samples for ABC showed eight cases (27%) with high ABC nuclear staining and 22 (73%) with low ABC staining. There was no significant difference in staining pattern between gender or mean age. Analysis of disease progression, as determined by metastasis at diagnosis/resection, showed a significant number of cases in the ABC high group demonstrated metastatic disease compared with the ABC low group.

Conclusions: Our results supports the potential to use ABC as a prognostic marker for OS progression. Using ABC as a prognostic marker in a larger, well powered study may further aid in determining its eventual utility/clinical adoption in routine pathology practice.
Genetic regulation of retinal cell subtype formation in the developing mouse retina.

Li Z, Hejazi M, Zagozewski J, Eisenstat D.

**Introduction:** We are interested in characterizing the DLX regulatory network that regulates specific cell fates from multipotent retinal progenitor cells (RPC) such as retinal ganglion cells (RGCs) and photoreceptors (PRs). Dlx1/Dlx2 double knock-out (DKO) mice have reduced RGC and increased and ectopic expression of Cone-Rod Homeobox (CRX) required for PR differentiation. Orthodenticle Homeobox 2 gene (OTX2) is essential in multiple developmental processes of the eye including PR generation. PRs fail to develop in all OTX2 loss of function conditions. We hypothesized that DLX2 represses CRX and OTX2 expression early during development to promote RGC specification and that later during development, OTX2 is an important upstream regulator of DLX2 and CRX transcription factors, promoting RPC differentiation to PRs at the appropriate developmental time point.

**Methods:** Chromatin immunoprecipitation (ChIP) was performed to identify DLX2 occupancy at the OTX2 and CRX promoters in situ. To identify specific DLX2 binding sites, electrophoretic mobility shift assay (EMSA) was completed. Quantitative real-time PCR (qRT-PCR) and immunofluorescence was performed on Dlx1/Dlx2 DKO retinas to examine changes in OTX2 and CRX expression in the absence of DLX gene function. Luciferase reporter assays examined transcriptional activity of DLX2 on OTX2 and CRX expression in vitro. The Crx-LacZ Reporter mouse was crossed with DKO mice to confirm CRX upregulation by performing X-gal staining and qRT-PCR experiments. To investigate reciprocal regulation, ChIP was performed to identify OTX2 occupancy at the DLX2 and CRX promoters in situ.

**Results:** ChIP demonstrated that DLX2 bound to specific regions of the CRX and OTX2 promoters in situ. EMSA showed specificity of DLX2 binding to CRX and OTX2 promoters in vitro. Reporter assays showed DLX2 repression of Crx and Otx2 expression in vitro. The CRXLacZ reporter showed increased expression at embryonic day 18 (E18) when crossed with the DKO. In the DKO, OTX2 expression was not significantly changed at E18, however, its expression was upregulated during early retinal development (E13) in vivo. ChIP demonstrated that OTX2 bound to specific regions of the CRX and DLX2 promoters in vivo.

**Conclusions:** Our data supports a transcriptional network exists between DLX2, OTX2 and CRX in regulating specific retinal fates during development. Specifically, a potential cell fate switch promoting PR differentiation over RGCs is observed in the Dlx1/2 DKO. Future directions include crossing Dlx1/2 DKO mice with OTX2 reporter mice to verify the biological significance of this regulatory network in vivo.
DLX regulation of pancreatic islet cell development.  

demonstrates that DLX2 occupies the mouse pre-proinsulin I & II and proglucagon promoters in neonatal and E18.5 pancreas in situ. The specificity of DLX2 binding was confirmed using EMSA in vitro. Luciferase reporter assays demonstrated that DLX2 acts as a transcriptional repressor of the proglucagon gene promoter in vitro. Cell counting using immunofluorescence studies performed on cryosections demonstrate reduced insulin and glucagon expression in DLX1/2 DKO islets compared to WT. Radioimmunoassay (RIA) showed plasma insulin levels that are significantly reduced in the DLX1/2 DKO mice compared to WT littermates.

Conclusions: DLX2 plays a role in pancreatic islet cell development by direct transcriptional regulation of insulin and glucagon expression. Decreased insulin and glucagon may be due to reduced islet cellularity, specific loss of β and α cell numbers or reduced insulin and glucagon gene transcription. Future directions include performing q-PCR to assess and quantify the mRNA expression levels of insulin and glucagon in wild type and DLX1/2 knock out mice. We will also assess expression of other TFs required for proper pancreatic development. We will also perform flow cytometry on dissociated embryonic pancreas to accurately quantify the cell cycle, comparing the DLX1/2 DKO to WT littermates. This research may be relevant towards identifying other TF-dependent types of Maturity Onset Diabetes of the Young (MODY).
No. 11 - ABSTRACT – POSTER PRESENTATION

Role of DLX genes in regulation of cell fate decisions in the developing forebrain: Implications for understanding normal oligodendrocyte development and pediatric high-grade glioma.

Nevin M, Gallego J, Song X, Becher O, Godbout R, Underhill DA, Eisenstat DD.

Introduction: DLX1 and DLX2 are homeodomain transcription factors that are both required for proper development of the forebrain for the differentiation and migration of GABAergic interneurons. In addition to major defects in interneuron development, the forebrain of the Dlx1/2 double knockout (DKO) mouse displays an increased production of oligodendrocyte progenitor cells (OPCs), which occurs at the expense of interneuron generation. As such, we hypothesized that in addition to its requirement for interneuron development, DLX signaling represses oligodendroglial cell fate in forebrain progenitor cells, and we are currently in the process of identifying transcriptional targets that may be repressed by DLX1/2 to mediate this. Here, we investigated whether DLX2 represses expression of myelin transcription factor 1 (MyT1), a zinc-finger transcription factor involved in oligodendroglial development. We also examined the role of DLX2 in driving differentiation in diffuse intrinsic pontine glioma (DIPG), a pediatric brain tumour that is considered in some cases to arise from an OPC.

Methods: Bioinformatics approaches were used to identify regions of the MyT1 promoter containing candidate homeodomain binding sites. Chromatin immunoprecipitation (ChIP) with a DLX2 antibody was performed on E13.5 mouse ganglionic eminence, followed by PCR using primers to amplify candidate binding regions. We also performed qPCR on RNA extracted from WT and DKO E13.5 forebrain to compare Myt1 expression levels. To examine effects of DLX2 signaling on DIPG, we overexpressed DLX2 in a murine DIPG cell line and assessed expression of oligodendroglial and GABAergic interneuron genes, and carried out in vitro migration, invasion, and colony formation assays.

Results: We found that DLX2 occupies several regions of the Myt1 promoter in E13.5 forebrain, and observed a trend towards upregulation of Myt1 expression in the DKO forebrain. Overexpression of DLX2 in a murine DIPG cell line resulted in downregulation of several oligodendroglial genes and upregulation of GABAergic interneuron genes, and reduced migration, invasion and colony formation in vitro.

Conclusions: In vivo occupancy of the Myt1 promoter by DLX2 in E13.5 forebrain upregulation of Myt1 in the DKO forebrain are both consistent with our hypothesis that DLX signaling represses Myt1 expression during forebrain development.

The observed phenotypic and gene expression changes with DLX2 overexpression in a murine DIPG cell line suggests that there is potential for DLX signaling to promote differentiation and modify the cancer cell phenotype in this disease. Experiments with patient-derived cell lines are ongoing.
Physical therapy interventions in children and adolescents before, during and following treatment for cancer: A Cochrane Systematic Review.
Ospina PA, McComb A, Pritchard-Wiart LE, Eisenstat DD, McNeely ML.

Introduction: Children and adolescents with cancer are at high risk of experiencing severe side effects from cancer treatment; many of which are amenable to physical therapy. Evidence exists evaluating physical therapy in childhood cancer patients; however, factors such as small sample sizes, varying intervention protocols and differences in cancer types among trials make it difficult to draw conclusions about efficacy. This review aimed to evaluate the efficacy of physical therapy on quality of life and functional outcomes in childhood cancer.

Methods: Searches were conducted in five databases (CENTRAL, MEDLINE, Embase, CINAHL, PEDro), ongoing trial registries, and conference proceedings on February 2019. We included randomized controlled trials (RCT), cross-over trials, and controlled clinical trials that evaluated the efficacy of physical therapy on quality of life and functional outcomes in children and adolescents with cancer between the ages of 0 and 19 years. The comparison group included children with cancer receiving standard care, no physical therapy intervention or a comparison intervention. Two reviewers independently identified eligible studies, performed data extraction, assessed the risk of bias using a standardized tool, and rated the quality using the Grading of Recommendation Assessment, Development, and Evaluation criteria. The outcomes of interest were quality of life, adverse events, fatigue, pain, peripheral neuropathy, balance, gait, functional mobility, motor performance, range of motion, and strength.

Results: Of 1619 studies, five studies met the inclusion criteria. Three were single-centre RCTs, one was a prospective pilot controlled trial, and one was a crossover randomized controlled pilot trial. A total of 155 children and adolescents diagnosed with acute lymphoblastic leukemia, brain tumors, and lower extremity sarcoma were analyzed. Results demonstrated considerable heterogeneity in terms of the chosen interventions across studies, variation in timing of physical therapy interventions, variable cancer diagnoses, and study aims. Based on the risk of bias assessment, many studies were classified as unclear to high risk of bias. No significant intervention effects were found on quality of life and functional outcomes. None of the studies assessed outcomes specific to peripheral neuropathy, balance, gait, fatigue, and pain.

Conclusions: Results demonstrate that research evidence to date is inadequate to inform clinical practice. More rigorous studies are warranted to produce high-quality research evidence that can be translated into clinical practice. Recommendations for future research include the need for high quality, large scale studies that examine common side-effects seen in clinical practice such as peripheral neuropathy, cancer-related fatigue, and balance and gait deficits.
Rojas Vasquez M, Lemire K, Lotey N, Diachinsky M, Desai S.

**Background/Objectives:** JMML is a rare leukemia associated with poor prognosis, treatment usually requires hematopoietic stem cell transplantation for cure. JMML is characterized by mutations on the Ras pathway gene: NF1, NRAS, KRAS, PTPN11, and CBL. We present a case with congenital JMML with a new mutation and good response to chemotherapy. Design Case report.

**Results:** We describe a newborn, 33 weeks gestation age, born from C section, Cree ancestry and consanguinity likely, mother 19 years/old, G1P0, smoking and gestational diabetes (treated with diet), prenatally presented with intrauterine growth retardation and intrabdominal calcifications. Clinically, he was small for gestational age, no dysmorphic features except for absence of 4th right finger, splenomegaly, imaging confirmed diffuse intracranial and liver calcifications, splenomegaly and portal hypertension. TORCH was ruled out.

Genetic work up ruled out syndromes including Down and Noonan. Multiple cell blood counts (CBC) revealed anemia, thrombocytopenia, both transfusion dependant and progressive leucocytosis (>70 x 109/L) with blasts. He met criteria for JMML: splenomegaly, absence of the BCR-ABL1 fusion gene, monocytosis, <20% blasts in the peripheral blood and bone marrow, circulating myeloid precursors, no evidence of mutation in the RAS pathway, a germline SH2B3 mutation (homozygous) was found, both parents had the same mutation (heterozygous). He was treated with cytarabine (3mg/kg/dose) twice weekly with no response, mercaptopurine 2.5mg/kg/day was instituted with improvement on the CBC and transfusion independence and resolution portal hypertension. He is currently 12 month old with normal development and thriving well, on weaning dose of mercaptopurine with normal CBC.

**Conclusions:** We report a case of congenital JMML with homozygous germline mutation of SH2B3 with unknown significance (has been implicated with leukemogenesis), who responded well to mercaptopurine. An archive of these new mutations with clinical follow up is required to further understand the significance of this mutation.
Trends in the Management of Iron Deficiency Anemia by Pediatric Hematologists.
Dang M, Anwar D, Pedersen S, Lau S, Bruce A.

Introduction: Iron deficiency anemia is a condition that affects individuals worldwide; particularly, women and children are observed to be high risk populations. Inadequate iron intake or excessive blood loss (including heavy menstrual bleeding) are the two leading causes of iron deficiency. Depleted iron stores lead to the decrease in hemoglobin and oxygen supply to the body. Symptoms that manifest from iron shortage include a decline in motor, organ, and cognitive functions, in addition to fatigue and weakness. Oral iron has been the most commonly used therapy for treating iron deficiency, but it may not always be the most effective. Alternatively, research has found that intravenous (IV) iron and its newer formulations show less adverse effects. It has also been shown that IV iron is an effective and safe alternative therapy for pediatric patients when oral iron is not sufficient. Whether IV iron therapy utilization is increasing for pediatric iron deficiency patients is unknown.

Research Question: Has the number of children with a diagnosis of heavy menstrual bleeding, iron deficiency, iron deficiency anemia referred to the Stollery Children’s Hospital Pediatric Hematology Program (SCH PHP) receiving IV iron increased between 2012 and 2018?

Methods: Retrospective chart review between May 31, 2012 to June 1, 2018. University of Alberta Ethics Board approved. Inclusion criteria: children (1 month to 18 years old), with a diagnosis of iron deficiency, iron deficiency anemia, heavy menstrual bleeding, or IV iron therapy. Exclusion criteria: IV iron therapy treatment by a team other than SCH PHP.

Results: 95 records were reviewed. There was a bimodal distribution in age of presentation with iron deficiency; adolescent females and children between 2 and 5 years showed higher rates of iron deficiency than the rest of the included population. The leading cause of iron deficiency was due to nutritional deficiency (41.9%) and second to that was blood loss (38.7%). The most common therapy overall was oral iron. However, there was an increase in children receiving IV iron therapy from 2014-2017 (33.3%).

Conclusions: As the tolerability and effectiveness of IV iron therapy has improved, the use of this treatment for children by hematologists in the SCH PHP has increased from 2014-2017.
No. 15 - ABSTRACT – POSTER PRESENTATION

The study of pollutant mixtures and adverse birth outcomes using innovative spatial data mining methods as a case to explore collaborative research.

Wine O, Zaiane OR, Osornio Vargas A. (on behalf of DoMiNO Project Team).

Introduction: Environmental health research is gaining interest due to the global concern of environmental factors impacting health. This research is often multifaceted and becomes complex when trying to understand the participation of multiple environmental variables. It requires the combination of innovative research methods, as well as the collaboration of diverse disciplines in the research process. The application of collaborative approaches is often challenging for interdisciplinary teams, and much can be learned from in-depth observation of such processes.

Methods: Based on a recently published manuscript (Wine et al. Challenges 2019), we share a case report describing initial observations and reflections on the collaborative research process of the Data Mining and Neonatal Outcomes (DoMiNO) project (2013–2018), which aimed to explore associations between mixtures of air pollutants and other environmental variables with adverse birth outcomes by using an innovative data mining approach. The project was built on interdisciplinary and user knowledge participation with embedded evaluation framework of its collaborative process. We describe the collaborative process, the benefits and challenges encountered, and provide insights from our experience.

Results: We identified that interdisciplinary research requires time and investment in building relationships, continuous learning, and engagement to build bridges between disciplines towards co-production, discovery, and knowledge translation.

Conclusions: Learning from interdisciplinary collaborative research experiences can facilitate future research in the challenging field of environmental health.
A spatial scoping review of the outdoor environment and SGA and LBW in the U.S.A. and Canada.

Nielsen C, Amrhein C, Osorno-Vargas A.

Introduction: Global health issues of concern are newborns that are small for gestational age (SGA: birth weight below the 10th percentile) and low birth weight (LBW: birth weight below 2,500 g) because they are vulnerable to mortality and morbidity. Maternal exposures during pregnancy may contribute to SGA/LBW. We combined a scoping review and geographical analysis of the distribution of publications describing spatial associations of SGA/LBW with outdoor environmental exposures.

Methods: We searched peer-reviewed scientific literature to determine what location-based hazards have been linked with SGA/LBW in the industrialized nations of Canada and the U.S.A. Based on our inclusion/exclusion criteria, we selected studies and entered relevant details into an evidence table. We summarized the articles and classified the type of environment and general category of environmental variables studied (e.g. air pollution, chemical, water contamination, waste site, agriculture, vegetation, race, SES, etc.). In a GIS, we mapped the studies by geographic area to visualize the distributions and frequencies. We also mapped LBW percentages and ubiquitous environmental hazards, and compared them with the studies to determine where gaps may exist.

Results: The majority of the 159 studies had been completed in the U.S.A. (states=41) than in Canada (provinces =6), but have been increasing overall from 1992 to 2018. The type of environment was classified as (built=108, natural=10, and social=41). The environmental hazards were identified as the following general categories of variables (from most-to-least frequent): air pollution (n=53), SES (n=17), chemical (n=16), race (n=11), individual (n=10), water contamination (n=9), waste site (n=8), vegetation (n=8), agriculture (n=6), roads (n=3), urban-rural (n=3), food (n=2), mining (n=2), neighborhood (n=2), weather (n=2), immigration (n=2), alcohol (n=1), noise (n=1), power (n=1), transmission lines (n=1), health care (n=1).

Conclusions: The distribution of studies clearly showed that there are areas requiring future research, especially the states bordering the Mississippi River and Canada’s northern territories. Our geographic inquiry demonstrated a novel spatially-focused review framework to promote understanding of the human ‘habitat’ of shared environmental exposures that have been associated with SGA/LBW.
Burnett D, Yap J, Kao D, Turner J.

Introduction: Fecal microbiota transplantation (FMT) has become an accepted therapy for recurrent Clostridium difficile infection (rCDI), with strong evidence for its efficacy. Reports of FMT for rCDI have mostly focused on colonoscopic administration, with limited description of nasogastric (NG), nasojejunal (NJ) or gastric-tube (GT) delivery. We present results from our pediatric rCDI-FMT program, which primarily uses NG or GT administration.

Methods: We retrospectively reviewed all cases of FMT for rCDI at Stollery Children’s Hospital since 2015. In all cases, Health Canada’s FMT guidance document was used to determine indication and potential contraindications for FMT, as well as screening processes for donors. An FMT protocol was developed that included bowel preparation, and was used in all cases. Total fecal slurry dose administered was 37.5-100g.

Results: In total, 5 individual patients received FMT (7 procedures), including via NG (1), GT (4), NJ (1) and into cecum via colonoscope (1). At time of first CDI, all patients were on either immune modulating medications (3/5), had a recent course of antibiotics (4/5), or both (2/5). Average age at first FMT was 9.0 years (5.2-13.9), with an average of 4 (3-6) toxin positive CDIs prior to first FMT, and 1.2 years (0.5-2.1) from first CDI to FMT. Following FMT, one day of abdominal pain and a single emesis were described in one patient, otherwise no short term complications were documented. Two CDI relapses occurred within 3 weeks of first FMT, requiring repeat FMT (1 NJ, 1 colonoscope). After FMT (including repeated FMT in 2/5 cases), we report all 5 patients (100%) had successfully eradicated CDI, defined as no rCDI within 12 weeks of FMT. With average follow up of 12 months (2.3-34.4), only the 2/5 cases that required a repeat FMT for early relapse have had further CDI, one spontaneously at 15 months and one following antibiotic exposure 4 months post second FMT.

Conclusions: We describe FMT via the upper-GI route for 5 pediatric patients with rCDI, with no serious short term complications identified. The overall 100% success rate reported is higher than described elsewhere in the literature, although the small sample size is acknowledged. The upper GI route of FMT delivery has advantages for children, particularly those with an existing GT. However, additional work is required to determine the optimal route of delivery (upper vs lower GI), optimal dose (expressed in g/kg for pediatric patients) and whether bowel prep is required for FMT treatment of rCDI in children.
Characterizing Pain in Children with Acute Gastroenteritis in the Emergency Department

Maki C, Ali S, Xie J, Lee BE, Graham TAD, Vanderkooi O, MacDonald SE, Poonai N, Thul-Freedman J, Rajagopal M, Dow N, Sivakumar M, Freedman SB (on behalf of the Alberta Provincial Pediatric EnTeric Infection Team (APPETITE Team) and Pediatric Emergency Research Canada (PERC)).

Introduction: Although acute gastroenteritis is an extremely common childhood illness, there is a paucity of literature characterizing the associated pain and its management. Our primary objective was to quantify the pain experienced by children with acute gastroenteritis in the 24-hours prior to emergency department (ED) presentation. Secondary objectives included describing maximum pain, analgesic use, discharge recommendations, and factors that influenced analgesic use in the ED.

Methods: Study participants were recruited into this prospective cohort study by the Alberta Provincial Pediatric EnTeric Infection TEam between January 2014 and September 2017. This study was conducted at two Canadian pediatric EDs; the Alberta Children’s Hospital (Calgary) and the Stollery Children’s Hospital (Edmonton). Eligibility criteria included < 18 years of age, acute gastroenteritis (≥ 3 episodes of diarrhea or vomiting in the previous 24 hours), and symptom duration < 7 days. The primary study outcome, caregiver-reported maximum pain in the 24-hours prior to presentation, was assessed using the 11-point Verbal Numerical Rating Scale.

Results: We recruited 2136 patients, median age 20.8 months (IQR 10.4, 47.4); 45.8% (979/2136) female. In the 24-hours prior to enrollment, 28.6% (610/2136) of caregivers reported that their child experienced moderate (4-6) and 46.2% (986/2136) severe (7-10) pain in the preceding 24-hours. During the emergency visit, 31.1% (664/2136) described pain as moderate and 26.7% (571/2136) as severe. In the ED, analgesia was provided to 21.2% (452/2131) of children. The most commonly administered analgesics in the ED were ibuprofen (68.1%, 308/452) and acetaminophen (43.4%, 196/452); at home, acetaminophen was most commonly administered (77.7%, 700/901), followed by ibuprofen (37.5%, 338/901). Factors associated with analgesia use in the ED were greater pain scores during the visit, having a primary-care physician, shorter illness duration, fewer diarrheal episodes, presence of fever and hospitalization.

Conclusions: Although children presenting to the ED with acute gastroenteritis experience moderate to severe pain, both prior to and during their emergency visit, analgesic use is limited. Future research should focus on appropriate pain management through the development of effective and safe pain treatment plans.
No. 19 - ABSTRACT – POSTER PRESENTATION

Humanoid robot-based distraction to reduce pain and distress during venipuncture in the pediatric emergency department: A randomized controlled trial.

Introduction: Intravenous insertion (IVI) is identified by children as extremely painful and the resultant distress can have lasting negative consequences. There is an urgent need to effectively manage such procedures. Our primary objective was to compare the pain and distress of IVI with the addition of humanoid robot-based distraction to standard care, versus standard care alone.

Methods: This two-armed randomized controlled trial (RCT) was conducted from April 2017 to May 2018 at the Stollery Children’s Hospital emergency department (ED). Children aged 6 to 11 years who required IVI were included. Exclusion criteria included hearing or visual impairments, neurocognitive delays, sensory impairment to pain, previous enrollment, and discretion of the ED clinical staff. A total of 426 pediatric patients were screened and 340 were excluded.

Results: We recruited 86 children, median age 9 years (IQR 7,10), of which 55% (47/86) were male; 9% (7/82) were premature at birth; 82% (67/82) had a previous ED visit; 30% (25/82) required previous hospitalization; and 78% (64/82) had previous IV placement. 96% (78/81) received topical anesthesia prior to IVI. A statistically significant reduction in distress was observed with the addition of robot-based distraction to standard care. The mean total distress score measured via the Observational Scale of Behavioral Distress (OSBD-R) was 1.49±2.36 (standard care) compared to 0.78±1.32 (robot group) (p=0.047). The median Faces Pain Score (FPS-R) during the IV procedure was 4 (IQR 2,6) in the standard care group alone, compared to 2 (IQR 0,4) with the addition of humanoid robot-based distraction (p=0.13). Parental anxiety, measured by the State Trait Anxiety Inventory immediately after IVI, was 36.7 (11.9) (standard care) versus 31.3 (8.5) (robot) (p=0.04). Parental satisfaction with the IV start was 93% (39/42) in the robot arm compared to 74% (29/39) in the standard care arm (p=0.03). Parents were also more satisfied with management of their child’s pain in the robot group (95% very satisfied) compared with standard care (72% very satisfied) (p=0.002).

Conclusions: Humanoid robot-based distraction therapy has a positive impact on child distress and pain as well as parental anxiety for pediatric IVI. Further trials are required to confirm utility in other age groups and settings.
Golden-Plotnik S, Moir M, Van Manen M, Drendel A, Poonai N, Ali S.

Introduction: Fractures are a common childhood injury. While the pain associated with fractures has been well-described, the related functional impact is less understood. When a child’s function is impaired due to fracture, his or her ability to participate in day-to-day life is restricted. Eighty percent of children with fractures experience compromise in at least one domain of daily function. While there is clear value in measuring function, no studies have provided an in-depth assessment of functional limitations related to childhood limb fractures. Furthermore, none have identified the specific outcomes that are important from the perspective of patients and families.

Methods: We performed a qualitative study employing interviews of caregivers of children (5 to 11 years) who received care for acute, non-operative long bone fractures at the Stollery Children’s Hospital emergency department (ED). Audio-recorded, semi-structured, one-on-one telephone interviews were completed one to two weeks following the ED visit. Open-ended interview questions focused on areas of function identified by existing literature and expert opinion. Qualitative analysis was completed using content analysis theory. Our aim was to describe the phenomenon of functional change following fracture. Transcripts were read and coded by two researchers concurrent with data collection.

Results: Twenty-five interviews were included in our final analysis. Most children (23/25) were diagnosed with upper extremity fractures, and most participants were female and mothers (21/25). All caregivers reported a change in their child’s function. The most commonly affected areas included: sleep, activities of daily living, and play. Caregivers reported that their children were also impacted by pain and related negative emotional responses. All children required additional help or effort from their caregivers to carry out day-to-day tasks; this required adaptive strategies such as planning, changes to household routine and missing work. Key concerns from caregivers included pain management, fracture healing or complications, and regression of their child’s independence.

Conclusions: Function is universally impaired in younger children with fractures. Caregivers were also impacted by these limitations and often had to provide significant support in order to successfully adapt. Caregiver impact was often described within the context of a disrupted family dynamic. Successful healing, child wellbeing, and adaptation to disruptive changes were described as important goals. The impact of a fracture on a child’s function (including sleep, activities of daily living, play), and improvement thereafter, should be a key patient-oriented outcome for pediatric fracture research.
Surgical Pediatric Temporal Epilepsy: more than meets the eye!
Kassiri J, Wheatley M, Schmitt L, Rajapakse T, Elliott C, Sinclair DB.

Introduction: Temporal lobe epilepsy (TLE) accounts for approximately 15%–20% of pediatric cases. Of those, many are considered medically intractable and require surgical interventions. In this study, we hypothesized that mesial temporal sclerosis (MTS) was less common in patients who had undergone surgery for intractable pediatric TLE. We further hypothesized that there was a radiological and pathological discordance in identifying the cause of pediatric TLE.

Methods: We retrospectively reviewed the charts of pediatric patients with TLE who had undergone surgical treatments as part of the University of Alberta’s Comprehensive Epilepsy Program between 1988 and 2016. Along with preoperative magnetic resonance imaging (MRI) reports, post-surgical pathology results and seizure outcomes were studied.

Results: Of the 83 pediatric patients, who had undergone temporal lobe epilepsy surgery, 28% had tumors, 22% had dual pathologies, 18% had MTS, 11% had focal cortical dysplasia, and 22% had other pathologies. In addition, for 36% of these patients, discordances between their pre-surgical MRI reports and post-surgical pathology reports were found.

Discussions: To our knowledge, this was one of the largest retrospective cohort studies of pediatric patients who had undergone surgery for intractable TLE. This study showed that tumors, and not isolated MTS, were the most common pathology in surgical pediatric TLE. Furthermore, the study found that it was often difficult to distinguish pathology from a preoperative MRI alone.
No. 22 - ABSTRACT – POSTER PRESENTATION

Creation of a Rapid Access Clinic – Improving Urgent Care for Pediatric Neurology Patients.
Yaworski A, Yager, Mailo J, Richer L, Rajapakse T, Kassiri J.

Background: Pediatric neurology referral wait times are increasing, interfering with neurologists ability to diagnose and treat urgent conditions in a timely manner. This often leads to increased utilization of the emergency department (ED). On average 5% of ED patients present with neurological symptoms and approximately 35% of ED neurological diagnoses are revised after specialist review. To improve these issues a Stollery Rapid Access Neurology (RAN) clinic was created. Our goal was to decrease wait time for urgent neurological consultation, and initiate a more efficient referral process.

Methods: At the Stollery Children’s Hospital in Edmonton, the RAN clinic ran once a week from March 2018 until February 2019. This was a prospective study approved by the University of Alberta ethics board. Inclusion criteria was met prior to referral being accepted. Information regarding patient symptoms, test results, diagnoses and ED visits was collected and later reviewed for analysis. This included confidential patient satisfaction surveys.

Results: Seventy-five patients were referred to the RAN clinic. Forty-nine percent were referred from the ED, the other half from primary care or other subspecialties. Wait time averaged 6 weeks. The most frequent referral reason was seizures, with 60% of referring diagnosis being correct. Prior to RAN appointment, 61% of patients presented to the ED, whereas only 0.1% returned in the following 3 months. Neurology follow up was deemed necessary in 81% of patients. Overall satisfaction was ranked 9.6/10 by family.

Conclusions: The RAN clinic created an effective urgent triage method. Neurologist review revised 40% of diagnoses. This ongoing study reveals that a RAN clinic can significantly reduce visits to the ED following appointment and initiate appropriate follow up. Future evaluation to understand cost effectiveness and long distance appointments via telehealth are needed.
No. 23 - ABSTRACT – POSTER PRESENTATION


Introduction: Infliximab (IFX) is an effective therapy for Crohn’s disease (CD), but pharmacokinetic data during induction are sparse. The objective of this study was to model the pharmacokinetic (PK) and use individual clearance (CL) estimates to explore relationships between PK and clinical remission in children with CD receiving IFX induction.

Methods: A prospective study was conducted at 3 Canadian Children IBD Network sites. Baseline data collected included simple endoscopic score (SES-CD) and weighted Paediatric CD Activity index (wPCDAI). IFX doses ranged 5-10 mg/kg. Up to 8 IFX levels per subject were collected: trough and peak at doses 2 and 3, trough prior dose 4, between doses 3 and 4, and trough prior to dose 5. Free antibody to IFX (ATI) levels measured at doses 3, 4, and 5. Faecal calprotectin (FCP), wPCDAI, CBC, albumin (ALB), ESR, and CRP samples were also collected at each dose. NONlinear Mixed Effects Modelling was used to develop a population PK model using standard model building approaches. Covariate factors had to be significant at p<0.001 and clinically relevant (>20% change in CL) to be retained. Dose and frequency may be adjusted clinically or based on preceding trough levels.

Results: 35 subjects, 18 males, were recruited and followed for up to 22 weeks over 5 doses. Median age was 12.3 years (IQR: 10.2–14.8). Median dose for Dose 1 was 6.0 mg/kg (IQR: 5.0–7.0) and increased to 7.0mg/kg (IQR: 5.0–8.3) for Dose 5. 80% of patients did not follow the standard induction and maintenance regimen of 0, 2, 6, and 14 weeks. Dose 4 had the most variability in frequencies with the median of Q6W. IFX CL was marked varied between subjects and improved during follow-up. Median baseline CL was 0.31 (IQR: 0.24, 0.40). During single covariate evaluations, the following factors were identified as potentially predictive of IFX CL: ALB (negative correlation) and FCP, CRP, SES-CD, wPCDAI, and ESR (positive correlation). On back elimination, only ALB and CRP were important predictors. CL had a nonlinear correlation with weight where CL/kg was higher in those weigh <30kg vs. those >30kg (p =0.005). 29 subjects (83%) went into complete remission (wPCDAI <12.5). IFX CL of ≤0.39 l/day was a good predictor of remission status determined by wtPCDAI at Dose 5 (AUC [95% CI] = 0.828[0.63–1.00], p = 0.013). ATI levels drawn at Doses 4 and 5 were all negative

Conclusions: IFX CL is variable and affected by factors including weight, ALB, disease activity and endoscopic severity. Under dosing is common in lower age bracket, due to higher drug CL/kg using current weight-based dosing. Paediatric IBD patients may benefit from precision medicine using PK model-based (dashboard) dose adjustments where individualized dosing can be calculated based on individual patient factors.
No. 24 - ABSTRACT – POSTER PRESENTATION

Making child health evidence usable to the public: What do parents want?
Anzinger H, Elliott SA, Hartling L.

Introduction: Connecting parents to research evidence is known to improve health decision making. However, guidance on how to develop effective knowledge translation (KT) tools which synthesize child health evidence into a form understandable by parents is lacking. The purpose of this study was to conduct a comparative usability analysis of three online KT tools to identify differences in tool efficacy, identify which format parents prefer, and to better understand what factors affect usability for parents.

Methods: We evaluated a Cochrane plain language summary (PLS), blogshot, and a Wikipedia page, on a specific child-health topic (Acute Otitis Media). A mixed methods approach was used involving a knowledge test, written usability questionnaire, and a semi-structured interview. Differences in knowledge and usability questionnaire scores for each of the KT tools were analyzed using Kruskal-Wallis tests, considering a critical significance value of p=0.05. Thematic analysis was used to synthesize and identify common parent preferences among the semi-structured interviews. Key elements parents wanted in a KT tool were derived through author consensus using questionnaire data and parent interviews.

Results: Sixteen parents (9 female) aged 39.6 ± 11.9 years, completed the study. Parents preferred the blogshot over the PLS and Wikipedia page (p=0.002) and found the blogshot to be the most aesthetic (p=0.001), and easiest to use (p=0.001). Knowledge questions and usability survey data also indicated the blogshot was the most preferred and effective KT tool at relaying information about the topic. Four key themes derived from thematic analysis, describing elements parents valued in KT tools. Parents wanted tools that were 1) simple, 2) quick to access and use, 3) trustworthy, and 4) informed how to manage the condition. Out of the three KT tools assessed, blogshots were the most preferred by parents, and encompassed these four key elements.

Conclusions: It is important that child-health evidence be available in formats accessible and understandable by parents to improve decision-making, use of healthcare resources, and health outcomes. Further usability testing of different KT tools should be conducted involving broader populations and other conditions (e.g. acute vs chronic) in order to generate guidelines to improve KT tools for parents.
INTRODUCTION: Perinatal arterial ischemic stroke (AIS) is the most common stroke in children occurring in 1 in 4000 live births. Consequences include seizures and a spectrum of cognitive and motor disability. Infantile spasms (IS) is an epileptic encephalopathy of infancy with an incidence of 2 per 10,000 live births. Approximately 5% of IS is caused by perinatal AIS. Patterns of ischemic injury that may predispose infants to IS and predict treatment response have not been identified.

METHODS: This retrospective case series of infants with AIS and IS provides detailed descriptions of ischemic distribution, seizure presentation, treatment and outcomes. Inclusion criteria were: term birth, ischemic stroke or encephalomalacia in an arterial distribution identified or presumed to have occurred in the perinatal period, a diagnosis of infantile spasms. Patients with a watershed pattern of injury were excluded. The modified pediatric ASPECTS was used to qualify and quantify the type and distribution of stroke. Areas of injury were identified on MRI and scored from T2/Flair or DWI sequences.

RESULTS: Eleven patients with AIS and IS were identified. Of nine who fit inclusion criteria, all had MCA territory involvement with 6/9 having basal ganglia injury. Five had ischemia identified retrospectively after developing IS and four presented as neonates. The highest ASPECTS (bilateral deep MCA) was associated with the worst outcome in motor function and epilepsy control. However, the second-highest ASPECTS (unilateral MCA, bilateral ACA) had mild motor deficits and no seizure recurrence after IS resolution. The three lowest ASPECTS (<10) involved unilateral cortical MCA strokes sparing the deep structures. These patients also had the best motor outcome and seizure control.

CONCLUSIONS: The co-occurrence of perinatal AIS and IS often results in significant neurologic disability. Although there was no defined pattern of regional homogeneity, there was a trend towards basal ganglia injury with progression of epilepsy after IS. This study highlights that size of ischemic injury may be less important than location as a predictor of motor outcome and seizure intractability. Future research will focus on identifying areas of injury that may confer increased risk of IS compared to stroke patients who remain seizure-free.
2019 Pediatric Research Day May 15, 2019 – Edmonton, AB

No. 26 - ABSTRACT – POSTER PRESENTATION

Infographics to promote trialists’ awareness and uptake of the Standards for Research in Child Health: development and usability evaluation.

Gates A, Dyson MP.

Introduction: In 2012, Standards for Research in (StaR) Child Health published six evidence-based Standards to guide the rigorous design and conduct of pediatric trials. While comprehensive, their format is not practical for many trialists. With the aim of promoting trialists’ awareness and uptake of the Standards, we (a) identified the key messages in each Standard, (b) translated the key messages into six one-page infographics, and (c) evaluated their usability among clinicians, researchers, and trainees.

Methods: We extracted key messages from each published Standard. Next, we collaborated with a graphic design team who drafted an initial set of six infographics based on the key messages. At each stage, we sought feedback from academic colleagues and members of the Standard Development Groups to ensure the accuracy and comprehensiveness of the messages. Based on the feedback we received, graphic designers revised the infographics, creating two prototypes for evaluation. The prototypes contained identical information but differed in their design: Prototype A followed a “map-like” layout while Prototype B was linear. Over one month (April 2018), we invited members of the Maternal Infant Child and Youth Research Network (MICYRN) and the Women and Children’s Health Research Institute (WCHRI) to evaluate the prototypes across eight usability domains via an online survey. We computed descriptive statistics to characterize the survey results using Microsoft Office Excel.

Results: There were 15 respondents to the survey (33% researchers, 13% clinicians/health professionals, 33% clinician-scientists, 20% students/trainees, 20% other). On a scale of 1 (strongly disagree) to 10 (strongly agree), respondents agreed that the infographics: had a clear purpose (median, range: 9, 3-10); contained relevant images and text (8, 6-10); used clear language (9, 7-10); seemed credible (9.5, 6 to 10); were preferable over detailed articles (10, 8-10); and would be helpful in designing and conducting a trial (9, 4-10). Respondents disagreed that the infographics were missing essential information (2, 1-6) and took too long to read (4.5, 2-9). Most respondents preferred the layout of Prototype A (53%) and thought that compared to Prototype B, it was more visually appealing (80%), enjoyable to read (67%), and important information was easier to find (53%).

Conclusions: In collaboration with the Standard Development Groups and graphic designers, we translated the StaR Child Health guidance into a format that appealed to the end users. Next steps will involve ongoing refinement and evaluation of the infographics and dissemination to networks of clinicians, researchers, and trainees.
Severe Obesity and Global Developmental Delay in Preschool Children: Preliminary Findings from a Canadian Paediatric Surveillance Program.


Introduction: Existing evidence suggests severe obesity (SO) and global developmental delay (GDD) are related. No Canadian studies have examined SO and GDD in children. Understanding the frequency and severity of the association between SO and GDD is needed to inform health services and policies for clinicians to tailor their care for these patients. Our objective was to characterize SO and GDD in preschool children in Canada.

Methods: A monthly survey was distributed to practicing general paediatricians and paediatric subspecialists (~2,500) participating in the Canadian Paediatric Surveillance Program (CPSP) from February 2018 to January 2019 to report new cases of SO and GDD among children ≤5 years of age.

Results: To date, 38 cases have been reported. Eleven confirmed cases (64% female; 3.5±1.2y; 28.6±5.2kg/m²) were included. CPSP participants reported age of GDD diagnosis at 2.3±1.0 years and age of first weight concerns at 2.7±1.3 years. The most common health problems reported were snoring (50%) and asthma (40%). Dietitians (91%) and developmental paediatricians (64%) were also involved in their care. The biggest challenges reported in supporting children with SO and GDD included (1) a lack of developmental and obesity health services and (2) the wait time between referral access to services.

Conclusions: Concerns about SO among children with GDD tended to begin around 2.7 years of age. Multidisciplinary service provision was common; however challenges to access in care were identified. Monthly surveillance remains ongoing until January 2020. Final analysis will include incidence, risk factors, and health care needs.
No. 28 - ABSTRACT – POSTER PRESENTATION

Effectiveness of digital technologies as a distraction for acute pain in children: a systematic review and meta-analysis.

Background: Evidence supports distraction as a pain-reduction strategy for children undergoing painful procedures but it is unclear whether the type of distraction might affect its efficacy. Our objective was to answer the question: For children with an acutely painful condition or who are undergoing a painful medical procedure, what is the effect of digital technology as a distraction on their pain and distress compared to no distraction, or other forms of distraction?

Methods. In November 2018 we searched 8 online databases and grey literature sources for quantitative primary studies. Two reviewers screened records for eligibility, extracted data (one reviewer with verification) and appraised study-level risk of bias, then established consensus. We pooled the findings of randomized controlled trials with suitable data via meta-analysis for the primary outcomes (pain and distress) and judged the certainty of the evidence in duplicate using GRADE.

Results: Of 3247 unique records, we included 108 studies (7890 children) that utilized a wide range of digital technologies (e.g. audiovisual aids; audiovisual eyeglasses; virtual reality; video games; computer tablets) for various painful procedures (e.g., needle-related, dental procedures, burn treatments). Evidence of low-to-very low certainty supported a reduction in self-reported pain (SMD -0.48, 95% CI -0.66 to -0.29, 46 RCTs, n=3200), observer-reported pain (SMD -0.68, 95% CI -0.91 to -0.45, 17 RCTs, n=1199), behavioural pain (SMD -0.57, 95% CI -0.94 to -0.19, 19 RCTs, n=1173), self-reported distress (SMD -0.49, 95% CI -0.70 to -0.27, 19 RCTs, n=1818), observer-reported distress (SMD -0.47, 95% CI -0.77 to -0.27, 10 RCTs, n=826), and behavioural distress (SMD -0.35, 95% CI -0.59 to -0.12, 17 RCTs, n=1264) with digital technology distraction compared to usual care. There was little-to-no difference in pain with digital technologies compared to non-digital (e.g., blowing bubbles, puppet show) distraction (2 to 8 RCTs, n=81 to 771, low-to-very low certainty), though self-reported distress (but not observer-reported or behavioural measures) was lower among children distracted with digital technologies compared to non-digital distraction (SMD -0.92, 95% CI -1.43, -0.41, 3 RCTs, n=235, very low certainty).

Conclusions: Healthcare providers should strongly consider digital and non-digital distractors to reduce children’s pain and distress during common painful medical procedures (e.g., needle-related, burn treatments, dental procedures). Until further evidence on comparative effectiveness becomes available, healthcare providers should use distractors that are convenient and appealing to patients. Only two studies reported on acutely painful conditions, but clinicians should see distraction as a viable option for these children.
Acute Kidney Injury and Fluid Overload in Critically Ill Children
Alobaidi R, Morgan C, Majumdar SR, Bagshaw SM.

**Background:** Acute kidney injury (AKI) and fluid overload (FO) are associated with considerable mortality, morbidity and increased use of health care resources. However, the precise epidemiologic characteristics and the incremental risks associated with the interaction between AKI and FO have not been well described in the pediatric population.

**Methods:** We conducted a population-based multicentre cohort study inclusive of all patients admitted to PICUs in Alberta, Canada over a 12-month period (between January-December 2015), utilizing prospectively collected demographic, clinical and laboratory data from bedside clinical information system and critical care data repository. Exposures were AKI (defined according to Kidney Disease: Improving Global Outcomes criteria) and FO (defined as peak FO% > 10% during the first 10 days of PICU admission). The primary outcome was PICU mortality. Secondary outcomes included receipt and duration of mechanical ventilation, duration of vasoactive support and length of PICU and hospital stay.

**Results:** A total of 1017 patients were included. AKI developed in 314 patients (30.9 %; 95% confidence interval [CI], 28.1 % to 33.8 %) and severe AKI (KDIGO stage 2 and 3) developed in 124 patients (12.2 %; 95% CI, 10.3 % to 14.4 %). The incidence rate for critical illness associated AKI was 34.6 per 100,000 children/year (95% CI, 30.9 to 38.7). FO occurred in 333 patients (32.7 %; 95% CI, 30.0 %– 35.7 %). Independent predictors of severe AKI included: Pediatric Index of Mortality 3 (PIM3) score, FO and need for vasoactive support. Severe AKI and FO were independently associated with increased PICU mortality (Adjusted odds ratio [aOR] 6.08, 95%CI 2.76 to 13.40) and (aOR 3.70; 95% CI 1.48 to 9.28), respectively. In addition, severe AKI and FO were independently associated with increased length of mechanical ventilation, duration of vasoactive support and length of PICU and hospital stay.

**Conclusions:** AKI and FO are common in critically ill children and are strongly associated with worse outcomes and increased health resource utilization. We found strong independent association between AKI and FO. These findings suggest that FO may represent a modifiable target of intervention. Future research aimed at evaluating strategies to prevent and mitigate FO is warranted.
Abstract

Intestinal epithelial injury is associated with systemic inflammation in vertically HIV-1 infected children


Introduction: Infection of gut associated lymphatic tissue in human immunodeficiency virus 1 (HIV-1) infection permits microbial translocation (MT) from the GI lumen to the circulation which drives systemic inflammation and endothelial activation (EA). Intestinal fatty acid binding protein (I-FABP) is an epithelial cytosolic protein, abnormally released into the circulation with MT, and elevated in the plasma of HIV-1 infected adults, even with sustained viral suppression (SVS) on combination anti-retroviral therapy (cART). I-FABP has not been extensively studied in HIV-1 infected children. Nonetheless, children face decades of chronic immune activation, which may predispose to cardiovascular disease and/or malignancy.

Hypothesis: We hypothesize that quantitative levels of I-FABP will be correlated with markers of inflammation in HIV-1 infected children with suppressed viral load on cART.

Methods: Cross-sectional analysis of I-FABP and markers of inflammation: tumour necrosis factor (TNF) and interleukin-6 (IL-6). Plasma samples were collected from vertically HIV infected children who achieved SVS (<40 copies/mL) with cART from the Early Pediatric Initiation – Canadian Child Cure cohort study (EPIC4). Commercial ELISA assays (R&D Systems) were used to quantify biomarker levels.

Results: We included 63 vertically HIV-1-infected children from 9 Canadian tertiary pediatric HIV treatment centres. 35/63 (56%) were girls, with median age 13 years (range 4-19). All had a suppressed viral load on cART at the time of testing. Biomarkers of inflammation were correlated with each other: TNF with IL-6 (p=0.91, p<0.001). Given the high degree of correlation between the biomarkers of inflammation, we used principal component analysis to derive an index of systemic inflammation. I-FABP was positively correlated with this index of inflammation (p=0.70, p<0.001).

Conclusions: Despite excellent virologic control with cART, intestinal epithelial injury (as reflected by elevated I-FABP) was associated with systemic inflammation in pediatric HIV-1 infection. Future studies should examine long-term outcomes (e.g., cardiovascular events) in children with elevated I-FABP.
No. 31 - ABSTRACT – POSTER PRESENTATION

Safety and Efficacy of Stereoelectroencephalography in Pediatric Epilepsy Surgery.
Elliot C, Wheatley BM, Narvacan K, Kassiri L, Carline S, Sinclair DB.

Introduction: There are few published reports on the safety and efficacy of stereoelectroencephalography (SEEG) in the presurgical evaluation of pediatric drug-resistant epilepsy. Our objective was to describe institutional experience with pediatric SEEG in terms of (1) insertional complications, (2) identification of the epileptogenic zone and (3) seizure outcome following SEEG-tailored resections.

Hypothesis: We hypothesize that quantitative levels of I-FABP will be correlated with markers of inflammation in HIV-1 infected children with suppressed viral load on cART.

Methods: Retrospective review of 29 pediatric drug resistant epilepsy patients who underwent presurgical SEEG between 2005 and 2018.

Results: 29 patients (15 male; 12.4 ± 4.6 years old) who underwent SEEG were included in this study with mean follow-up of 6.0 ± 4.1 years. SEEG-related complications occurred in 1/29 (3%)—neurogenic pulmonary edema (Jacob et al., 2010, Can J Neurol Sci., 37(6):885-71). A total of 190 multi-contact electrodes (mean of 7.0 ± 2.5 per patient) were implanted across 30 insertions which captured 437 electrographic seizures (mean 17.5 ± 27.6 per patient). The most common rationale for SEEG was normal MRI with surface EEG that failed to identify the EZ (16/29; 55%). SEEG-tailored resections were performed in 24/29 (83%). Engel I outcome was achieved following resections in 19/24 cases (79%) with 5.9 ± 4.0 years of post-operative follow-up.

Conclusions: Stereoelectroencephalography in presurgical evaluation of pediatric drug-resistant epilepsy is a safe and effective way to identify the epileptogenic zone permitting SEEG-tailored resection.

Background/Aims: Caesarean section delivery is a well-known factor for microbial gut dysbiosis up until mid-infancy. However, little is known about the impact of other birth events such as prolonged labour or rupture of membranes on infant gut microbiota. This study investigates the direct and indirect effects of birth mode, prolonged labour and other perinatal exposures on infant gut microbiota.

Methods: In a subsample of 999 infants born at or near-term in the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort, stool samples were collected at 3-4 months of age and microbial taxa profiled with 16S rRNA sequencing. Generalized structural equation model was employed to examine directional relationships between birth mode and prolonged stage 2 labour, and microbial diversity (Shannon index) and taxon abundance, taking into account primigravida status, pre-pregnancy obesity, prolonged rupture of membranes, intrapartum antibiotics prophylaxis, gestational age, exclusivity of breastfeeding and infant age at stool collection.

Results: Four early life factors were associated with reduced total gut microbiota diversity in infants: vaginal birth ($\beta$=-0.10, p=0.043), prolonged stage 2 labour ($\beta$=-0.11, p=0.01), early term birth ($\beta$=-0.07, p=0.056) and exclusive breastfeeding ($\beta$=-0.34, p<0.001). Prolonged stage 2 labour mediated the association between reduced microbial diversity and birth mode, prolonged stage 1 labour and rupture of membranes. A first pregnancy was associated with reduced colonization of *Bifidobacterium* (OR = 0.70, p<0.001) in the infant gut via 2 pathways: lower likelihood of exclusive breastfeeding and prolonged stage 2 labour.

Conclusions: Aside from the physiologic effects of exclusive breastfeeding, prolonged labour and early term birth have the capacity to reduce microbial diversity in the infant gut. Maternal primigravida status is a risk factor for childhood allergic disease. By reducing *Bifidobacterium* abundance in the infant gut, this study suggests that prolonged labour, which is more common in first pregnancies, could be a pathway to allergic disease.
No. 33 - ABSTRACT – POSTER PRESENTATION

Risk Factors for Respiratory Infections at Three Months of Age in the CHILD Cohort.

Introduction: Early life respiratory infections have been associated with an increased risk for a development of severe asthma later in life. A recent report in humans found there was an association between development of asthma and presence of respiratory infections in early life, independent of virus type. In this study, we used data from the CHILD cohort to investigate the preliminary associations between various risk factors and respiratory infections at 3 months of age.

Methods: A sample of 2502 term infants from the Vancouver, Edmonton and Winnipeg sites of the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort study were studied. sIgA levels in infant stool samples at 3-4 months were assayed using the Immundiagnostik sIgA ELISA kit. Other co-variates including respiratory infection, sex, gravidity, birth-mode, home environment, maternal asthma, maternal allergies, pregnancy weight, and antibiotics were obtained via standardized questionnaire. Using STATA v15, each of these co-variates were entered into either a linear or logistic regression model to determine the risk associated with these pre/postnatal factors and respiratory infections in the first three months of life.

Results: About 3.5% of infants had recorded respiratory infections in the first 3 months of life. Infants with prenatal smoke exposure were three times more likely than infants without to have a respiratory infection within the first three months (OR 3.17; 95% CI: 1.74, 5.79; p<0.001). Notably, postnatal smoke exposure was not significant (p>0.05). Breastfeeding (exclusive or partial) at 3 months was associated with a 51% decreased risk for respiratory infections in the first three months of life compared to non breastfeeders (OR: 0.49; 95% CI: 0.25, 0.97; p=0.04). Risk for respiratory infections increased with increasing numbers of inhabitants in the home (p<0.05). No differences in respiratory infections in 3 month old infants were observed in relationship to birthmode, fecal sIgA, antibiotics, sex, maternal asthma or allergy, pregnancy weight, or number of pets. Despite being a known risk factor for child development of asthma, mothers having asthma during pregnancy was not significantly associated with respiratory infections in the first three months of when controlling for breastfeeding status (OR: 1.74; 95% CI: 0.88, 3.45; p<0.11).

Conclusions: Prenatal smoke exposure, not breastfeeding and increasing numbers of inhabitants in the home were associated with increased risk for development of respiratory infections in the first three months of life. Due to these associations, these early life influence may put infants at increased risk of later development of asthma.
No. 34 - ABSTRACT – POSTER PRESENTATION

Dose-dependent Relationship between Infant Antibiotic Exposure and the Gut Microbiota Composition at 12 Months Age.

Introduction: Greater prescribing of antibiotics to infants has coincided with an epidemic of allergic diseases such as asthma in developed countries. Asthma is a respiratory disorder characterized by chronic airway inflammation and hyper-responsiveness that leads to episodic airflow obstruction. Infant antibiotic exposure, as well as gut microbiota dysbiosis, are linked to future risk of asthma (1,2). Stronger association observed with multiple courses of antibiotics and asthma suggests biological plausibility (3). The relationship between early life antibiotics and later childhood allergic asthma may be explained by a disturbed gut microbiota. The purpose of this study was to determine the dose-response relationship between antibiotic exposure and gut microbiota composition at 12 months of age.

Methods: This study included a representative sample of full-term infants (n=190) in Manitoba from the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort. Infant antibiotic exposure was obtained from hospital records (maternal intrapartum, newborn) and the provincial prescription database (infant). Birth method was also obtained from hospital records. Fecal samples were collected at approximately 12 months of age, and gut microbiota were profiled using illumina 16S rRNA gene sequencing. Spearman’s correlation was used to measure the strength and direction of association between number of antibiotic courses and median abundance of gut microbiota.

Results: About 61% of infants had been exposed to antibiotics during their first year of life and over 12% had received 3 or more courses. Maternal intrapartum antibiotic and intravenous administration to the newborn was considered as the first antibiotic course, and accounted for 47% of antibiotic exposure. As the number of antibiotic courses increased, the median abundance of genus Streptococcus, Dorea and Lachnobacterium was observed to rise successively in gut microbiota. After stratification by birth method, more statistically-significant dose-related associations were observed in vaginally-born infants, seen as increased levels of Lachnobacterium (Spearman’s correlation(r) = +0.20; p = 0.02) and decreased abundance of Clostridia (r = -0.22; p = 0.01), Bacteroides and Ruminococcus. In caesarean-delivered infants, Blautia and Ruminococcus were observed to decrease in abundance with increasing antibiotic courses.

Conclusions: Multiple courses of antibiotics affect the gut microbiota composition and this association is more pronounced in vaginally-born infants. Dose-dependent associations have been reported between antibiotics and childhood asthma and allergic diseases (3). Hence, affected gut microbes may play an important role in this association by affecting infant immunity and health outcomes.
No. 35 - ABSTRACT – POSTER PRESENTATION


Introduction: Autism spectrum disorder (ASD) is associated with impaired emotion regulation (ER), defined as the ability to maintain homeostasis in response to positive and negative events. Research on the early development of ASD has shown that infants at risk for ASD have difficulty regulating their emotions by 12 months. The early control of emotion may be critical to the development of later social-communicative abilities and, consequently, may affect the onset of ASD symptomology. Given that ER is a multicomponent process, a behavioral-physiological approach is warranted. This study aimed to examine the relationship between behavioral affect and heart-rate during an ER task, and whether these indices predict ASD symptoms in high-risk (HR) infants.

Methods: Participants: Participants were 35 HR infants with an older sibling with ASD, assessed at 12 months.

Emotion Regulation: The ER task (adapted from LabTAB) is comprised of activities designed to elicit positive (bubbles, toy play) and negative (toy removal, masks) emotions. Behavioral affect was coded using Noldus Observer software. Affect was coded for valence (positive or negative) and intensity (to differentiate mild from intense displays of affect). Heart-rate was recorded using Thought Technologies Procom5 Infiniti. Data were processed and transformed into a metric of average change in heart-rate from baseline.

ASD Symptoms: The Autism Observation Scale for Infants (AOSI) was used to measure early signs of ASD.

Analytical Approach: Average values were calculated for behavioral affect and heart-rate across 5-second time bins. Data were analyzed using a series of Spearman rank-order correlations to determine the relation/congruence between behavioral affect and heart-rate, as well as between affect intensity and heart-rate with AOSI score.

Results: A significant correlation between behavioral affect and heart-rate was found for the grooming activity ($r_s=-0.458$, $p=0.003$), but not other ER activities ($p’s>0.05$). Behavioral affect was significantly correlated with AOSI score for bubbles ($r_s=-0.692$, $p<0.001$), toy play ($r_s=-0.337$, $p=0.026$), and grooming activities ($r_s=-0.337$, $p<0.026$). No significant correlations were observed between heart-rate and AOSI score on any ER activities.

Conclusions: Results suggest modest congruence between behavioral affect and heart-rate indices of ER in 12-month-old HR infants. Behavioral affect during positive and negative activities was correlated with ASD symptom expression in HR infants, whereas heart-rate was not. Further work is warranted on modeling physiological responses to various emotion-eliciting activities in HR infants. Using this approach, we may be able to discern behavioral and physiological differences between infants who are diagnosed with ASD from those who are not.
Surgery ABSs: A Healthcare Podcast for Kids
*Marsden N, Marshall J, White J.*

Surgery ABCs is an educational healthcare podcast targeted at pre-school and elementary aged kids to engage them in discovering how their bodies work! Podcasts are becoming increasingly popular as an educational alternative to screen time. While many science-based podcasts are available for this age group, healthcare focused ones are lacking. This gap provides a unique opportunity to create a podcast to empower kids to learn about their bodies, become better patients when they encounter the healthcare system and inspire them to pursue careers in healthcare. The 11 Surgery ABC episodes are centered around questions kids have about the body and what it does! During each episode, the host, her daughter and a medical student explore a body part related to the episode focus question and learn how that area of the body works. Kids also get to learn about a “Doctor of the Day” which highlights a practitioner that works on that area of the body. The podcast, which is available on Spotify and iTunes, has been successful with over 2500 downloads. Future directions include getting feedback from parents and kids and evaluating what they are learning from Surgery ABCs.
Antimicrobial lock solutions for prevention of central venous catheter infections in pediatric patients with intestinal failure.

*Gibson B, McNiven C, Sebastianski M, Featherstone R, Persad R, Robinson J.*

**Introduction:** Children with intestinal failure are dependent on parenteral nutrition (PN) via a central venous catheter (CVC) for survival, and are at high risk of catheter-related bloodstream infections (CRBSIs). Prevention of these infections is imperative, as they result in line removal and loss of access sites. Eventually, there may be no available sites for a CVC, and the child will need an intestinal transplant. Antimicrobial locks (AML) are solutions instilled in CVCs to prevent CRBSI. Presently, there are many solutions available, and limited evidence guiding the optimal use of prophylactic AML solution in children with intestinal failure. A guideline for appropriate prophylactic AML use has the potential to decrease rates of CRBSIs and reduce morbidity and mortality in pediatric intestinal failure patients.

**Methods:** A systematic review of available literature on AMLs used for CRBSI prophylaxis in children with intestinal failure was performed. Studies that used comparator groups with participants including children (age 0-17) with intestinal failure, who have a CVC for PN were screened for inclusion.

**Results:** The primary outcomes are the rate of new CRBSI with AML versus controls, as well as a comparison of each AML type versus controls. Secondary outcomes include: any CVC removal, recurrence of CRBSI, all adverse events attributed to antimicrobial lock solutions, development of infections with antibiotic resistance at any point, length of hospital stay attributed to CRBSI, need for intensive care, any other morbidities or outcomes that were compared in cases and controls. Our preliminary data shows that in 19 studies with a variety of AML solutions, all but one study found a trend toward less CRBSI in the AML lock group. Sample sizes were not adequate and the studies were too heterogeneous to statistically compare lock solutions.

**Conclusions:** This research in progress aims to provide clinicians with guidance on the use of AML for prophylaxis of CRBSI in pediatric patients with intestinal failure. We will provide data for the efficacy of this practice and clarify which solutions have the best outcomes. Some limitations include varying co-morbidities, exposure to prior antibiotics, antimicrobial resistance, and limited patient numbers within the pediatric intestinal failure population.
Lengths of Stay in Children Presenting to High Volume Emergency Departments Varies by Type of Facility.
Rosychuk R, Rowe BH.

Introduction: Emergency Department (ED) crowding is believed to be influenced by multiple factors and no single ED crowding metric has been universally accepted. The study describes ED crowding metrics based on presentations by children to high volume (non-rural) EDs in Alberta, Canada.

Methods: This population-based retrospective study extracted all presentations made by children (age <18 years) between April 2010 and March 2015 to 15 high volume EDs: 5 regional, 8 urban, and 2 academic/teaching children’s hospitals. Time to physician initial assessment (PIA), length of stay (LOS) for discharge and admission dispositions, and proportions left without being seen (LWBS) and against medical advice (LAMA) were calculated based on the start of visit and ED facility. The mean, median, and 90th percentiles for hourly, facility-specific PIA and LOS metrics were obtained. Statistical analyses were descriptive.

Results: Nearly half (48.9%) of the 819,887 presentations were made to the academic/teaching EDs in Calgary and Edmonton; 52.9% were by females and the average age was 8.8 years. The three categories of EDs had similar distributions on most characteristics; however, urban and academic/teaching EDs had more severe triage scores and higher proportions of admissions. Across all EDs, the mean of the median PIA metric, median LOS for discharges, and median LOS for admission were 1h 22m, 2h 46m, and 8h 13m, respectively. Generally, regional hospitals had shorter wait times than urban and academic/teaching hospitals. The mean daily LWBS occurred in 4.5% of presentations (median=0) and LAMA occurred in 0.7% (median=0). There was some variation among ED category. For regional, urban, and academic/teaching hospitals, the daily means were 4.9%, 4.4%, and 4.2% for LWBS, respectively, and 0.6%, 0.6%, and 1.1% for LAMA.

Conclusions: Metrics for PIA were similar across ED category whereas LOS for discharges and admissions varied by ED category. Academic/teaching EDs see the highest volumes and suffer the most severe overcrowding. The impact of crowding on outcomes for children requires further study.
Enhanced Branched Chain Amino Acid catabolism improves contractile function in the failing heart.


Alterations in cardiac energy metabolism can have a profound impact on the establishment and severity of cardiac pathologies including heart failure. In the failing heart, Branched Chain Amino Acids (BCAAs) are markedly elevated causing impaired BCAA oxidation, which can further progress heart failure and influence insulin resistance. Key enzymes in the BCAA catabolic pathway, such as Branched-chain α-keto acid dehydrogenase (BCKDH), are controlled by phosphorylation via kinases such as BCKDH kinase (BCKDK), rendering them inactive. We hypothesized that increasing BCAA catabolism by pharmacologically inhibiting BCKDK would decrease BCAAs and improve the pathophysiology of heart failure. Adult mice were subjected to a transverse aortic constriction or sham surgery to induce pressure overload hypertrophy, and injected with either BCKDK inhibitor (BT2) or vehicle 1-week post surgery. Echocardiography data were obtained after 4 weeks to assess cardiac function, following which hearts were subjected to isolated working heart perfusions. There was a significant decrease in cardiac function (45.8±3.1 vs 54.3±3.8% ejection fraction) in TAC mice compared to sham. The BT2 injection significantly improved cardiac function in both sham and TAC mice (63.0±1.8 and 56.9±3.8% ejection fraction respectively. BCAA oxidation showed improvement with the treatment but only in the sham inhibitor treated hearts, with no changes in cardiac work. Furthermore, a significant decrease in BCKDH phosphorylation due to BT2 injection supports an increase in BCAA catabolism. Additionally, BCKDK expression was significantly decreased in the BCKDK inhibitor treated groups. We conclude that BCKDK inhibition by BT2 results in the improvement of BCAA oxidation and cardiac function in the failing heart. Improving BCAA catabolism may provide a potential future therapeutic approach in treating heart failure.
Mitochondrial protein kinase B (Akt) translocation mediates insulin-stimulated cardiac glucose oxidation.

Karwi QG, Wagg CS, Altamimi T, Lopaschuk GD.

Introduction: Insulin stimulates glucose oxidation, an effect which is associated with simulating pyruvate dehydrogenase (PDH). However, how the insulin signal is transduced from the cell membrane to the mitochondria to stimulate PDH is not known. Protein kinase B (Akt), protein kinase C-delta (PKCδ) and glycogen synthase kinase-3beta (GSK-3β) are main components of the cytosolic insulin signalling pathway and it has been suggested that they can be translocated to the mitochondria following insulin receptor activation in noncardiac tissue. Therefore, we investigated whether any of these kinases has a role mediated cardiac insulin-stimulated glucose oxidation in the heart.

Methods and Results: Male and female C57BL/6 mice were anesthetized and hearts were collected and perfused in the isolated working heart mode. Hearts were perfused with [5-³H] glucose and [U-¹⁴C] glucose to simultaneously measure glycolysis and glucose oxidation rates, respectively, in the presence and absence of insulin. Insulin enhanced the phosphorylation and translocation of Akt¹⁷⁷⁷⁷, PKCδᵀᵣᵣ₃¹¹ and GSK-3B⁹⁹ to the cardiac mitochondria along with enhancing PDH activity by decreasing its phosphorylation. Pharmacological inhibition of Akt using AktiVIII completely abolish the stimulatory effect of insulin on cardiac glucose oxidation rates (354 ± 145 vs 2307 ± 185 nmol. g dry wt⁻¹. min⁻¹ in vehicle-treated hearts, p<0.05). However, pharmacological inhibition of either PKCδ or GSK-3β using Bisindolylmaleimide I or 3F8, respectively, did not have a significant effect on insulin-stimulated glucose oxidation rates. None of the pharmacological inhibitors had any significant effect on cardiac glycolysis.

Conclusions: Insulin mediates its stimulatory effect on cardiac glucose oxidation via a mechanism which involve the activation and translocation of Akt to the mitochondria.
No. 41 - ABSTRACT – POSTER PRESENTATION

Youth and Parent Motivation to Change Lifestyle Habits: Preliminary Findings from the Readiness and Motivation Interview for Families (RMI-Family) Study.


Introduction: Motivation plays a key role in how youth and parents manage pediatric obesity. The Readiness and Motivation Interview for Families (RMI-Family) was conceptualized to better understand youth-, parent-, and family-level motivation to change lifestyle habits known to influence weight and health. The objective of this study was to characterize and compare motivation in youth and parents at the time of entry to a weight management clinic.

Methods: This preliminary analysis of baseline data from a longitudinal study includes information collected between Dec, 2017 and March, 2019 from pediatric weight management clinics in Edmonton and Calgary. Youth (13–17y; BMI ≥97th percentile) and parents were interviewed separately and the importance of lifestyle habits and readiness to change youth lifestyle habits was assessed.

Results: In total, 26 youth (50.0% female; 14.8±1.2y; 33.5±4.4kg/m²) and 25 parents (88.0% female; 45.2±9.9y; 32.8±6.9kg/m²) participated. Parents reported higher ratings of importance (all p<0.05) than youth for physical activity, screen time, intake of treat foods, overeating and eating when not hungry, but not for sleep (p>0.05). Parents also reported higher readiness to change youth lifestyle habits for physical activity, screen time, intake of treat foods and overeating (all p<0.05) than youth; however, no differences were reported for eating when not hungry (p>0.05).

Conclusions: In these preliminary analyses, parents tended to report higher levels of importance and readiness to change youth lifestyle habits than youth. The relevance of these differences in predicting youth health outcomes and health service use over time will be examined in future analyses as our study remains ongoing until 2020.
No. 42 - ABSTRACT – POSTER PRESENTATION

RETAIN board game training simulator as a summative tool to evaluate professionals’ neonatal resuscitation knowledge.
Ghoman S, Cutumisu M, Brown MRG, Schmölzer GM.

Introduction: Healthcare professionals (HCPs) must be trained in neonatal resuscitation to improve outcomes for newborns (1 million infants die at birth annually, 60-70% deaths caused by communication errors and deviations from protocol). Currently, HCPs use the neonatal resuscitation textbook while answering a Multiple Choice Questionnaire about neonatal resuscitation knowledge. This approach is insufficient. Our objective is to examine if the RETAIN board game training simulator can be used as a summative assessment tool to objectively assess HCPs’ neonatal resuscitation knowledge.

Methods: HCPs from the Royal Alexandra Hospital Neonatal Intensive Care Unit were recruited. Participants completed i) a pre-test (open-answer neonatal resuscitation scenario), ii) a short tutorial, and ii) one round of the RETAIN board game. Sessions were video-recorded. The RETAIN board game (https://playretain.com, RETAIN Labs Medical Inc., Edmonton, Canada) consists of a game board with an image of an infant, where learners use equipment, supplies, action cards, and adjustable monitors to prepare and perform evidence-based neonatal resuscitation simulations. Performance on the pre-test and during the game was scored using Neonatal Resuscitation Program 2015 guidelines and compared using Spearman Pearson correlation. Data is reported as mean (Standard Deviation (SD)).

Results: 20 HCPs participated (19 female; Nurse n=8, Respiratory Therapist n=4, Nurse Practitioner n=4, Neonatal fellow n=4; mean (SD) 11.3 (9.1) years of experience). The mean (SD) pre-test score was 8.35 (1.81) out of 16 (52%), while the game performance score was 18 (5.27) out of 40 (45%). Participants’ pre-test and game performance scores were moderately correlated (r=0.45, p=0.05).

Conclusions: Although the game scenario was more difficult than the pre-test, HCPs’ performance on the RETAIN board game was moderately associated with their scores on a traditional summative assessment tool (i.e., open-answer resuscitation scenario). With further refinements of the game and comparable-difficulty scenarios for the pre-test and the post-test, RETAIN could be used as an alternative summative assessment tool to evaluate HCPs’ knowledge. Potential applications of the RETAIN summative assessment tool include evaluating HCPs’ knowledge after completing the neonatal resuscitation provider course, or evaluating HCPs’ competencies for the purpose of quality measurement of healthcare delivery.
No. 43 - ABSTRACT – POSTER PRESENTATION

Varying Peak Inflation Pressures during Sustained Inflation with Chest Compressions and their Effect on Return of Spontaneous Circulation in a Porcine Model of Asphyxia.
Patel MS, Cheung P-Y, Lee TF, O'Reilly M, Schmölzer GM.

Introduction: The current resuscitation guidelines recommend a 3:1 compression to ventilation ratio (3:1 C:V) during cardiopulmonary resuscitation. We have described a novel chest compression technique in using sustained inflation during chest compressions (CC+SI), which significantly improved Return of Spontaneous Circulation (ROSC) compared to the 3:1 C:V in asphyxiated newborn piglets. While this is encouraging, the optimal peak inflation pressure needed during CC+SI is unknown. The study aimed to examine the optimal peak inflation pressure during CC+SI, which will improve time to ROSC. We hypothesized that a peak inflation pressure of 20 cmH2O compared to 30 cmH2O will improve time to ROSC.

Methods: Newborn piglets were intubated via tracheostomy, and femoral vessels were catheterized for drug administration and hemodynamic measurements. Newborn piglets were allowed to recover from surgery for an hour, which was followed by 30min hypoxia and asphyxia. Asphyxia was achieved by clamping the endotracheal tube until cardiac arrest defined by zero carotid blood flow. Piglets were randomized to CC+SI with peak inflation pressure of 10, 20, or 30 cmH2O (CC+SI 10, CC+SI 20, or CC+SI 30) using computer generated randomization. During resuscitation, piglets received CC+SI with peak inflation pressure of 10, 20, or 30 cmH2O according to group allocation. The primary outcome was time to ROSC. Statistical analysis was done using one-way ANOVA with bonferroni post-test.

Results: The median (IQR) time to cardiac arrest was 240s (156-415s), 522s (338-600s), and 500s (364-557s) for CC+SI 10, CC+SI 20, and CC+SI 30 (p=0.06) respectively. Time to ROSC was similar between groups with 75s (63-193s), 94s (78-210s), and 85s (70-90s) for CC+SI 10, CC+SI 20, and CC+SI 30 (p=.56) respectively. However, the time to cardiac arrest following asphyxia was shorter in the CC+SI 10 group compared to the other intervention groups. Overall, 5/8, 7/8, and 3/8 piglets achieved ROSC for CC+SI 10, CC+SI 20, CC+SI 30 (p=.012) respectively. Although, fewer CC+SI 30 piglets achieved ROSC, this did not reach statistical significance.

Conclusions: The time to ROSC was similar between CC+SI 10, CC+SI 20, or CC+SI 30 groups.
Prophylactic Indomethacin: The impact on brain and gut injury may be gestational age dependent

Introduction: Extremely low gestational age newborns (ELGAN) have higher rates of mortality and brain or gut injury. Prophylactic indomethacin (PI) has been shown to reduce severe neurological injury (SNI); however, studies suggest an association of indomethacin with spontaneous intestinal perforation (SIP). To evaluate association of PI on early mortality (<10 days of age) or SNI and early mortality or SIP across gestational age groups in babies born at <29 weeks’ (w) GA.

Methods: Data from the Canadian Neonatal Network (CNN) database were reviewed for neonates born at GA 23⁰ - 28⁶ weeks and admitted to participating Neonatal Intensive Care Units (NICU) in Canada during 2010 – 2017. Infants with major malformations and moribund on admission were excluded. Infant characteristics were compared between groups with and without receipt of PI. The impact of PI on the primary outcomes (early mortality/SNI and early mortality/SIP) across GA was assessed using multivariable logistic regression model with Generalized Estimating Equations (GEE) approach to account for the clustering of infants within each site, after adjustment for confounders.

Results: Of 12515 included eligible infants, 1,435 were exposed to PI. The rate of receipt of PI was 28.79% at 23w, 26.59% at 24w, 18.82% at 25w, 9.76% at 26w, 5.68% at 27w and 2.35% at 28w GA. The PI group were of lower GA, lower birth weight, and had higher severity of illness (Score for Neonatal Acute Physiology with Perinatal extension, SNAP II PE score) on admission (Table 1). Univariate analysis showed PI was associated with significantly lower early mortality/SNI in infants born at 23w GA and lower early mortality/SIP at 23-24w GA but increased early mortality/SIP at 28w (Table 2). Multivariable analysis revealed that PI was associated with reduced early mortality/SNI, early mortality/SIP and death before discharge at 23-25w, 23-24w and 23-24w GA respectively. PI was associated with increased risk of early mortality/SIP at 26-28w GA (Table 3; Figure 1).

Conclusions: In a large national cohort of ELGANs, and after adjustment for known confounders, PI for neonates at 23-25w GA was associated with lower mortality with SNI or SIP. Use of PI at 26-28w GA, was associated with harm.
No. 45 - ABSTRACT – POSTER PRESENTATION

Skeletal muscle-specific knock-out of succinyl-ketoacid-CoA transferase (SCOT) prevents the decline in cardiac function during heart failure.

Dijk S, Valcheva E, Jarman M, Lawley M, Armstrong H, Carroll M, Huynh H, Wine E.

Introduction: The failing heart has defects in metabolic processes that normally allow for proper ATP production which is necessary to maintain contractile function. Recent studies have shown that the failing heart upregulates ketone metabolism and relies on ketones, namely β-hydroxybutyrate (βOHB), as a fuel, presumably to increase overall energy production. Ketones, also referred to as ketone bodies, and comprised of βOHB and acetoacetate, are most notably produced by the liver in conditions of low glucose, such as fasting. Furthermore, the oxygen sparing effects of βOHB are thought to be beneficial for the failing heart, alongside other beneficial signaling effects. Thus, regardless of the role that endogenous βOHB plays in heart failure (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 in HF.

Methods: To determine whether elevating circulating ketones may improve cardiac function in HF, we utilized a tamoxifen-inducible skeletal muscle-specific knockout of succinyl-CoA:3-ketoacid-CoA transferase (smSCOT-KO), the rate limiting enzyme in ketone catabolism. We then subjected these smSCOT-KO and wild-type littermate mice to transverse aortic constriction (TAC) surgery to generate pressure overload-induced HF. Echocardiography was used to assess heart function, and levels of circulating glucose and βOHB were also measured. Lastly, protein expression of SCOT was confirmed by immunoblot analysis.

Results: SCOT expression was significantly reduced in skeletal muscle of smSCOT-KO compared to wild-type mice to 5% and 4% in gastrocnemius and soleus, respectively (p<0.001); there were no appreciable changes in cardiac SCOT expression. Given that ketones are largely utilized in skeletal muscle, the smSCOT-KO results in a 1.5-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 (47% vs 32% ejection fraction; p=0.0042) and diastolic (E/E'; p=0.002) function in smSCOT-KO compared to wildtype littermates.

Conclusions: Together, these data are the first to show that smSCOT-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.
Understanding self-regulation strategies in adolescents with FASD: An intervention study.

Kryska K, Pei J, Joly V, Kapasi A, Hodgetts S, Abele-Webster L, Rasmussen C.

Introduction: Fetal Alcohol Spectrum Disorder (FASD) is a diagnosis describing individuals who have been exposed to alcohol prenatally and consequently present with impairments in many areas, including the ability to regulate behaviours. The Alert program® is an evidence-based self-regulation intervention that supports the identification of arousal levels and the exploration of self-regulation strategies. In this study we aimed to describe: 1) the types of strategies chosen by the adolescents with FASD in this intervention, and 2) whether strategy use is generalized outside of the intervention.

Methods: Adolescents (n = 23) aged 11 to 18 years with FASD participated in the Alert program® intervention, which consisted in weekly individual sessions with a trained interventionist over a ~12-week period. Information collected from each intervention session including: 1) self-regulation strategies chosen in-session, and 2) reported strategy use outside of session. Participants also completed a satisfaction questionnaire following the intervention.

Results: Adolescents used both cognitive (e.g. card games and puzzles) and sensory (e.g. listening to music and colouring) self-regulation strategies throughout the intervention. Developmental trends were noted, as younger adolescents (11-13 years) preferred sensory (66%) strategies, but many still used cognitive (27%) strategies. Older adolescents (14-17 years) relied much more on sensory strategies (78%) compared to cognitive strategies (17%). Caregiver and adolescent reports of strategy use outside of sessions revealed steadily increasing use of self-regulation strategies throughout the intervention, from 25% at the beginning of the intervention to 75% at the end. Additionally 90.9% of adolescents report that self-regulation strategies learned during the intervention were helpful in daily life, 81.8% report using strategies at school, and 68.2% report using strategies at home.

Conclusions: Among adolescents with FASD, both younger and older adolescents preferred sensory strategies to cognitive strategies. Cognitive strategies were preferred more by younger adolescents compared to older adolescents. As the intervention progressed, self-regulation strategies were integrated and viewed as helpful tools in daily life. Self-regulation strategies appear to be more generalizable in school settings, compared to at home. It is not too late for adolescents with FASD to develop awareness of self-regulation, and use effective strategies that reach outside of clinical intervention.
No. 47 - ABSTRACT – POSTER PRESENTATION

The Paediatrician as a Leader: An Educational Intervention for High-Value Care.
Foulds J, Forbes K, Rajani H.

Introduction: The CanMEDS framework for physician competency defines necessary competencies of medical practice, laying the foundation for medical education and subsequent practice in Canada to meet patient needs. The role of Leader highlights the importance of quality improvement, stewardship, health care resource allocation and ability to apply evidence and management processes to facilitate cost-appropriate care. Educational innovations in this domain have not previously been described.

Methods: We sought to evaluate the impact of an educational intervention developed to foster stewardship of health care resources for paediatricians in training. An educational workshop on high-value care was created for general paediatric residents. Prior to workshop development, the study team procured local costing information from microbiology, general chemistry/laboratory, pharmacy, and radiology. During the workshop, individual, small group and interactive activities were used to explore clinical decision making and associated costs, radiation dosing, and non-monetary implications of care. A pocket-card reference was developed for use during the exercises. To assess the impact of the workshop, participants completed a post-workshop reflection asking them to identify lessons learned and an action plan for providing high-value care. Qualitative exploration of statements was conducted using thematic analysis; individual responses were coded and grouped into three overarching themes for both lessons learned and action plan.

Results: Forty-three learners participated in the workshop. Post-workshop reflections yielded 93 lessons learned statements, and 67 action plan statements. Lessons learned were grouped into three themes: Scope, Content and Judgement Statements. Within Scope, most statements were general (80%) versus specific. Content areas most frequently cited included cost (61%), diagnostic imaging (28%) including radiation exposure (14%), and non-monetary costs of care (17%). Inferences about aspects of learnings, such as those referring to expense, value or waste, were labelled as Judgement Statements, and were present in 50% of the responses. Action plan statements were grouped into themes of Scope, Content and Action Words. Responses were again generally focused (87%). Most frequent Content subtheme responses were: tests (37%), non-monetary costs of care (21%), and diagnostic imaging (12%). Action words were grouped into seven categories with Consider as most frequent (46%).

Conclusions: Reflections on non-monetary costs and action plans that consider how investigations might change management seemed to resonate with our single-centre paediatric trainees. Longitudinal follow-up may help identify most effective practice-impacting components of this educational workshop.
No. 48 - ABSTRACT – POSTER PRESENTATION

Availability of the therapeutic oxygen on pediatric wards in Uganda and Eastern Democratic Republic of the Congo

Clarke C, Opoka RO, Sophie N, Claude KM, Huang Y, Mian Q, Hawkes MT.

Introduction: Pneumonia is the leading cause of child mortality globally. Oxygen therapy is a vital component of treatment of pediatric pneumonia. Despite its importance, poor availability of oxygen therapy exists in many resource-limited settings. This is primarily due to difficulty in restocking cylinder oxygen and finding reliable electricity sources which oxygen concentrators need to function. Previous studies have demonstrated that oxygen concentrators powered by solar panels are an effective alternative to oxygen cylinders in reducing mortality and recovery time among children with pneumonia.

Methods: To determine if a gap in oxygen therapy exists, and the potential scalability of solar powered oxygen delivery in Uganda and Eastern Democratic Republic of Congo (DRC), we collected data at 55 rural hospitals and clinics. At these sites we interviewed and administered a standardized questionnaire to one or more key informants (e.g., charge nurse, clinician).

Results: We conducted a cross-sectional survey of oxygen delivery capabilities of pediatric wards at 55 district hospitals and health centers (39 in Uganda and 16 in the DRC). Between July 2017 and July 2018, we visited 55 health facilities in Uganda and Eastern DRC with inpatient pediatric services. While cylinder oxygen was available at 24/55 (44%) of sites, dedicated cylinders were not available on the pediatric wards of any health facility. Oxygen concentrators were present at 48 (87%) of sites. Of these, 37 concentrators (86%) were operational. Of these, only 18 (58%) produced oxygen with >= 80% purity. Additionally, only 23% of sites had oxygen concentrators available on pediatric wards. 39/54 (72%) of sites reported that power outages were frequent. While 49/55 (89%) of sites had generators available, only 9/49(18%) turned them on when children needed oxygen. Because electricity is necessary to run oxygen concentrators, this suggests access to a reliable power source is a major obstacle in delivering oxygen therapy. Overall, only 28/55 (51%) of sites had oxygen available for pediatric use.

Conclusions: These findings suggest that a high proportion of health facilities that treat children do not have reliable access to therapeutic oxygen. Solar powered oxygen delivery, generated autonomously on-site, may be a viable alternative.
Effect of perinatal iron deficiency on neonatal cardiac mitochondrial function.

Holody C, Woodman AG, Carpenter R, Lemieux H, Bourque SL.

Introduction: Iron deficiency during gestation can predispose offspring to chronic disease in later life. Pregnant women are at a high risk for developing iron deficiency due to increased iron demands; an estimated 38% of women worldwide will develop anemia throughout pregnancy. Thus, iron deficiency likely contributes significantly to the global burden of chronic disease. Given that iron is essential for oxygen transport and a component of the electron transport system, we hypothesized that perinatal iron deficiency would permanently alter cardiac mitochondrial function through the neonatal period.

Methods: Female rats were fed either an iron-restricted diet (3-10mg/kg) or an iron-replete diet (35mg/kg) before and during pregnancy. At birth, all dams were fed standard rat chow; pups were weaned onto standard rat chow at postnatal day (PD) 21. At PD 1, 14, and 28, hearts from male and female offspring were collected. Electron transport system and fatty acid β-oxidation capacities were assessed in permeabilized cardiac fibres using High-Resolution Respirometry. Data were analyzed by 2-way ANOVA for the effects of iron-restriction and PD, with Tukey’s post hoc test.

Results: Hemoglobin levels were reduced in iron-deficient pups at PD-1 (P<0.001) and PD-14 (P<0.05), but not at PD-28 (P>0.05). Body weights of iron-deficient pups were reduced at all ages compared to control pups (P<0.05). Heart weight relative to body weight was larger in iron-deficient pups at all ages (P<0.001). Mitochondrial respiration (O₂ flux per fiber mass) increased with age; flux control ratios suggest this may be due to differences in mitochondrial content. Overall, mitochondrial respiration was similar between iron-deficient and control groups. However, iron-deficient females showed an increased capacity to oxidize medium vs. long chain fatty acids (P=0.006) compared to controls. A similar trend was observed in male offspring (P=0.08).

Conclusions: Perinatal iron deficiency is associated with minor changes in cardiac mitochondrial function compared to other tissues (i.e. kidney, liver), albeit energy substrate utilization may be altered.
No. 50 - ABSTRACT – POSTER PRESENTATION

Perinatal Iron Deficiency and High Salt Diet in Adulthood Sex-Dependent Hypertension, Renal Mitochondrial Dysfunction and Oxidative Stress.

Introduction: Susceptibility to cardiovascular disease in later life can be programmed by stressors during pregnancy, such as perinatal iron deficiency (ID). ID is the most common nutritional deficiency worldwide, affecting an estimated 23% of pregnant women in developed nations. We have previously shown perinatal ID causes fetal kidney mitochondrial dysfunction and oxidative stress, although it remains unclear whether these effects persist. Here, we studied the effects of perinatal iron-deficiency on adult blood pressure, kidney mitochondrial function and reactive oxygen species in male and female offspring; furthermore, we sought to determine if these effects are exacerbated by a high-salt diet — a cardiovascular stress common in developed nations.

Methods: Sprague Dawley rats were fed either an iron replete (control; CTL) or low iron diet (perinatal ID) 2 weeks prior to and throughout pregnancy. Upon giving birth, all dams and offspring were fed an iron replete diet. Six weeks prior to experimentation, ID and CTL offspring were fed either a normal-salt (NS; 0.26% NaCl w/w) or high-salt (HS; 5% NaCl w/w) diet. Blood pressure measurements were made under isoflurane anesthesia using indwelling catheters. Isolated kidneys were separated into medullary and cortical homogenates for mitochondrial respiration (Oroboros Oxygraph-2k respirometer) and content assessments via citrate synthase (CS) activity assay. Cytosolic superoxide and nitric oxide (NO) were assessed by dihydroethidium and DAF-FM diacetate fluorescence staining, respectively, in cryopreserved kidney sections.

Results: ID resulted in growth restriction and a 52% decrease in offspring hemoglobin at birth. Systolic blood pressure was increased in male, but not female, 6-month-old offspring by both ID (P=0.01) and HS (P=0.02). Male offspring medulla exhibit increased CS activity (P=0.003) and global respiration (P<0.05) due to HS, and reduced succinate-dependent respiration due to ID (P<0.05). Complex IV activity was reduced by the combination of ID and HS in the cortex of male offspring (interaction P=0.03). ID resulted in increased cytosolic superoxide (P<0.001) concomitant with decreased NO (P<0.001) in the medulla and cortex, whereas HS further increased cortical superoxide (P=0.04). Female offspring exhibited no alterations in mitochondrial function or quantity or NO levels, albeit there was subtle but significant interaction effect (P<0.05) in both the cortex and medulla

Conclusions: Perinatal ID combined with a HS diet induces sex-dependent renal mitochondrial dysfunction and oxidative stress, which is associated reductions in renal NO bioavailability and hypertension in male offspring.
No. 51 - ABSTRACT – POSTER PRESENTATION

Tricuspid valve prolapse in children with hypoplastic left heart syndrome patients requiring tricuspid valve repair is due to leaflet mal-adaptation, not sub-valve changes – a quantitative three-dimensional echocardiography study.


Background: Tricuspid valve regurgitation (TR) is associated with morbidity and mortality in hypoplastic left heart syndrome (HLHS). Over 25% of HLHS patients require tricuspid valve (TV) repair within 10 years, while the mechanism of TR remains poorly understood. This study explores TV remodeling in HLHS requiring surgical repair, using novel quantitative three-dimensional echocardiography (3DE) to further understand the mechanisms of TV failure in HLHS.

Methods: This case-control study with prospectively acquired 3DE in 72 children with HLHS, 36 children prior to TV repair (group 1) and 36 age- and stage-matched controls with no TV repair and mild or less TR (group 2). All 3DE were analyzed using a specific custom TV software (MATLAB) to quantitate TV annulus and leaflet area (Figure), prolapse and tethering volumes, and bending angle. TV leaflets were segmented into the anterior (AL), septal (SL) and posterior (PL) to measure regional areas and volumes. We also measured position of papillary muscle (PM) and chord length. Variables were indexed by body surface area (BSA), and comparison was performed using t-test with significance at p<0.05.

Results: Group 1 and 2 had similar age and BSA (mean: 2.3 years; 0.47 m²) at assessment. Group 1 had larger total annulus (10.3 vs 8.4 cm²/m², P< 0.001) and leaflet (11.7 vs 9.3 cm²/m², P= 0.002) area. SL area (2.66 vs. 2.00 cm²/m², p= 0.009) was larger and AL trended to being larger (5.2 vs 4.2 cm²/m², P= 0.05). Group 1 had larger total prolapse volume and for each leaflets (Total leaflet 140 vs 5.8 μl/m², P= 0.002; AL: 39.4 vs 2.2 μl/m², p= 0.004; SL: 2.2 vs 0.16 μl/m², p= 0.017; PL: 2.7 vs 0.12 μl/m², p= 0.032). No difference in tethering volume for total or each leaflet. Group 1 had greater bending angle (156.6 vs 151.8 degree, p= 0.034), hence a flatter annulus. No difference in PM angle and length, nor chord length between the groups.

Conclusions: Failing TV in children with HLHS had larger annulus and leaflet size, specifically in SL and AL, and greater prolapse of all the leaflets compared to HLHS with competent TV. Despite increased leaflet prolapse, there is no difference in chord or PM length, suggesting that failing TV prolapse is due to leaflet mal-adaptation, rather than chord or PM changes. This novel insight suggests future research into TV leaflet mal/adaptation in HLHS may be important.
No. 52 - ABSTRACT – POSTER PRESENTATION

Left Ventricular Dysfunction is a Common Feature of Neonatal Ebstein’s Anomaly and Tricuspid Valve Dysplasia but not Pulmonary Atresia with Intact Ventricular Septum.
Teramachi Y, Hornberger LK, Howley L, van der Velde ME, Eckersley LG.

Introduction: Neonates with severe Ebstein’s anomaly and tricuspid valve dysplasia (EA/TVD) are often hemodynamically unstable with low systemic perfusion and hypoxia; whereas, this is uncommon in another critical right heart lesion, pulmonary atresia with intact ventricular septum (PAIVS). We have recently demonstrated left ventricular (LV) dysfunction and dyssynchrony to be common in fetal EA/TVD but not PAIVS. In the current study we sought to explore LV function and mechanics in neonatal EA/TVD with comparison to PAIVS in the early neonatal period.

Methods: We identified cases of neonatal EA/TVD (n=30) and PAIVS (n=17) encountered from 2004-2018. We assessed LV function using 2D, Doppler-derived, longitudinal and circumferential deformation (6-segmental Vector Velocity Imaging) and dyssynchrony indices (standard deviation of time-to-peak, T2PSD) and a novel global dyssynchrony index (DI) in the first 48 hours after birth. Results are described as mean ± standard deviation, or median (95% confidence intervals). Comparisons between diagnostic groups were performed using t-test and Wilcoxon test.

Results: Gestation at birth was earlier in EA/TVD than PAIVS (36.4 ± 2.2 weeks vs 38.1±2.4 weeks p=0.03). Five cases of EA/TVD required extra-corporeal membrane oxygenation. 1 EA/TVD and 1 PAIVS died in the first 30 days. 16 cases in EA/TVD had antegradate flow from the right ventricle.[LH1]The LV fractional area change and global circumferential strain were reduced in EA/TVD [EA/TVD 41.9% (37.9-48.1) vs PAIVS 51.9% (48.1-54.5) p=0.002; EA/TVD -15.9% (-12.1 - -17.7 vs PAIVS -24.1% (-19.9 - -24.5) p<0.001), and the septum was flattened (eccentricity index EA/TVD 1.33 (1.26-1.46) vs PAIVS 1.04 (1.01-1.17), p<0.001). There was increased dyssynchrony in EA/TVD (DI of Radial Strain 0.14 (0.12-0.3) vs 0.05 (0.02-0.17) p=0.006; DI of Circumferential Strain 0.17 (0.16-0.35) vs 0.08 (0.05-0.1) p=0.003). Left ventricular ejection fraction, global longitudinal strain, cardiac output and LV Tei index were not different between EA/TVD and PAIVS.

Conclusions: LV radial and circumferential deformation was impaired in cases of EA/TVD, with increased dyssynchrony. Further work will examine the impact of LV mechanics on outcome and requirements for medical support in early life.
A novel measure of dyssynchrony outperforms traditional methods during RV pacing in pediatric patients.

**Background:** Electromechanical dyssynchrony is common in pediatric patients with cardiomyopathies and congenital heart disease and is associated with reduced cardiac output. Assessment of dyssynchrony in pediatric patients guides potential for response to resynchronization therapy, however current echocardiography measures are laborious, angle-dependent and poorly predict response to resynchronization. In this study, we aimed to compare a novel deformation-based measure to standard approaches.

**Methods:** We prospectively recruited seven patients with normal cardiac anatomy undergoing electrophysiological study under general anesthetic for ablation of supraventricular tachycardia. Following successful ablation, a baseline echocardiogram was performed. The right ventricular apex was then paced at 10bpm above baseline to create dyssynchrony, and the echocardiogram was repeated. Offline analysis included global measures of cardiac function (LV output by Doppler continuity equation, Simpson’s biplane ejection fraction, global longitudinal and circumferential strain (LS, CircS) and measures of dyssynchrony (long and short axis (papillary muscle level) septal-posterior wall motion delay (SPWMD), time to peak longitudinal and circumferential strain standard deviation (T2PSD), novel DI (Figure).

**Results:** Patient ages ranged from 6.9 to 15.7 years. Baseline QRS duration was 88±9, and paced QRS duration was 133±21ms, p<0.001. Pacing resulted in impaired global function, with reduced peak global LS, CircS, ejection fraction and stroke volume. Longitudinal and Circumferential DI increased with pacing. LS T2PSD was also increased. Other measures of dyssynchrony were not significantly different (Table).

**Conclusions:** Right ventricular pacing minimally above baseline heart-rate resulted in impaired measures of LV global function. A novel dyssynchrony index was more sensitive than standard measures in detection of pacing related dyssynchrony.
### BASELINE vs PACED:

<table>
<thead>
<tr>
<th>Metric</th>
<th>Baseline</th>
<th>Paced</th>
<th>Percent Change</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STROKE VOLUME (ML)</strong></td>
<td>52.0</td>
<td>36.0</td>
<td>-31%</td>
<td>0.05</td>
</tr>
<tr>
<td><strong>CARDIAC INDEX (L/MIN/M2)</strong></td>
<td>3.11</td>
<td>2.61</td>
<td>-16%</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>LVEF (%)</strong></td>
<td>52.2</td>
<td>46.8</td>
<td>-10%</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>PEAK GLOBAL STRAIN (%)</strong></td>
<td>-15.7</td>
<td>-11.1</td>
<td>-29%</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>PEAK GLOBAL CIRC. STRAIN (%)</strong></td>
<td>-15.2</td>
<td>-9.8</td>
<td>-36%</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Q TO MVOI</strong></td>
<td>571</td>
<td>667</td>
<td>17%</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>Q TO AVOI</strong></td>
<td>107</td>
<td>199</td>
<td>86%</td>
<td><strong>0.001</strong></td>
</tr>
<tr>
<td><strong>Q TO PVOI</strong></td>
<td>81</td>
<td>108</td>
<td>33%</td>
<td>0.14</td>
</tr>
<tr>
<td><strong>Q TO AAVCI</strong></td>
<td>490</td>
<td>611</td>
<td>25%</td>
<td><strong>0.005</strong></td>
</tr>
<tr>
<td><strong>SPWD LONG AXIS (MS)</strong></td>
<td>61.0</td>
<td>113</td>
<td>85%</td>
<td>0.25</td>
</tr>
<tr>
<td><strong>SPWD SHORT AXIS (MS)</strong></td>
<td>72.0</td>
<td>112</td>
<td>56%</td>
<td>0.49</td>
</tr>
<tr>
<td><strong>GLOBAL LS DI</strong></td>
<td>0.05</td>
<td>0.13</td>
<td>160%</td>
<td><strong>0.03</strong></td>
</tr>
<tr>
<td><strong>LS T2P (MS)</strong></td>
<td>386</td>
<td>371</td>
<td>-4%</td>
<td>0.28</td>
</tr>
<tr>
<td><strong>LS T2PSD (MS)</strong></td>
<td>39</td>
<td>72</td>
<td>85%</td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td><strong>CIRC. STRAIN DI</strong></td>
<td>0.12</td>
<td>0.29</td>
<td>142%</td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td><strong>CIRC. T2P (MS)</strong></td>
<td>354</td>
<td>376</td>
<td>6%</td>
<td>0.39</td>
</tr>
<tr>
<td><strong>CIRC.T2PSD (MS)</strong></td>
<td>92</td>
<td>106</td>
<td>15%</td>
<td>0.50</td>
</tr>
</tbody>
</table>
Cardiac magnetic resonance parameters associated with surgery in a pediatric and young adult population with chronic aortic regurgitation.

Moray A, Pagano J, Tham E.

Introduction: The timing for intervention in patients with significant chronic aortic regurgitation (AR) is based on symptoms and 2-dimensional echocardiography measurements of LV diameters and function. However, threshold dimensions in adults do not apply to children. Because of its high accuracy and reproducibility cardiac magnetic resonance imaging (CMR) is being increasingly used in the evaluation of AR. However there is limited data on the use of CMR parameters to guide surgical decision making in pediatrics. We examined associations between CMR quantification of AR and left ventricular (LV) volumetric function and the need for surgical intervention.

Methods: Forty-one children and young adults with aortic regurgitation who had undergone CMR at our institution were retrospectively divided into two groups based on subsequent need for aortic valve surgery. CMR consisted of bSSFP cine imaging for assessment of ventricular volumes, mass, and ejection fraction, and phase contrast imaging for quantification of aortic regurgitant fraction (RF) and indexed regurgitant volume (RVi). Left ventricular (LV) dimensions were taken in end diastole (LVEDD) and end systole (LVESD) from the 3 chamber view to compare with ventricular volumes using Pearson correlation coefficient. For patients in the surgical group, the CMR immediately prior to the intervention was included, while the most recent CMR was used for those in the non-surgical group. Differences in CMR parameters between the 2 groups were compared using unpaired t-tests. Receiver operating characteristic (ROC) analysis identified CMR parameters with discriminatory ability towards primary end point of surgery (area under the curve AUC >0.7). Cutoff values were determined using the Youden index.

Results: The demographic and CMR features of the two groups are shown in Table 1. Patients who underwent surgery (n=20) had significantly larger ventricular dimensions, volumes and aortic regurgitant fraction than those without surgery (n=21). Results of ROC analysis (Table 2) demonstrated that aortic RF and RVi had the highest discriminatory power (AUC of 0.93 and 0.92 respectively). Indexed LV volumes had good but slightly reduced discriminatory power (AUC 0.85 and 0.89 for indexed end diastolic and end systolic volume respectively) towards surgery. 2D measurements showed moderate correlation with ventricular volumes (LVEDD vs LVEDV, r=0.5, p = 0.0008 and LVESD vs LVESV r=0.57,p=0.0002).

Conclusions: Guidelines for surgical intervention in children with chronic aortic regurgitation are lacking. Furthermore, adult 2D echo measurements of LV dimensions and AR quantification may not apply to the pediatric population. Our study highlights the significant differences in CMR parameters between patients who underwent aortic valve surgery and those who were managed conservatively. We identified potential threshold values for surgery and this provides an opportunity for further research to formulate guidelines for aortic valve surgery in children with chronic AR.
No. 55 - ABSTRACT – POSTER PRESENTATION

Survival and Neurodevelopmental Outcome after Non-Cardiac Extracorporeal Life Support in Children.
Ryan L, Joffe A.

Introduction: As extracorporeal life support (ECLS) survival has improved there has been a growing interest in evaluating neurodevelopmental outcomes of children who have undergone ECLS. Recent studies have focused on survival to discharge, or survival to follow up, with little description of neurodevelopmental outcomes beyond survival. Some have developed tools to predict in-hospital mortality, but their practicality has yet to be determined. The objective of this study is to describe the survival and neurodevelopmental outcomes of children who underwent non-cardiac ECMO using follow-up data collected from The Registry. We will also evaluate the P-PREP and Ped-RESCUERS prognostic tools on our population.

Methods: This study will be conducted as a retrospective chart review using data from The Registry database, which includes all patients under 6 years of age who received non-cardiac ECMO from January 1999 to December 2016. All survivors received multidisciplinary neurodevelopmental assessments through existing follow-up clinics performed at 2 and 4 years. Pre- and post-ECMO variables will be collected and analysed using univariate analysis (linear regression for continuous outcomes; logistic regression for categorical outcomes) to elucidate which variables have predictive power for neurodevelopmental outcome. The neurodevelopmental outcomes will be assessed by measurement of early outcomes, including duration of ECMO, PICU admission days post-ECMO, duration of hospital admission, death in hospital and at 30 days, as well as late outcomes, including early and late mortality, and the Bayley Scale of Infant Development-II at age 2 and 4 years follow up.

Results: The primary outcomes of interest will be neurodevelopmental status using the Bayley Scales of Infant Development-II, as well as disability, including visual and/or auditory impairment, cerebral palsy, or delay on motor or psychomotor developmental indices. The secondary outcomes will be early and late mortality and morbidity.

Conclusions: Despite greater interest in assessing long-term outcomes following ECMO, there is a deficit in understanding of the long-term neurodevelopmental and functional outcomes for pediatric patients undergoing non-cardiac ECMO. Our objective is to report our centre’s experience with pediatric non-cardiac ECMO, including survival, morbidity, and neurodevelopmental outcome. We also seek to identify independent variables that predict these outcomes and test the P-PREP and Ped-RESCUERS prognostic scoring tools against our population. We anticipate that greater understanding of long-term sequelae will facilitate more appropriate rehabilitation therapies, identify important variables associated with poorer outcomes, and provide guidance when counseling parents.
No. 56 - ABSTRACT – POSTER PRESENTATION

Undiagnosed Atypical Kawasaki Disease Presenting with Sudden Cardiac Arrest due to Myocardial Ischemia.


Introduction: Sudden cardiac arrest (SCA) due to isolated myocardial ischemia is rare in children. Accurate coronary artery (CA) imaging in children is challenged by small size, and multiple modalities may be required for accurate diagnosis.

Methods: 12 month old male with a remote history of febrile illness and mucocutaneous changes at 4 months, presented with an out of hospital cardiac arrest preceded by a three week history of irritability and poor feeding. He received cardiopulmonary resuscitation with return of spontaneous circulation. He had significantly elevated troponin but normal inflammatory markers. ECG showed intermittent ST segment depression in V2-V3. Echocardiogram showed bilateral CA ectasia, proximal CA aneurysms and decreased left ventricular function with regional wall motion abnormalities. He was fully anticoagulated but had 2 in hospital ischemia-induced ventricular tachycardia arrests and was electively cannulated onto extracorporeal membrane oxygenation support.

Results: CA angiography revealed complete right CA occlusion distal to a 2.5mm proximal segment with collateral formation; severe stenosis of proximal left anterior descending (LAD) <0.5mm; ectasia of the left main CA; and a small aneurysm of proximal left circumflex artery. This was consistent with a remote occurrence of atypical Kawasaki Disease. In conjunction with adult cardiology we felt that he would benefit from LAD intervention due to evidence of ongoing myocardial ischemia. Because the risk of stenting was felt to be unacceptable (LAD diameter 1.0 mm with smallest coronary stent available 2.25 mm), LAD angioplasty alone was performed to 1.5 mm with markedly improved calibre (1.1 mm) and flow within the LAD. The patient’s troponin and rhythm normalised for 48 hours post-intervention but due to proximal right CA occlusion and concern for recurrence of left CA lesions he underwent bilateral CA bypass grafts with clinical stabilization.

Conclusions: This case demonstrates the value of invasive CA imaging to accurately define disease and therapeutic options in pediatric patients presenting with SCA, the ability to successfully perform CA intervention in small children, and the need for multi-specialty collaboration.
High prevalence of allergic disorders but no specific immune phenotype pattern in children awaiting transplantation.


Introduction: After transplantation (Tx), children show a higher frequency of allergic disorders (AD) compared to healthy children, reflecting an imbalance of the immune system, in the context of immunosuppression including immune cell-depleting induction, which may also be due to heritable factors present before Tx. We previously found a lack of naïve regulatory T cells (Tregs) and other alterations of lymphocyte phenotypes associated with AD in children after heart Tx. We assessed whether these patterns are present pre-Tx by comparing immune profiles of children awaiting Tx with and without AD.

Methods: This multicenter collaboration was conducted within the POSITIVE study, part of the Canadian National Transplant Research Program. Clinical data were collected into a REDCap database. Lymphocytes were isolated from pre-Tx blood via density gradient centrifugation and subtyped by flow cytometry with a focus on regulatory cells. Cell distributions were compared between patients with and without AD across kidney, heart and liver Tx groups (KTx, HTx, LTx) and in correlation to age.

Results: Of the 114 patients, 33% experienced one or more allergic disorders pre-Tx, with prevalence of 40% in KTx, 34% in HTx and 21% in LTx listed children. Of patients with one or more AD, 24% experienced asthma, 47% experienced rhinitis and 47% experienced eczema pre-Tx. Tregs, regulatory B cells, memory T cells and memory B cells were not significantly different between AD and non-AD groups. Within the HTx group, CD45RA+ naive Tregs were in trend less frequent in patients with AD than patients without AD ($p = 0.079$).

Conclusions: AD is more common in children awaiting HTx, KTx, and LTx compared to the general population with lowest prevalence in LTx listed children. The AD-associated immune phenotype alterations previously described were not present in these children, except in trend in HTx children. This indicates that the AD-associated imbalance evolves or manifests with transplant and immune suppression.
Cardiac Glucose Oxidation Rates are Impaired and a Possible Pharmacological Target for Mitigating Heart Failure in Barth Syndrome.

Introduction: Heart failure (HF) presents as the leading cause of infant mortality in individuals with Barth syndrome (BTHS), a rare genetic disorder due to mutations in the tafazzin (TAZ) gene, which encodes for a phospholipid transacylase critical in the remodelling of the mitochondrial phospholipid, cardiolipin. Despite well-characterized mitochondrial dysfunction, information regarding perturbations of cardiac energy metabolism in individuals with BTHS remains limited. Hence, our objective was to identify potential metabolic perturbations and determine whether optimization of cardiac energetics may be a novel approach to attenuate cardiomyopathy development in BTHS children.

Methods: Cardiac function in a mouse model of BTHS (tetracycline-inducible Taz knockdown (TAZKD) mice) was assessed via ultrasound echocardiography in mice ~2 months of age. Hearts were subsequently extracted from ~2.5-month-old TAZKD mice and their wild-type littermates for mRNA/protein expression profiling, or for isolated working heart perfusions to assess energy metabolism.

Results: TAZKD mice exhibited early development of a hypertrophic cardiomyopathy as evidenced by increased left ventricular (LV) anterior (0.95±0.04 vs. 0.82±0.03 (mm)) and posterior (0.85±0.05 vs. 0.79±0.09 (mm)) wall thickness during diastole, and impaired LV volumes during both systole and diastole. Conversely, no signs of systolic dysfunction or HF were apparent. Of interest, inhibitory phosphorylation of pyruvate dehydrogenase (PDH), the rate-limiting enzyme for glucose oxidation, was increased in hearts from TAZKD mice. This change coincided with increased protein expression of PDH kinase 4 (PDHK4, gene name Pdk4), the primary PDHK isoform in the heart inhibiting PDH activity, but did not coincide with an increase in Pdk4 mRNA expression. Moreover, TAZKD mouse hearts exhibited a marked reduction in glucose oxidation rates.

Conclusions: Our findings point to a marked reduction in myocardial glucose oxidation prior to the development of overt HF in TAZKD mice, which may represent a pharmacological target for mitigating HF development/progression in BTHS.
No. 59 - ABSTRACT – POSTER PRESENTATION

Sulforaphane protects Neurons from Oxygen & Glucose Deprivation.
Ladak Z, Garcia E, Armstrong EA, Yoon J, Persad S, Yager J.

Introduction: Perinatal brain injury results in developmental disabilities (DDs) inclusive of cerebral palsy, autism, attention deficit disorder and others. The placenta is responsible for transporting nutrients and oxygen to the fetus. Placental insufficiency results in a hypoxic-ischemic (HI) environment. A significant HI state in-utero leads to perinatal compromise, characterized by fetal growth restriction and brain injury. Given that over 80% of perinatal brain injury leading to DD occurs prior to birth, preventive approaches are needed to reduce or eliminate the opportunity for injury and the incidence of DDs. Sulforaphane (SFN), derived from cruciferous vegetables such as broccoli sprouts (BrSp), is a phase-II enzyme inducer that acts through cytoplasmic NrF2 to enhance the production of anti-oxidants via the glutathione pathway. We previously showed a profound neuro-preventive effect of BrSp/SFN as a dietary supplement in pregnant rats. We explored the dosing range of SFN for neuronal and glial protection and toxicity in normal and oxygen/glucose deprived (OGD) cell culture.

Methods: OGD simulates in-vitro, in-vivo HI conditions. We developed a rodent newborn cell culture model of primary cortical neuronal, astrocyte, and mixed cell cultures. These cultures are exposed to an OGD environment for different durations of time to determine the LD50 (duration of OGD required for 50% cell death). Using the LD50, different doses of SFN are evaluated to determine the most efficacious dose for neuroprotection and minimum dose for neurotoxicity. Control cultures are exposed to normal media without OGD. Cell specific markers are evaluated by Western blot and immunofluorescence (IF). Cell viability is assessed by IF/high content and cytotoxicity by Alamar blue/colorimetric MTT.

Results: Primary cortical neuronal/astroglial cell cultures have been established. We determined the LD50 to be 2 hours for neurons (p<0.001) and 4 hours for astrocytes (p<0.002). The protective effect of SFN on neurons was 2.5uM (p<0.0001), and for astrocytes, 5uM (p<0.0001). Significant toxicity doses were also confirmed as 50uM (p<0.05) for neurons, and 100uM (p<0.005) for astrocytes. One Way ANOVA was used for statistical analysis.

Conclusions: Our results indicate that cell death is significantly reduced in neurons and astrocytes treated with low doses of SFN. Higher SFN doses were toxic. The findings suggest that: 1. SFN shows promise as a preventative agent for fetal ischemic brain injury, 2. Dosing parameters are required for safety. This study will influence the development of innovative therapies for the prevention of childhood DD.
No. 60 - ABSTRACT – POSTER PRESENTATION

Developing Skills for Developmental Disabilities: Pre-clinical elective experience enhances medical students’ confidence in various settings.
Simin I, Fong-Leboeuf A, Le A, Andrews D.

Introduction: Medical students feel they are not adequately trained to care for patients with developmental disabilities (PWDD). At present, there is a paucity of literature on effective teaching methods on the subject (Troller et al. 2016; Salvador-Carulla et al. 2015). Students may have poor clinical skills and experience discomfort when assessing patients with developmental delays. Consequently, PWDD may not receive the timely, empathetic care from their future clinicians (Sahin and Akyol 2010).

“Developing Skills with Developmental Disabilities” (DSDD), is a pre-clinical elective designed to improve student knowledge, skills, and attitudes toward pediatric PWDD. Initial elective cohorts worked with preschoolers. These cohorts displayed improved confidence working with PWDD (Penner et al. 2017). The current project examines the efficacy of DSDD using a hospital-based day-school for elementary-aged children and compares the results to previous cohorts.

Methods: The DSDD module was an elective offered to preclinical medical students. The curriculum consisted of the following: 1) 6 hours of didactics on child development, assistive technologies, and breaking bad news, and 2) 6 clinical hours at the Glenrose Rehabilitation Hospital, where students observed school-aged PWDD in a classroom and interacted with an interdisciplinary team, and family interviews.

Students completed 10-question pre- and post-elective surveys administered on a 5-point Likert scale. Questions involved student self-perceived comfort and knowledge regarding PWDD. Scores pre- and post-elective were compared using t-test analysis. Results were compared to those from previous cohorts (using the same survey).

Results: 24 students registered for DSDD, and 14 surveys were suitable for analysis. Statistically significant (p<0.01) increases were present in 9/10 domains, with the statistically insignificant score pertaining to confidence using positive reinforcement techniques. There was no significant difference in pre- and post-elective score improvement when comparing this cohort with past cohorts, across all scores.

Conclusions: The critical components of DSDD were maintained across setting changes with significant (p<0.01) increases in students’ self-reported confidence and knowledge in working with PWDD. This elective demonstrates effectiveness in different settings and ages. The general structure and principles of this elective may be applied by Pediatricians in medical education. Examples include having students attend developmental programs, using a short set of parent interview questions and/or a child observation to guide developmental teaching, and allocating time for interaction with allied health professionals to enhance students’ understanding of the interdisciplinary nature of care for PWDD.
Assessing the role of appetite hormones in pediatric populations with overweight and obesity and Autism Spectrum Disorder (ASD)

Dhaliwal K, Triador L, Richard C, Haqq AM, Zwaigenbaum L.

Introduction: Obesity and its associated complications are among the most common and severe health risks in children with Autism Spectrum Disorder (ASD). There is a higher prevalence of obesity in children with ASD in comparison to children without ASD. Research suggests possible differences in specific satiety hormones in populations with ASD, in comparison to controls, such as a decrease in ghrelin and an increase in leptin concentrations. Current research, although limited, suggests the possibility of neuroendocrine influences on abnormal eating behaviors exhibited by children with ASD. The aim of this study will be to assess for differences in hormones (ghrelin, leptin, GLP-1, insulin) and feeding behavior scores in ASD, in comparison to age- and weight-matched typically developing (TD), control populations.

Methods: Participants aged 5-12 years old will complete one study visit to the Clinical Research Unit at the University of Alberta. Anthropometric measurements (height, weight, waist circumference) will be completed during the visit. There will be 20 participants in each group, and they will be assigned to one of four groups: obese/overweight and ASD, normal weight and ASD, obese/overweight and without ASD, and normal weight without ASD. Participants will fast for 8 hours prior to the study visit. During the visit, blood will be drawn and later assessed for hormone concentrations (ghrelin, leptin, GLP-1, insulin) and glucose. Participants will also complete The Brief Autism Mealtime Behavior Inventory (BAMBI) in order to better understand any differences in challenging eating behaviors between ASD and TD populations.

Expected Results: It is hypothesized that we will find differences in the hormonal profiles of children with ASD, when compared to TD controls. The different BMI subgroups will allow for a better understanding of the independent effect of being obese/overweight and ASD on shifts in hormonal factors. Through this study we hope to understand how key appetite hormones are affected and may be leading to weight gain.

Conclusions: This study may provide further insight into specific biological drivers of increased weight gain in children with ASD and help to better understand the role of potentially modifiable factors, such as diet, and how they relate to the development of obesity. This could lead to the identification of novel prevention and treatment strategies and help to further explain why children and adults with ASD are at a higher risk of developing obesity at a very young age, likely progressing to its associated chronic health problems later in adulthood.
No. 62 - ABSTRACT – POSTER PRESENTATION

The Effect of Post-Ischemic Hypothermia (PIH) on Energy Regulation in the Core and Penumbra following Perinatal Brain Injury.
Doosti MH, Przyslupski AMT, Armstrong E, Yager J.

Introduction: Perinatal hypoxic-ischemic (HI) brain injury is a risk factor for mental retardation, epilepsy, and cerebral palsy. The only available therapy for neurologically compromised neonates is PIH. This treatment however is only partially protective in newborns with moderate injury and not protective in severe HI. Current research is focused on complementing hypothermia with medications to enhance its benefits. Survivability of injured brain cells is highly dependent on energy production in the form of adenosine triphosphate (ATP). As a master regulator of energy homeostasis, AMP-activated protein kinase (AMPK) determines survival or death of cells after HI. The concentration of ATP delineates the extent of brain injury Core (complete cell death) and Penumbra (injured cells that may or may not die). Despite saving more ATP through decreasing brain metabolism, the impact of hypothermia on AMPK in the core vs penumbra remains poorly investigated. AMPK activation (pAMPK) occurs when ATP is incompletely depleted (penumbra), allowing for recovery of ATP and cell survival. However, AMPK activation in areas of complete ATP depletion is detrimental to cells. Hypothermia inhibits p-AMPK. Therefore AMPK inhibition during recovery may have beneficial effects in the core, but detrimental effects in the penumbra.

Hypothesis: We hypothesize that hypothermia will inhibit AMPK following HI and allow for the determination of supplemental drugs therapies, to enhance hypothermic neuroprotection.

Methods: Carotid artery ligation was conducted on postnatal 7 days Long-Evans rats. After recovery, pups were placed in hypoxia for either 60 (penumbra) or 150 (core) min. Immediately after hypoxia pups were split into either hypothermia (HT, 31°C) or normothermia (NO, 37°C) groups for 24 hours. AMPK and Bim, a pro-apoptotic protein, were evaluated at several times post HI.

Results: There were no significant differences in p-AMPK in core. There was a significant difference in Bim at 24 and 25 hours in core HT and core NO (p<0.05). There was a significant decrease in p-AMPK after 4 and 24 hours of HT in penumbra compared to the NO group (p<0.05). There was significantly less Bim expression in the HT compared to NO at 4 and 24 hours.

Conclusions: AMPK suppression at 4 and 24 hours of PIH in penumbra may have a detrimental effect on overall outcome. Further downstream proteins need to be evaluated to determine the exact effect of these changes. However, therapeutic agents that activate or inhibit AMPK given at appropriate times during recovery may improve outcome.
No. 63 - ABSTRACT – POSTER PRESENTATION

Examining the usage, perceived impact and user experience of an Internet-based cognitive behavioural therapy program for adolescents with anxiety: Results from a randomized controlled trial. Radomski A, Bagnell A, Curtis S, Hartling L, Newton A.

Introduction: Internet-based cognitive behavioural therapy (iCBT) is a novel treatment option for adolescent anxiety. More understanding of experiences related to its use is still needed. ‘User experiences’ include an adolescent’s self-reported satisfaction and acceptability, credibility and impact, adherence to and usage of iCBT, and how users rate changes in their anxiety as a result of iCBT (minimal clinically important difference; MCID). These experiences are important for understanding treatment effects, but have been understudied. This study examined adolescents’ experiences with iCBT for anxiety.

Methods: A national randomized controlled trial was conducted with adolescents aged 13-19 years reporting mild-to-moderate anxiety problems. Enrolled adolescents were randomly allocated to treatment (6-session iCBT program) or control (anxiety resource webpage). Self-reported demographics and anxiety (Multidimensional Anxiety Scale for Children-2nd edition [MASC-2]) were collected pre-intervention. Self-reported anxiety (MASC-2), user experiences (purpose-built questionnaire; score range 0[poor]-84[positive] user experience), overall change in anxiety (global ratings of change scale [GRCS]), and intervention usage (number of iCBT sessions completed, webpage visits) were collected after 6 weeks (post-intervention). Descriptive statistics summarized user characteristics and experiences, and independent sample t-tests and Pearson correlations tested relationships between them. The MCID was calculated using the mean change in MASC-2 scores among adolescents reporting “somewhat better” changes in anxiety on the GRCS.

Results: Enrolled adolescents (n=530) were predominantly female (71.3%) with an average age of 16.6 years (SD=1.7). Baseline anxiety symptoms were ‘very elevated’ at 92.2 (SD=18.1; n=411). The average intervention dose was 2.2 iCBT sessions (SD=2.3; n=258) and 2.1 webpage visits (SD=2.7; n=278). A significantly (p<.001) more positive user experience was reported by iCBT users than webpage users. Commonly-reported challenges among iCBT users were ‘finding time’, ‘remembering to do it’ and ‘avoiding exposure activities’. Enjoyable aspects of iCBT included ‘learning about anxiety, new coping techniques’ and ‘seeing progress’. User experience did not significantly correlate with intervention usage for iCBT (p=0.16) or webpage participants (p=0.18); however, specific iCBT features (e.g., content relatability, reminder emails) were significantly correlated with the number of sessions completed (p’s<0.05). The MCID was defined as a mean anxiety change score of 13.75 on the MASC-2 (SD=18.13).

Conclusions: Adolescent users reported a positive iCBT experience despite low program usage. Users’ perceived impact of iCBT suggests that more sessions may not be required for adolescents to experience an important anxiety reduction post-iCBT. Future studies can validate the user experience questionnaire and use it to understand factors influencing iCBT use and impact in different conditions.
Waldner R, Doulla M.

Introduction: The ABCC8 gene encodes the sulfonylurea receptor 1 subunit of the ATP-sensitive potassium channel of the pancreatic beta cell and is integral in insulin secretion. Monogenic diabetes secondary to ABCC8 mutations have variable responsiveness to sulfonylurea (SU) treatment, with individuals stable on SU monotherapy while others requiring insulin due to persistent hyperglycemia. We present a case of a nuclear binding domain 2 heterozygous ABCC8 missense mutation, non-responsive to SU therapy and postulate that this nuclear binding location renders the mutation unresponsive to SU therapy.

Case Description: A non-obese 12-year-old female presented with hyperglycemia (36.1 mmol/L) and elevated HbA1C (15.5%) in the absence of ketones. Her hemoglobin A1C was elevated 1 year prior to presentation (8.7%). Glutamic acid decarboxylase (GAD65) antibodies were negative and C-peptide was detectable. She had a three generational family history of diabetes. Insulin therapy was initiated and genetic testing was pursued, revealing a heterozygous mutation in ABCC8 (A1537V). This is a known pathogenic mutation but responsiveness to SU therapy is unknown. A SU trial was initiated with Gliclazide 20 mg daily and maximized to 160 mg daily, with cessation of insulin. Hyperglycemia persisted on monotherapy and Gliclazide was discontinued with the need for insulin re-initiation.

Conclusions: We review the clinical presentation for a dominant loss-of-function ABCC8 mutation (A1537V) causing monogenic diabetes and show sulfonylurea unresponsiveness. We also review the known literature on sulfonylurea response in ABCC8 mutations and summarize the known pharmacogenomic correlations.
Use of flash glucose monitoring to screen for dysglycemia in pediatric patients with cystic fibrosis: a Feasibility Study.

Potter K, Rusnell L, Korbutt G, Rosolowsky E, Kherani T, Haqq A, Senior P.

Introduction: Early intervention in cystic fibrosis-related diabetes (CFRD) can limit adverse impacts on nutrition, respiratory function, and longevity. Diagnosis is challenging in asymptomatic patients since oral glucose tolerance testing (OGTT) is inconvenient and subject to high intra-individual variability. We assessed the feasibility of flash glucose monitoring to screen for dysglycemia in pediatric patients with cystic fibrosis (CF).

Methods: We recruited CF patients aged 10 to 18 years without pre-existing diabetes. Study participants underwent OGTT with measurement of glucose, insulin, and C-peptide at 0, 30, 60 and 120 minutes. Serum was collected for biomarker analysis. Participants wore a Freestyle Libre sensor for up to 14 days following OGTT.

Results: Of 41 patients contacted, 10 (24%) underwent OGTT. Seven of 10 participants (70%) wore a sensor. The mean age was 12.1 ± 0.9 years and 43% were female. The average BMI z-score was 0.8 ± 1.2 and the average FEV1 was 85.6 ± 7.9%.

Fasting blood glucose levels were normal in 6/7 patients (mean 5.4 ± 0.2 mmol/L). One patient had impaired fasting glucose. Dysglycemia was identified by OGTT in 4/7 subjects; indeterminate glycemia (n=1), impaired glucose tolerance (n=2), and diabetes (n=1). The participant who screened positive for CFRD was not on insulin or oral or IV corticosteroids during the study. The change in BMI z-score over the preceding 6 months was -0.04 ± 0.05 (normal glucose tolerance) and -0.34 ± 0.13 (indeterminate/impaired glucose tolerance).

Participants wore sensors for 9.8 ± 1.7 days and performed 6.8±0.9 scans/day. Mean sensor glucose was 5.3 ± 0.5, 6.3 ± 0.2, and 6.9 mmol/L for normoglycemic (n=3), indeterminate/impaired fasting glucose (n=3), and diabetes participants (n=1), respectively. The proportion of time above 8 mmol/L was: 7.0 ± 3.2%, 12.7± 0.5%, and 18%, respectively.

Conclusions: Increased mean glucose or time above range detected by flash glucose monitoring may be a useful screening tool to detect early dysglycemia in children with CF. Its use may be limited by cost and patient acceptability.
ABO Tolerance Following Treatment of Infant Mice with A-Expressing MHC-Identical Erythrocytes.
Motyka B, Fersovich J, Adam I, Pearcey J, Tao K, Cairo CW, Cowan PJ, West LJ.

Introduction: ABO-incompatible heart transplantation (ABOi HTx) is safe in young children and increases donor access. Post-ABOi HTx, B cell tolerance develops to donor ABO blood group antigen(s) by mechanisms not fully defined. To study ABO tolerance, we developed A-transgenic mice (A-Tg) that express A-antigen on vascular endothelium, erythrocytes (RBCs) and lymphocytes. Recently, we showed ABO tolerance could be intentionally induced in WT mice after ip injection of infant mice with intact A-Tg blood cells (BCs). Herein, we sought to determine specific A-Tg cell type(s) capable of inducing tolerance.

Methods: WT BALB/c (BALB) mice at 7 days of age were left untreated or injected ip (weekly×3) with either unfractionated BCs, erythrocytes (RBCs), peripheral blood mononuclear cells (PBMCs), or splenocytes from A-Tg BALB mice. At 5 weeks of age, mice were injected ip (weekly×5) with human A-RBC (A-antigen challenge) in an attempt to elicit anti-A antibody (Ab) production. Serum anti-A and third-party (non-A anti-human) Ab were assessed by hemagglutination or ABH glycan microarray.

Results: In response to challenge with A-antigen, high levels of anti-A Ab were produced both in untreated mice and in mice previously treated with A-Tg PBMCs or splenocytes. In contrast, anti-A Ab remained undetectable/very low in mice treated as infants with A-Tg BCs or RBCs. Third-party Ab responses were high for all groups.

Conclusions: A-Tg RBCs induced robust A-antigen-specific tolerance in infant mice, whereas A-Tg lymphocytes (PBMCs, splenocytes) did not. Future studies will explore mechanisms of A-Tg RBC tolerance induction with the goal to design synthetic ABH-multivalent polyethylene glycol (PEG) glycoconjugates for intentional ABO tolerance to allow subsequent ABOi HTx safely.
Investigating the difference in inorganic and organic phosphate bioavailability.

MacDonald T, Saurette M, Alexander T.

Introduction: Hyperphosphatemia, *i.e.* elevated serum phosphate (Pi), is a nearly universal feature of advanced chronic kidney disease (CKD) and end-stage renal disease (ESRD) and is correlated with all-cause mortality. Thus, lowering blood Pi is a cornerstone of treating patients suffering with CKD/ESRD. Currently, this is accomplished via dietary Pi restriction and oral Pi binders. However, dietary Pi restriction may lead to protein malnutrition and is difficult given the high Pi content in the western diet. In addition, Pi binders are associated with a recognized host of adverse side-effects. This warrants investigation into how Pi is absorbed from the intestinal lumen. Inorganic Pi is recognized to be more orally bioavailable than its organic counterpart. It is hypothesized that this is due to inorganic Pi being absorbed predominantly via the unsaturable paracellular pathway, with organic Pi being absorbed via the saturable transcellular pathway. Preliminary data have suggested Claudin-12 (Cldn-12), a protein expressed in the tight junctions of intestinal enterocytes, to behave as a paracellular Pi blocker. As such, we hypothesized that Cldn-12 expression attenuates the absorption of inorganic Pi, with nominal effect on organic Pi absorption.

Methods: To investigate our hypothesis, wild-type (WT) mice, and Cldn-12-null mice were generated. Mice were fed an organic Pi-based diet for 72 hours, whereupon they were transferred to an inorganic-Pi based diet for 72 hours. Euthanasia was performed prior to tissue extraction. To determine Pi bioavailability, urinary and fecal Pi was measured for each respective dietary treatment. Kidney and intestinal segments were tested for expression of transcellular Pi transporters NaPi2a-c, Pit1 and Pit2 using RT-PCR.

Results: In accord with our hypothesis, inorganic Pi was more orally bioavailable in Cldn-12-null mice than WT mice. Also consistent with our hypothesis was the nonsignificant difference in organic Pi bioavailability between WT and Cldn-12-null mice.

Conclusions: Our results are consistent with inorganic Pi being absorbed primarily via the paracellular intestinal epithelial pathway, and organic Pi absorption occurring predominantly via the transcellular pathway. In addition, our findings are consistent with Cldn-12 behaving as a paracellular Pi blocker.
Environmental immunotoxicants and autism.
Bryan S, Osornio Vargas A, Nielsen C, Clark B, Zwaigenbaum L, Goez H.

Introduction: Autism spectrum disorders (ASD) represent neurodevelopmental entities wherein up to a third of patients demonstrate developmental regression between 18-24 months of age. This variant is known as autistic regression (AR), and although poorly understood, an emerging theory suggests that immune dysregulation may be involved in its pathogenesis. Indeed, we previously showed a higher familial incidence of autoimmunity - in particular maternal autoimmunity - and increased incidence of febrile illness in AR. The prevalence of ASD increased more than two-fold between 2000 and 2010 in the United States, and while genetics is a recognized factor, there remains unaccounted contributions, among which environmental influences are likely. Indeed, while recent evidence points to air pollution as a potential risk factor for ASD and autoimmune disease, a possible link between immune dysregulation caused by environmental immunotoxicants and prevalence of ASD is not yet fully explored.

Objective: The purpose of this study is to determine whether geographical proximity to facilities releasing immunotoxicants to air and water is associated with a child having ASD in general, and AR in particular, in Alberta, Canada.

Methods: Using a retrospective case-series of children diagnosed with ASD (based on DSM-V criteria) between 2014 to 2018, we compare ASD with and without the AR-variant in terms of (1) patient factors (perinatal features, postnatal complications, parental education/occupation) and (2) child address proximity to industrial facilities releasing immunotoxicants to air and water. We calculate the latter from the integration of wind dispersion mapping and hydrological modelling of known/suspected immunotoxicants in Alberta from 2013-2017. Logistic regression models adjusted for sex, parental education, and postnatal complications will help predict how a patient’s geographical location in relation to emitting facilities affects the odds of the patient having ASD in general, and AR in particular.

Results: This study is ongoing. We seek to share and discuss these ideas and our progress with our University of Alberta Department of Pediatrics colleagues.
Identifying Characteristics Associated with Children with Complicated Glenn Procedures and Outcomes in a Single Institution.
Khaira G, Joffe A, Guerra G, Robertson C.

Introduction: The bidirectional cavopulmonary shunt (BCPS, also known as the Glenn) is one procedure, in a trio of staged procedures, which has been utilized as a method of palliating children with single ventricle physiology and anatomy. It is most often employed as the second stage of three procedures used to palliate children with Hypoplastic Left Heart Syndrome. Some attempts at describing those children for whom a higher chance of failure post-Glenn exists have been made. We aim to add to this body of literature by describing a single institution’s experiences of patient characteristics that are more likely to result in complications post Glenn.

Research Question: Are there pre-operative, cath-derived and intra-operative predictors of a complicated Glenn course (cGP, defined as: death less than 30 days post Glenn, transplant free survival at two years, need for ECLS, need for Glenn take down or addition of another source of pulmonary flow) during primary hospitalization? Are outcomes affected?

Methods: We will conduct a retrospective cohort study of all Glen procedures procedures of children at Stollery Children’s Hospital from January 2012-December 2017. Included will be all children who underwent a Glenn procedure at Stollery Children’s Hospital from January 2012 to November 2017. Children with data sources that are incomplete will be excluded. Our data collection will be aimed at identifying the following groups of features we feel may be associated with a higher likelihood of a cGP:

- Patient related:
  - Patient Demographics: GA at birth, sex, and age at Glenn, chromosomal abnormalities, chylothorax (at any stage of course), abnormal MRI (at any stage of course)
  - Stage I variables: ICU and Hospital LOS, CPR, ECMO, Dialysis
  - Stage II variables: inpatient (ICU vs ward) immediately prior to Stage II; intubated pre-operatively
- Pre-operative anatomical or hemodynamic related:
  - Residual lesions prior to Glenn: residual arch obstruction, pulmonary vein anomalies, systemic venous anomalies (e.g. bilateral SVCs)
  - Cath data: PVR/SVR ratio, Qp/Qs
  - Echo data: AVVR, ventricular function
- Intra-operative predictors:
  - Any procedures performed at same time as Glenn
  - CPB time, DHCA used, DHCA duration, Aortic-cross-clamp time, re-CPB needed in the OR

In addition, we will be collection outcome data
- Alive at two years: Y/N
  - Two year functional outcome: General Adaptive Composite on ABAS-II
  - Two year Bayley III Outcomes:
For analysis, we will look at univariate predictors of our composite end point of cGP and all univariate predictors with a p<0.1 of cGP will be evaluated using a multivariate logistic regression analysis. The cut off for significant predictors in the multivariate model will be set at p<0.05.
Alterations in Brain Structure in Pediatric Migraine.

Rajapakse T, Kassiri J, Mathieu E, Lindsell M, Xin T, Matta M, Katliariwala P, Beaulieu C, Richer L.

Introduction: Migraine is a prevalent and disabling condition with limited understanding in the developing brain. Adults with chronic migraine show structural alterations in pain and sensory processing regions. Similar data is lacking in children and required for early intervention.

Methods: Case-control feasibility study assessing structural brain differences between adolescents with chronic migraine and healthy controls using 3T Siemens structural volumetric MRI analysis. Fifteen subjects with chronic migraine were compared to 25 age and sex matched healthy controls. Non-parametric statistics (Kruskal-Wallis).

Results: Migraine subjects had reduced volumes in total brain (grey and white matter) (KW p <0.03), total thalamus (KW p <0.01) and hippocampal regions (KW p <0.03). Unilateral (right) cerebellar grey matter volumes were significantly reduced in migraine subjects versus controls (KW p<0.05).

No significant differences found in other regions, including basal ganglia, cortical grey matter and brainstem.

Conclusions: Total brain, hippocampal and thalamic volumetric reductions are seen in adolescents with chronic migraine. The regions identified are involved in migraine pathogenesis. This volumetric imaging study should improve understanding of the causes and effects of pediatric migraine.
No. 71 - ABSTRACT – POSTER PRESENTATION

Certain properties of the natural mineral water suitable for hydration in children.
Avramovic D.

Introduction: The importance of hydration in maintaining good health has been increasingly recognized by the professional and scientific community. Daily requirement for sufficient intake of fluids differs from person to person and depends on the type of activity, climatic conditions in the immediate environment, eating habits, lifestyle, general health and age. Low daily fluid intake can adversely affect the health, and this is especially true in the most vulnerable groups, mainly children, but also for athletes, adults of working age and the elderly.

Methods: We compared basic physical and chemical characteristics including some of trace elements of analyzed samples of natural mineral water and drinking water from public water supply system to investigate potential benefits for consumption during childhood.

Results: Our results obtained show that except as a method for compensation of fluid loss, consuming natural mineral water in children may provide input of some mineral substances necessary for proper growth and development, which cannot be found in the same quantities in processed and purified drinking water.

Conclusions: For these reasons it is important to consider and properly interpret all aspects of the water analysis in accordance with the applicable regulations, and to take into consideration the possible positive impact on the health of certain properties of the natural mineral water.
Screening for pediatric malnutrition at hospital admission: Which screening tool is best?

Introduction: Malnutrition in hospitalized children has been linked to increased length of hospital stay, and increased morbidity and mortality. Identifying children at malnutrition risk on admission to hospital is described as best practice, however, there is no validated screening tool in use in Alberta pediatric facilities. The aim of this study is to identify a pediatric nutrition screening tool able to identify children with malnutrition risk on admission to hospital.

Methods: A nurse administered two pediatric nutrition screening tools, Screening Tool for Risk on Nutritional Status and Growth (STRONGkids) and Pediatric Nutrition Screening Tool (PNST) to patients admitted to medicine and surgery units (n=165) at the Stollery Children’s Hospital. The Subjective Global Nutritional Assessment (SGNA) was then completed by a dietitian, blinded to the results of the screens, as an indicator of true nutrition status. In a subset of patients both screening tools were completed a second time by a different nurse, blinded to the results of the first screens, to determine interrater reliability. Sensitivity, specificity, and kappa were calculated for both screening tools against the SGNA. An ROC curve assessed alternate cut-offs for each tool to potentially improve their ability to identify nutrition risk in this population. Length of hospital stay (LOS) was used to assess prospective validity.

Results: 29% of children admitted to hospital were malnourished based on the SGNA. Using the recommended cut-offs, the sensitivity of STRONGkids’ was 89%, specificity 35%, and kappa 0.483. The sensitivity of PNST was 58%, specificity 88%, and kappa 0.601. Using adjusted cut-offs based on ROC curve analysis, PNST’s sensitivity improved to 87%, specificity 71%, and kappa 0.681, and STRONGkids specificity improved to 61%, sensitivity 80%, and kappa 0.5. Children identified as malnourished stayed for 3 days longer than those who were well nourished (p < 0.05). Conclusion: This study showed neither tool was appropriate for clinical use based on published cut-offs. By adjusting the cut-offs using ROC curve analysis, both tools improved overall agreement with the SGNA without significantly impacting the prospective validity. The PNST with adjusted cut-offs is the most appropriate for clinical use in this population, with the best overall agreement and lowest rate of false positives. Use of the adjusted PNST in pediatric hospitals could aid in the early detection of children who would benefit from a nutrition intervention.
No. 73 - ABSTRACT – POSTER PRESENTATION

Referrals for Pediatric Weight Management – A Role for Public Health Nurses.

Nguyen N, Kebbe M, Ball G.

Introduction: Recently, public health nurses (PHNs) in the Edmonton-area were given the opportunity to directly refer children with obesity for weight management within Alberta Health Services (AHS). Our purpose was to (i) characterize referred children, including proportions of families who enrolled in pediatric weight management and (ii) explore PHNs’ experiences, perspectives, and recommendations regarding this new referral pathway. Method. This study included children (1–17 years of age; body mass index [BMI] ≥85th percentile) referred to the Pediatric Centre for Weight and Health (PCWH; Stollery Children’s Hospital, Edmonton, Alberta, Canada) from April 2017 to September 2018. We obtained referral and enrollment data from AHS databases, which we summarized using descriptive statistics. We used a semi-structured interview guide to conduct telephone interviews with PHNs; these were audio-recorded, transcribed verbatim by The Comma Police, managed using NVivo 12 (QSR International, Australia), and analyzed by two independent reviewers using manifest, inductive content analysis

Results: A total of 79 referred children (n=39, 52.7% male; 4.4±1.8 years old) were included in our sample, of which 47 children (59.5%) enrolled in care. Qualitative interview data (n= 10 PHNs) were grouped into five categories: (i) PHN’s perspectives on the referral form (e.g. simple and straightforward), (ii) benefits of the new referral process (e.g. increased opportunities for referral), (iii) barriers regarding the uptake of the new referral (e.g. lack of family receptiveness), (iv) recommendations for the referral process (e.g. receiving feedback on families’ referral status), and (v) recommendations to enhance the referral form (e.g. provide referral form in online-format)

Conclusions: Despite encountering challenges, PHNs acknowledged the importance of the new referral process in referring families for pediatric weight management. To benefit families and the health care system, our data can help to inform improvements in processes and procedures for pediatric weight management.
No. 74 - ABSTRACT – POSTER PRESENTATION

CMR assessment of aortopathy in pediatric Turner Syndrome.
Pajunen K, Suntratonpipat S, Rosolowsky E, Girgis R, Pagano J, Tham E.

Introduction: Turner syndrome is associated with aortopathy and risk of aortic dissection. Thresholds for risk of dissection are reported at an aortic size index (ASI) of 2-2.5 cm/m2. Clinical assessment using 2-dimensional measurements of aortic size does not reflect vascular function. Cardiac MRI (CMR) allows for evaluation of ventricular and vascular properties, thus we sought to evaluate the aortic properties of strain, compliance and ventriculoarterial (VA) coupling in pediatric patients with Turner syndrome.

Methods: Patients with Turner syndrome underwent CMR to evaluate the aortic anatomy, flow and ventricular function. Systolic blood pressure (SBP) and pulse pressure (PP) were obtained and the end systolic pressure (ESP) calculated as 0.9xSBP. Aortic root diameters were obtained from cine images. Magnitude images from phase-contrast imaging of the ascending aorta in cross-section was used to calculate: relative area change (RAC = max-min area); and ASI (maximum diameter) from the same image. Vascular properties were calculated as such: aortic strain = RAC/min area; aortic compliance = RAC/PP; aortic elastance (Ea = ESP/SV); LV elastance (Ees) = ESP/Esv; and VA coupling (VAC) = Ea/Ees. Pearson correlation coefficient examined the associations between aortic size and vascular properties.

Results: CMR was performed in 27 patients, age 14 ± 3 years, height 139 ± 12 cm, BSA 1.34 ± 0.32 m2, SBP = 116 ± 13 mmHg and DBP 76 ± 13 mmHg. Of these, 7 (26%) had bicuspid aortic valve, 1 aortic coarctation repair, 1 PAPVR, 3 L SVC. All patients had normal LV volumes, LVEF (62±5.6%), and aortic root size (z score -0.08±1.2). Mean ASI was 1.8±5 cm/m2 (z score 1.48±1.27), and 6 patients had a dilated ascending aorta (>2 cm/m2). Aortic elastance was 2.28±0.62 mmHg/ml and LV elastance 3.88±1.56 mmHg/ml, resulting in VAC 0.63±0.15. Increased ASI was associated with increased aortic compliance (r = 0.69), increased aortic elastance (r = 0.37), decreased aortic strain (r = -0.34) and increased LV elastance (r = 0.34) but not Ees. Higher max aortic area was associated with increased aortic compliance (r = 0.69) and increased aortic root diameter was associated with increased aortic elastance (r = 0.38). None of the parameters had a relationship with blood pressure.

Conclusions: Larger aortas displayed increased compliance, but they also demonstrated decreased strain, suggestive of increased aortic stiffness, which was not due to hypertension. The corresponding increased aortic elastance accompanied by increased LV elastance is consistent with preserved myocardial contractility in order to maintain optimal coupling (VAC <1). Evaluation of the biophysical properties of the aorta in Turner syndrome may provide early detection of patients at risk for dissection, which may guide earlier treatment.
No. 75 - ABSTRACT – POSTER PRESENTATION

Patient’s Satisfaction with Pediatric Nurse Practitioner at a Tertiary Hospital.


Objective: The purpose of this study was to understand parents’ perceptions and satisfaction with the care provided by Pediatric Nurse Practitioners (PNPs) at a pediatric tertiary care hospital.

Methods: A convenience sample of 1013 parents of children who saw a PNP were asked to complete the validated Parents’ Perception of Satisfaction with Care from Pediatric Nurse Practitioners Instrument (PPSC-PNP). Parents were recruited from both inpatient and outpatient settings within the same tertiary care hospital.

Results: A total of 537 surveys were completed resulting in a return rate of 53.01%. Overall, 89.6% of parents were aware that their child was receiving care from a PNP. Caregivers who saw a PNP were found to be highly satisfied with the care they received (129.61/140). Caregivers were most satisfied with the caring behaviors exhibited by PNP’s (28.49/30). Clinical competency (27.77/30), communication (27.97/30) and general satisfaction (18.29/20) were also rated as highly satisfied. Decisional control (27.09/30) was found to be slightly lower although still in the highly satisfied category.

Conclusions: This study demonstrates parents’ overall satisfaction with the care provided by PNP’s at a tertiary care hospital. Survey scores revealed that parents felt PNP’s communicated well, exhibited clinical competence, and cared about their children. This study provides important knowledge of the valuable role provided by pediatric nurse practitioners in both inpatient and outpatient settings.
No. 76 - ABSTRACT – POSTER PRESENTATION

All That Wheezes Isn’t Asthma: A Missed Opportunity
Valji, R and Hicks, A

Introduction: X-linked agammaglobulinemia (XLA) is a rare immunodeficiency caused by impaired B lymphocyte development.

Description: A previously healthy, immunized, developmentally normal 5-year-old male presented with a multifocal pneumonia, followed by a six-month history of cough and wheeze, not responsive to escalating doses of inhaled corticosteroids. He had intermittent purulent rhinorrhea and otorrhea, serous otitis media, low energy and mild weight loss. The family history was significant for the death of 4/5 maternal uncles in infancy. Chest x-rays demonstrated bilateral perihilar bronchial wall thickening, mucoid impaction and multifocal opacities.

Investigations included: normal CBC, negative HIV, absent immunoglobulins and vaccine response. Flow cytometry revealed absent BTK expression. Genetic testing demonstrated a BTK mutation, confirming XLA. CT revealed: right middle lobe collapse and mild lingular cylindrical bronchiectasis. Bronchoscopy showed diffuse airway impaction with thick orange secretions; bronchoalveolar lavage yielded Haemophilus influenza.

In spite of consistent chest physiotherapy and IVIG over the past 18 months, his chronic cough recurs within 1 week of stopping antibiotics. Chest x-rays show improvement but persistent right middle lobe collapse and lingular impaction.

The patient’s two brothers have the same BTK mutation, but with limited B cell and antibody production. His seven-year old brother has occasional otitis media, chronic nasal congestion and no vaccine response. His twenty-month old brother has chronic rhinorrhea, otitis media, asthma, minimal vaccine response and an elevated IgE.

Discussion: XLA presents with sinopulmonary infections, diarrhea, sepsis or cellulitis in >50% of cases by 1 year of age, but presentation is variable. Our index patient’s chronic cough, misattributed to asthma, led to diagnostic delay that may have contributed to bronchiectasis. The phenotypic variability between siblings in this case may be due to splice site mutation leakiness, which can allow for variable protein expression in XLA. A high index of suspicion with atypical asthma is critical for timely capture of rare diseases.

Conclusions:

1. Consider primary immunodeficiency in the differential diagnosis of treatment resistant “asthma”.
2. We describe a novel mutation of the BTK gene at c. 1349+4A>T.
3. XLA has variable genotype-phenotype correlation, including in siblings.