

ABSTRACT #1 **SPEAKER: Dr. Matthew Sibley** **Resident Year 3** **Resident Paper# 1**

In-center Practice Variation in the Treatment of Childhood Nephrotic Syndrome Affects Outcomes

Matthew Sibley, JA Sibley, T Kwok, J Jobsis, A Alshami, D Matsell, C Mammen [Division of General Pediatrics]

Background: In order to standardize care of childhood nephrotic syndrome (NS) patients across the province of British Columbia (BC), the Nephrology division at BC Children’s Hospital (BCCH) developed an evidence-based clinical pathway (CPW). An important step of this CPW development was to demonstrate the extent of practice variation locally and determine how this has impacted patient outcomes at our center.

Methodology: We performed a retrospective analysis of NS cases treated at BCCH from 1990-2010. We excluded those with a secondary cause of NS, those <1 year of age at diagnosis and those with steroid resistance. We explored cumulative prednisone dose (mg/m²) and duration of induction treatment (days) as sources of practice variation. We defined “low” and “high” dose prednisone groups as those prescribed less than or greater than the mean cumulative dose, respectively. We defined “short” and “long” duration groups as those prescribed prednisone for less than or greater than the mean duration of treatment, respectively. The primary outcomes were the total number of relapses in 3 years and the time to first relapse after completion of induction treatment (days).

Results: Mean (SD) cumulative prednisone dosing at induction was 2688 mg/m² (915 mg/m²). Mean (SD) duration of prednisone treatment was 118 days (47 days). The number of relapses was higher in the “low” vs “high” dose prednisone group (3.7 vs 2.5 relapses/patient) and in the “short” vs “long” prednisone group (3.9 vs 2.3 relapses/patient). Higher cumulative prednisone doses at induction and longer induction periods were also associated with better 3 year relapse-free survival.

Conclusions: Significant practice variation exists in the induction treatment of childhood NS within the province of BC. This has a direct impact on disease outcomes, including the number of future relapses and time to first relapse. The variation in practice and clinical outcomes support the development and implementation of a CPW for the treatment of childhood NS. This will standardize and improve patient care across the province. These results will also serve as a historical control for future evaluation of the CPW.

ABSTRACT #2 **SPEAKER: Dr. Brenden Hursh** **Division of Endocrinology** **Fellow Paper #1**

Autonomic Nervous System Function in Childhood Obesity

Brenden Hursh¹, M Fazeli², S Wang³, E Marchant⁴, P Woo¹, R Elango⁴, P Lavoie⁴, J-P Collet⁴, J-P Chanoine¹ [Division of Endocrinology¹, Clinical Support Unit², BCCH & UBC Faculty of Medicine³, Child & Family Research Institute⁴]

Background: One in four Canadian children is overweight or obese. Furthermore, medical complications related to obesity (such as type 2 diabetes), which were once the purview only of adults, are increasingly observed in children. Dysfunction of the autonomic nervous system (ANS) has been found to occur in obesity. Further studies are needed to clarify the relationship of obesity to autonomic function in children.

Objective: To describe the activity of the ANS in children with obesity compared to children with normal weight, as evaluated by heart rate variability and impedance cardiography.

Methodology: Fifteen healthy normal weight (NW) children and adolescents (BMI 15–85th percentile, 12–18 years) and 15 children with obesity (BMI >95th percentile, 12–18 years) have been recruited. Subjects met specified exclusion criteria. Anthropometric data and Tanner staging were recorded. Heart rate variability measurements included resting data, as well as the response to a perceived mental stress (mirror tracing task) and a physical stress (hand grip task). ANS parameters of interest included low frequency to high frequency ratio (LF:HF), high frequency normalized units (HFnu) and pre-ejection period (PEP).

Results: The normal weight and obese groups were similar in age (mean: obese 15.1; NW 15.8 years) and sex (male 47% and female 53% in each group). There was no statistically significant difference between the two groups with regards to the balance between sympathetic and parasympathetic tone, measured during rest, as assessed by LF:HF ratio (obese median 0.86, IQR 0.58–1.55; NW median 1.13, IQR 0.55–2.36; p=0.806). Additionally, there were no differences in other heart rate variability parameters at rest, including parasympathetic balance (HFnu: obese median 53.9, IQR 39.3–63.1; NW median 47.0, IQR 29.8–64.5) and sympathetic activity (PEP: obese median 121.41 msec, IQR 113.9–128.5; NW median 120.5 msec, IQR 116.4–127.6). Finally, there were no differences between groups in the percent change in HFnu or PEP in response to mental or physical stress.

Conclusion: In this small cross-sectional study, we were unable to detect a meaningful difference in ANS balance between obese and normal weight children at rest and in response to stress. Therefore, autonomic nervous system testing to assess for autonomic dysfunction in children with obesity cannot be recommended at this time.

ABSTRACT #3 **SPEAKER: Dr. Helen (Qi) Xu** **Neurology Resident Year 4** **Resident Paper # 2**

Pattern of Brain Injury Predicts Long Term Epilepsy Following Neonatal Encephalopathy

Helen (Qi) Xu, V Chau, K Muir, EWY Tam, SP Miller, DST Wong, J Zwicker, K J Poskitt, A Hill, S Belanger, J Rigney, E Roland [Division of Neurology]

Background: Hypoxic-ischemic (HI) encephalopathy is a major cause of neonatal seizures and long-term epilepsy. Extensive brain injury is usually associated with an increased risk. The objectives of this study were to determine the association between the patterns of HI brain injury and specific anatomical lesion, and the subsequent development of longer childhood epilepsy.

Methodology: This retrospective study included term newborns (>36 weeks gestation) with encephalopathy (n=181) seen between 2004 and 2012 at BC Children’s and Women’s Hospital. These neonates had standardized MR imaging performed between 3 and 5 days of life and 10 days of life. The predominant pattern of HI brain injury on MRI was recorded by a pediatric neuroradiologist, who was blinded to the clinical information, and classified as follows: Normal, Watershed, Basal Ganglia, Total, and Focal-Multifocal. Specific attention was directed to lesions in the hippocampus, motor cortex and occipital cortex. Clinical information, including demographics, use of systemic hypothermia, and occurrence of neonatal seizures, developmental outcome and incidence of childhood epilepsy, was collected by systematic chart reviews. Fisher exact test and Kruskal-Wallis analysis of variance were used for categorical and continuous variables respectively. Logistic regression was performed to examine the relationships between specific brain injury and long-term epilepsy.

Results: Of the 181 newborns, 122 (67%) had long-term clinical followed-up (median 24; interquartile range: 12 – 43 months of age) by a pediatric neurologist or pediatrician. Epilepsy diagnosed clinically and confirmed by an EEG was documented in 17 children. Review of clinical data demonstrated that children with epilepsy were sicker at birth, required more support during the immediate postnatal period and were more disabled at follow-up. A significantly higher proportion of newborns with Basal Ganglia or Total patterns developed epilepsy ($P < 0.001$). Specific injury in the motor cortex, hippocampus (both $P < 0.001$) and occipital cortex ($P = 0.005$) was strongly associated with the development of epilepsy. In a logistic regression model adjusting for the predominant pattern of HI injury, all 3 anatomical structures persisted as an independent risk factor. However, when they were added to the model at the same time, only involvement of the motor cortex and occipital cortex remained as an independent risk factor for epilepsy. Cooling did not affect these associations.

Conclusions: In term newborns with hypoxic-ischemic encephalopathy, injury to the motor cortex and occipital cortex on neonatal MRI is the best predictors of long term epilepsy, which are independent of the predominant pattern of hypoxic-ischemic brain injury and hypothermotherapy.

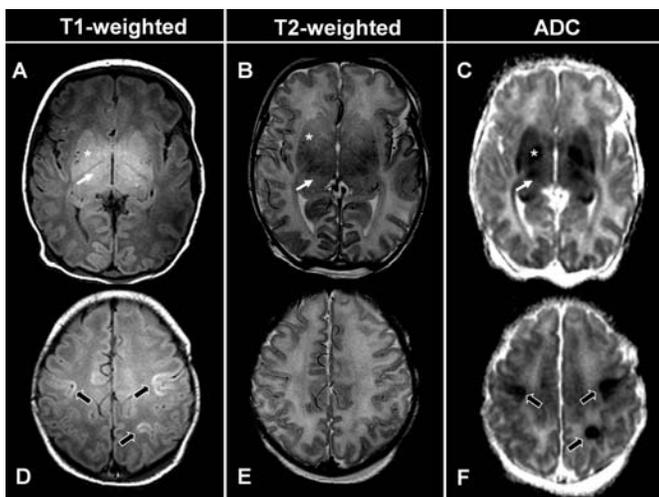
Table 1: Pattern of brain injury on Day 3 MRI in the newborns with and without epilepsy

Pattern of brain injury	Epilepsy (N = 17)	No epilepsy (N = 105)	P-value
Predominant pattern			
Normal, N (%)	2 (12)	56 (53)	<0.001
Watershed, N (%)	2 (12)	12 (11)	
Basal ganglia, N (%)	8 (48)	15 (14)	
Total, N (%)	4 (24)	3 (3)	
Focal-multifocal, N (%)	1 (6)	19 (18)	
Signal abnormalities in specific brain structure			
Hippocampus, N (%)	8 (44)	5 (4)	<0.001
Motor cortex, N (%)	11 (65)	14 (12.5)	<0.001
Occipital cortex, N (%)	8 (47)	16 (14)	0.005

N, number of cases

IQR, interquartile range

Figure 1: Brain MR scan on the third day of life, showing basal nuclei pattern with involvement of the motor cortex



Signal abnormalities are seen in the thalami (white arrow), the lentiform nuclei (star) bilaterally on both T1- and T2-weighted images (A, B). Higher up, there is also involvement of the motor cortex (black arrows) on T1-weighted image (D). On ADC map (C, F), brain injury is seen as areas of restricted diffusion in the corresponding structures.

Birth Weight Below 500 grams: Survival and Developmental Consequences

Rani Bashir, J Petrie Thomas², M MacKay², J Agnew², P Hubber-Richard², A Synnes^{1,2,3} [¹Division of Neonatology, ²Neonatal Follow-up Program, BC Children's & Women's Hospitals, ³Developmental Neurosciences & CFRI]

Background: Although survival of extreme premature infants at the threshold of viability is increasing, quality adjusted survival has plateaued in the last two decades. Antenatal counseling of parents and decisions about resuscitation can be made only after considering the survival, morbidities and disabilities of these babies. **Objectives:** To describe survival of babies with birth weight (BW) <500 grams (g) born 1985-2012 and long term outcomes of those babies born 1985-2008.

Methodology: Institutional survival rates were calculated for all births, live births and NICU admissions for epochs: 1985-87, '88-'92, '93-'97, '98-2002, '03-'07 and '08-'12. Terminations were excluded. All survivors with BW <500 g were invited to the Neonatal Follow-Up program (NFUP). Birth characteristics and neurodevelopmental outcomes at 18 months (m) corrected age (CA) and at 4.5 years (yr) were evaluated in the NFUP and analyzed descriptively. Definitions included: Cerebral palsy (CP) as abnormalities of tone and reflexes according to Bax; bilateral visual impairment (VI), hearing impairment (HI) as hearing aid or cochlear implant prescribed. Motor impairment (MI) was defined at 18 m CA as <70 on the Bayley I and II and <85 on Bayley-III and at 4.5 yr as <70 on the motor quotient of the Peabody PDMS 1 or 2 and/or Developmental Coordination Disorder (DCD) as <5%ile on the Movement ABC. Cognitive impairment (CI) was defined at 18 m CA as <70 on the BSID-I or II and adjusted Bayley-III score (Moore et. al., 2012), < 85 on unadjusted Bayley-III and at 4.5 yr as <70 on Wechsler testing (WPPSI-R and WPPSI III).

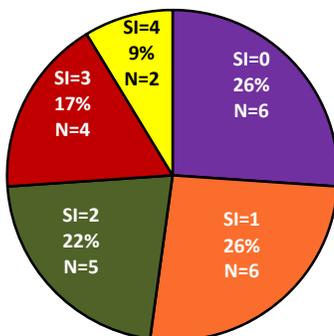
Results: Survival rates were 2.7% for all births (by epochs: 0.9%, 0%, 1.2%, 2.0%, 10.5%, 3.6%), 6.6% for live births (by epochs: 1.9%, 0%, 3.4%, 4.1%, 24%, 11.1%) and 48% for all NICU admissions (by epochs: 20%, 0%, 50%, 33%, 86%, 36%). Of 25 neonatal survivors, one died at 9 m CA (BW 492 g) and one refused follow-up. Data was extracted for 23 children. The earliest survivor was born in 1987 (male, BW 480 g). Babies had a median BW 465 g (range 380- 495) and gestation 26 1/7 weeks (range 22 4/7-30 2/7); 21 (84%) were inborn and 12 (48%) were male; 20% were of multiple pregnancy; 19 (76%) were small for gestational age (BW <3 %ile). Median 5 min Apgar was 7 (range 1-10).

Conclusion: Chance of impairment free survival is very low in babies <500 g and most of these survivors face a variety of developmental challenges. Antenatal counseling should address this outcome.

Table I- Follow up data

Significant Impairments	N (%)
Motor at 18 m	10/ 23 (48)
Motor at 4.5y	16/23 (69.5)
CP	4/23 (17)
DCD	6/23 (26)
Cognitive at 18 m (Bayley I& II <70 and Bayley III <85)	10/22(45)
Cognitive at 18 m (adjusted Bayley III <70)	12/22 (55)
Bayley cognitive score (Mean, SD)	73.6 (22.8)
Cognitive at 4.5 yr	11/23 (48)
3-5 yr IQ (Mean, SD)	75 (20.7)
Visual	6/22 (27)
Hearing	2/22 (9)

Figure 1: Number of Significant Impairments:



ABSTRACT #5**SPEAKER: Dr. Vicki Cook****Resident Year 2****Resident Paper #3****Clinical Characteristics of Seafood Allergy in Canadian Children**

Vicki Cook, ES Chan¹, A Clarke^{2,3}, G Shand³, M Ben-Shoshan⁴ [¹*Division of Allergy & Immunology, ²Department Medicine, Division of Clinical Immunology & Allergy, McGill University Health Center, Montreal, ³Department of Medicine, Division of Clinical Epidemiology, McGill University Health Center, Montreal, ⁴Department of Pediatrics, Division of Clinical Immunology & Allergy, McGill University Health Center, Montreal]*

Background: There is minimal data describing presentation of seafood allergy. We have characterized first reactions in seafood-allergic children. **Methodology:** Children with seafood allergy were recruited from allergy clinics at the Montreal Children's Hospital from March 2011 to May 2013. Questionnaires assessed demographics, cause, location, diagnosis, severity, and management of first reaction.

Results: Twenty-one fish and 18 shellfish-allergic patients responded (36.2% and 51.4% response rate). Age, sex, trigger and reaction severity were comparable between respondents and non-respondents. Median age at initial reaction was 2.0 and 4.8 years respectively. Almost 60% were males. Fish and shellfish reactions typically followed ingestion [90.5%(95%CI, 68.2%,98.3%) and 94.4%(70.1%,99.7%) respectively], and occurred more commonly to cooked fish [81.0%(57.4%,93.7%)] and shellfish [81.0%(57.4%,93.7%)]. Tilapia (28.6%) and shrimp (83.3%) were the most common causative foods. Most reactions occurred at home (61.9% and 83.3%). Average age at introduction was 1.5 years for fish and 3.2 years for shellfish. Mean time to diagnosis following initial reaction was 8 months (fish) and 10 months (shellfish). Most (85%) reactions were classified as moderate to severe, yet only 21% (9.6%, 39.4%) of these patients sought medical attention. At the time of questionnaire administration, all children had seen a physician, but 33.3% (15.5%, 56.9%) of patients with fish allergy and 52.9% (28.5%, 76.1%) of those with shellfish allergy were not prescribed an auto-injector. **Conclusions:** Seafood allergy presents at an early age and the most common causative foods are tilapia and shrimp. Following initial reaction, there appears to be a delay in physician diagnosis and low rates of auto-injector prescription.

ABSTRACT #6**SPEAKER: Dr. Carolina Escudero****Division of Cardiology****Fellow Paper #3****An Echocardiographic Study of Cardiac Size and Function in Adolescent Females with Anorexia Nervosa**

Carolina Escudero, P-Y Lam, AM De Souza, JE Potts, GGS Sandor [*Division of Cardiology*]

Background: Cardiac involvement occurs in the majority of patients with Anorexia Nervosa (AN), however, controversy still exists regarding systolic and diastolic function in females with AN. The purpose of our study was to investigate echocardiographic indices of cardiac dimensions, output, and systolic and diastolic function in adolescent females with AN.

Methodology: We performed a retrospective case-control study of adolescent females with AN compared to healthy adolescent controls. A complete echocardiogram including a detailed left ventricular (LV) function protocol was performed for controls and patients with AN during their acute phase of illness. LV dimensions, LV mass (LVM), LV mass indexed for body surface area (LVMI), left atrial (LA) size, stroke volume (SV), cardiac output (CO), and cardiac index (CI) were measured. LV systolic function was measured using fractional shortening (FS), mean velocity of circumferential fiber shortening (MVCf), and systolic tissue Doppler imaging (TDI) at the LV lateral wall (LVlateral), interventricular septum (IVS), and right ventricular free wall (RV). Diastolic function was measured using transmitral E and A wave velocity, pulmonary venous velocities, and diastolic TDI E' and A' wave velocities. BMI percentiles were calculated for patients and controls and patients were divided into those of BMI \leq 10th percentile (AN \leq 10th) and $>$ 10th percentile (AN $>$ 10th).

Results: We studied 95 adolescent AN patients (ANtotal) and 58 healthy adolescent female controls. There were 70 patients in the AN \leq 10th group. ANtotal and AN \leq 10th groups had reduced LV dimensions, LA size, LVM, LVMI, SV, CO, and CI compared to controls, with no differences between AN $>$ 10th and controls. There were no differences between controls and all AN groups in FS, MVCf, or systolic TDI. Pulmonary venous A wave velocity was significantly decreased in ANtotal and AN \leq 10th as compared to controls with no difference in transmitral E or A wave velocity or E/A. LVlateral E' and A', IVS E' and A', and RV A' were significantly decreased in ANtotal and AN \leq 10th, with only a decrease in RV A' in AN $>$ 10th as compared to controls.

Conclusions: Adolescent females with AN have downsized LV dimensions, LVMI, and CI, but systolic ventricular function remains preserved. Diastolic function is decreased in AN patients. This is the first study to show that patients with BMI \leq 10th percentile demonstrate changes in LV dimensions and diastolic function and warrant more careful monitoring.

ABSTRACT #7**SPEAKER: Dr. Amanda Li****Resident Year 4****Resident Paper #4****Pediatric Ependymoma and the Expression of EZH2, a Novel Prognostic Biomarker**

Amanda Li, C Dunham, U Tabori, AS Carret, D Mcneely, D Johnston, L Lafay-Cousin, B Wilson, D Eisenstat, N Jabado, S Zelca, M Silva, K Scheinmann, C Fryer, G Hendson, A Fotovati, C Hawkins, S Yip, SE Dunn, J Hukin [*Division of Hematology/Oncology & Division of Neurology*]

Background: Ependymoma is the third most common brain tumour in children, and prognosis is generally poor. Gross total resection followed by radiotherapy is presently the standard of treatment, but is often unachievable, particularly in young patients and in tumours located in the posterior fossa. Previous studies have not demonstrated significant benefit of conventional chemotherapy in improving survival or prevention progression of the disease. Therefore, there is keen interest in identifying novel biomarkers to guide the development of directed chemotherapy.

Methodology: We studied a cohort of 181 children diagnosed with intracranial ependymoma from 12 of 16 pediatric oncology centres from across Canada. Tissue microarray immunohistochemical techniques were performed on sample tissue cores to determine the expression of several markers of cell proliferation, cell death, and cell signalling postulated to play a role in ependymoma pathophysiology.

Results: EZH2 (Enhancer of Zeste Homologue 2), a protein involved in gene repression via histone methylation chromatin remodelling, was found to be expressed pediatric intracranial ependymoma. Kaplan-Meier analyses showed that strong EZH2 expression was significantly associated with poor 5-year overall survival in all intracranial ependymoma (35% vs 68%; $p=0.014$). In a subset of posterior fossa tumours, strong EZH2 expression was associated with both poor 5-year progression-free survival (21% vs 50%; $p=0.014$), and 5-year overall survival (31% vs 66%; $p=0.02$). Multivariate analysis showed that EZH2 was an independent marker of poor 5-year progression free survival (95% CI 1.03-51.7), along with younger age (95% CI 0.77 - 0.99). **Conclusion:** EZH2 is a novel biomarker in pediatric ependymoma associated with disease progression and poor overall survival. These findings suggest potential for therapeutic targeting of EZH2 in the treatment of pediatric ependymoma.

ABSTRACT #8	SPEAKER: Dr. Mary Dunbar	Neurology Resident Year 2	Resident Paper #5
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Can X-linked Creatine Transporter Deficiency be Treated?

Mary Dunbar, S Jaggamantri, S Stockler, C Van Karnebeek [Division of Neurology]

Background: Creatine transporter deficiency (CTD) is an X-linked inborn error of creatine metabolism characterized by reduced intracerebral creatine, developmental delay, intellectual disability, behavioral disturbance, seizures, and hypotonia in individuals harboring mutations in the SLC6A8 gene. Creatine transporter deficiency is one of three inborn errors of creatine metabolism including arginine:glycine amidinotransferase (AGAT) and guanidinoacetate methyltransferase (GAMT) deficiency. Oral supplementation of creatine alone or in combination with arginine and glycine has been successful in reversing some of the pathology in AGAT and GAMT deficiencies and has improved motor and intellectual development. Unfortunately, since it was first described in 2001, CTD has been generally viewed as untreatable, though reports of clinical improvements following treatment exist. A systematic literature review was needed to critically evaluate the response of CTD patients to treatment.

Methodology: Here we present a systematic literature review (1966–2013) comprising 7 publications collectively describing 27 patients with CTD. Three additional cases treated in our institution are also described. Extracted data were analyzed for cognitive ability, psychiatric and behavioral disturbances, epilepsy, and cerebral creatine measurements at pre-treatment and following treatment.

Results: Treatment regimens varied among the 28 included cases: 2 patients received creatine supplementation, 7 patients received arginine, 2 patients received creatine and arginine, and 17 patients received a combination of creatine, arginine, and glycine. Median treatment duration was 34.6 months (range 3 months - 5 years). An important minority of patients demonstrated clinical ($n=8$) or spectroscopic response ($n=5$) to therapy. Pre-treatment residual cerebral creatine levels (measured by magnetic resonance spectroscopy) appeared to influence response to therapy: only those with detectable pretreatment creatine improved. Patients exhibiting a $>10\%$ increase in cerebral creatine with treatment also demonstrated the greatest improvement in cognitive abilities. Treatment outcome was also affected by age; patients aged 9–16 years exhibited lower response.

Conclusions: Acknowledging the limitations of this systematic review, we conclude that CTD is an inborn error of metabolism that is amenable to treatment—particularly in milder cases with residual brain creatine, and therefore probable residual protein function. We propose standardization of low threshold screening for this diagnosis in patients with ID to allow early initiation of treatment with creatine, arginine, and glycine, with monitoring for safety and effect on relevant outcomes.

ABSTRACT #9	SPEAKER: Dr. Shira Harel	Division of Endocrinology	Fellow Paper #4
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Adrenal Suppression in Children Treated with Oral Viscous Budesonide for Eosinophilic Esophagitis

Shira Harel, B Hursh¹, ES Chan², V Avinashi³, C Panagiotopoulos¹ [¹Endocrinology & Diabetes Unit,² Division of Allergy & Immunology,³Division of Pediatric Gastroenterology, Hepatology & Nutrition, BCCH, UBC]

Background: Eosinophilic esophagitis (EoE) is an allergic inflammatory condition of the esophagus with increasing prevalence in children and adults. Oral viscous budesonide (OVB) is one of the topical corticosteroids considered first-line treatment due to its low systemic bioavailability. Adrenal suppression (AS) has not been previously reported with OVB treatment. Recent evidence suggests that active EoE is associated with reduced elimination of budesonide. Our aim was to determine the prevalence of and associated risk factors for AS in children with EoE treated with OVB for at least 3 months.

Methodology: We retrospectively reviewed a quality assurance initiative that took place in BC Children's Hospital between June 1, 2012 and November 30, 2013. Consensus was reached between the Endocrinology and Gastroenterology departments that all children with EoE, who were being treated with OVB for at least 3 months, needed to be referred for an Endocrine assessment, including a 1 μg ACTH stimulation test. We reviewed demographic and anthropometric data, medical problems and medication history, symptoms suggestive of AS and recent endoscopic inflammatory findings.

Results: Thirteen children (age range 3-17 years) have been assessed. Doses of OVB ranged from 0.5 to 2 mg/day and mean duration of treatment was 18.9 months (range 4-52 months). Five patients (38%) had suboptimal stimulated cortisol [range 343-497 nmol/L; mean (\pm SD) 426.8 nmol/L (\pm 58.3); normal ≥ 500 nmol/L], consistent with AS. We found no significant association between suboptimal cortisol levels and duration of treatment with OVB, ratio of dose to body surface area, dosing regimen (once versus twice daily) or use of concomitant inhaled/nasal/topical corticosteroids. There was also no association with symptoms suggestive of AS or with disease activity on endoscopy.

Conclusions: This study suggests that children with EoE treated with OVB for at least 3 months duration are at high risk for AS. These data highlight the need for clinicians to provide families with anticipatory counseling, ensure assessment for AS, and have a low threshold to provide stress dosing for endoscopies and intercurrent illness in these patients. The results of this study may also have clinical applicability for other inflammatory conditions that use topical preparations of budesonide.

ABSTRACT #10

SPEAKER: Dr. Katryn Paquette

Resident Year 3

Resident Paper #6

Active Tuberculosis Case Finding Using Chest Radiography in Homeless Populations: A Systematic Review and Meta-Analysis

Katryn Paquette, MP Cheng, MJ Kadatz, VJ Cook, W Chen, JC Johnston [UBC Department of Medicine]

Background: In low-incidence regions, tuberculosis (TB) often affects vulnerable populations. Guidelines recommend active case finding (ACF) in homeless and under-housed populations but there is no consensus on a preferred screening method. **Objective:** We performed a systematic review and meta-analysis to evaluate the use of chest radiography (CXR) screening in ACF for TB in homeless and under-housed populations.

Methodology: Articles were identified through EMBASE, Medline, and the Cochrane Library. Studies using symptom screens, CXRs, sputum sweeps, tuberculin skin tests, and/or interferon gamma release assays to detect active TB in homeless and under-housed populations were sought; 16 studies addressing CXR screening for active TB in low incidence regions were analysed. Of these, six studies with longitudinal registry data were analyzed for programmatic sensitivity. Data was extracted using a standardized method by two reviewers, and then reviewed by an independent reviewer.

Results: The pooled prevalence of active TB in the 16 study cohorts was 931 per 105 persons screened (95% CI: 565-1534) or 782 per 105 CXR (95% CI: 566-1079). In the six studies that used regional TB registry data, CXR-based screening programs identified 42% of active TB cases diagnosed in homeless people. Six of seven longitudinal screening programs reported a decrease in TB incidence.

Conclusions: Our data suggests that CXR screening is a good tool for ACF and should be incorporated into TB screening programs for homeless populations.

ABSTRACT #11

SPEAKER: Dr. Lara Malks-Jumba

Resident Year 4

Resident Research Project

Developing Learning Tools for Residents

Lara Malks-Jumba, S Freedman [Division of General Pediatrics], S Albersheim [Division of Neonatology]

Pediatrics is a large and diverse area of medicine and during residency there is considerable pressure to acquire knowledge and skills in all the areas of pediatric medicine. Although during residency there is a tremendous degree of clinical learning, the exact breadth and depth of learning is dependent on the particular cases one sees during any particular rotation, the time available for general reading, and the effectiveness of on the job teaching by more senior residents and physicians. It is very common that a resident comes to studying for their Royal College Exam in their 4th year of training and is surprised by how much of the information listed in the Royal College objectives (6) they have not yet learned and were not exposed to during their training.

Studies have highlighted that many residents prefer learning activities that are active and engaging versus ones that are passive and didactic. One study highlighted that "an experiential sense of the information being conveyed would appear preferable to the more passive and abstract features of lectures and literature review".

(1) It has been stated that students retain 20% of what they hear, 40% of what they see and hear, and 75% of what they see, hear and interact with (2,3). It has also been shown that pre-testing, post-testing, as well as multimedia learning tools, help the learner to integrate newly acquired information into his or her long-term memory (4,5). Grundman et al. conducted a study comparing didactic learning to learning via multimedia learning tools, and demonstrated that the multimedia tools consistently outperformed the lecture-based teaching format (4).

I will be presenting some education projects that I have created with the goal to facilitate long term learning of important pediatric topics in fun, interactive and effective ways.

References:

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Parental Decision Making Factors and Outcomes Regarding Fetal and Neonatal Lethal Anomalies

Esther Lee, S Stenekes, M Harlos [Division of Palliative Care]

Background: Perinatal palliative care is a relatively new field. There is a paucity of research regarding the care of neonates or fetuses diagnosed prenatally with lethal abnormalities. **Objective:** The purpose of this study was to obtain details about this patient population in the province of Manitoba, Canada. A retrospective chart review was undertaken to provide a description of the outcomes for patients and their families following the diagnosis of a lethal anomaly.

Methodology: Criteria for a lethal anomaly included the diagnosis of specific genetic conditions, renal and pulmonary diseases, central nervous system anomalies, and cardiac defects. With the aid of several databases, a total of 176 patients met the study inclusion criteria.

Results: The majority of the lethal diagnoses were in the genetic and CNS categories, with Trisomy 18 being the most predominant. Over half of all patients (n=103, 58%) made the decision to terminate the pregnancy. When a live birth occurred (n=39), the mean length of survival was 13.5 days (range 1-156 days), with the location of death primarily being in hospital (n=29). Ethnicity and geographical factors were associated with the decision to terminate a pregnancy. The involvement of the palliative care service was associated with decreased interventions when a live birth occurred.

Conclusions: Our study demonstrated similar findings as the literature in that the termination rates are similar and that the decision to terminate a pregnancy with a lethal anomaly was associated with specific ethnic backgrounds of the parents. We also found that urban home location was associated with increased termination rates, which has not been reported in any other studies. This study showed an association between the involvement of palliative care and less aggressive interventions for the infant. This supports the inclusion have palliative care as part of the interdisciplinary team.

Optical Coherence Tomography Identifies Coronary Abnormalities in Children

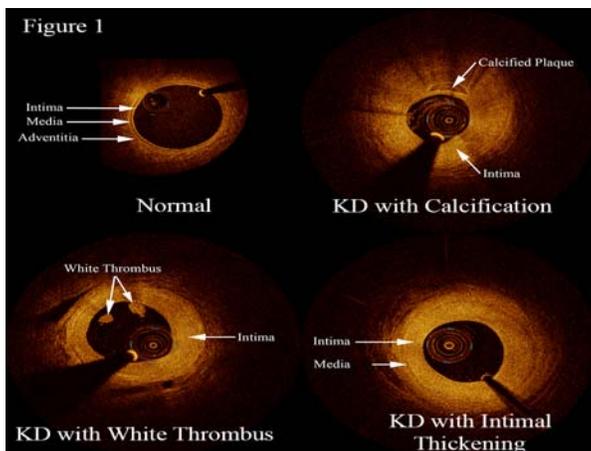
Anas Manouzi, M Hosking, A Fung, A De Souza, J Potts, K Harris [Division of Cardiology]

Background: Optical Coherence Tomography (OCT) is a high-resolution intravascular imaging technique used in adults. We tested the hypothesis that OCT could identify coronary abnormalities not seen by angiography in children with a history of Kawasaki Disease (KD) and pediatric heart transplant (TX) recipients.

Methodology: KD patients and TX recipients were evaluated between December 2012 and October 2013 with angiography and OCT (Ilumien System, LightLabs, St Jude Medical, Westford, MA). Modifications were made to the adult OCT protocol to adapt this technique for children. Serial cross sectional area (CSA) measurements of the lumen, intima and media were made. Entire imaging data was analyzed for the presence of qualitative changes.

Results: Seventeen children were evaluated (5 KD patients; 12 TX recipients). In KD patients angiography was normal. The lumen area was normal (z-score >-2 and $<+2$) at 95% of the 86 data collection points. However, significant vessel wall abnormalities were present in all children including intimal thickening (intima/lumen CSA ratio > 0.4), loss of the normal layered structure of the vessel wall, white thrombus, calcification and neovascularization. There was extensive destruction of the internal elastic lamina. In TX recipients angiography was normal; however, intimal thickening [intima/media (I/M) CSA ratio >1] was seen in 9/12 patients. The median I/M CSA ratio was 1.18.

Conclusion: In this initial experience with OCT in children, we have shown significant abnormalities in the coronary arteries of children with a history of coronary aneurysms due to KD and TX recipients that are not identified with conventional angiography.



ABSTRACT #14

SPEAKER: Dr. Emily Budd

Resident Year 4

Resident Research Project

Complex Dysautonomia in Adolescents: A Case SeriesEmily Budd, V Claydon, S Sanatani [Division of Cardiology], G Horvath [Division of Biochemical Diseases]

Background: Impairments in autonomic control have been implicated in numerous diseases. The most common of the dysautonomias are the disorders of reduced orthostatic tolerance, which include the reflex syncope, postural orthostatic tachycardia syndrome (POTS), and other orthostatic intolerance syndromes. These can be very disabling, are often misdiagnosed and can be challenging to manage. Little is known about the diagnostic criteria for these in children.

Methodology: We undertook a retrospective chart review of 15 patients who underwent head-up-tilt-table testing (HUT) for significant dysautonomia at BC Children's Hospital between 2008 and 2011. Inclusion criteria were symptoms of orthostatic intolerance, including any of the following dizziness, light-headedness, exercise intolerance, palpitations, chest pain, fatigue, abdominal pain, chronic nausea or vomiting. For this series, POTS was defined as an increase in heart rate in the first 5 minutes of HUT by 40 bpm.

Results: Fifteen patients fulfilled the criteria (13 female), median age was 14 years. The median time from onset of symptoms to time of referral was one year. The response to tilt showed that 6/15 patients fulfilled diagnostic criteria for POTS (all females). 4/15 had a working diagnosis of adolescent dysautonomia, 2/15 had dysautonomia with psychiatric comorbidities (anxiety, depression), 2/15 had a primary genetic syndrome with secondary autonomic dysfunction and 1/15 was diagnosed with abdominal migraine. None of the patients had orthostatic hypotension in the first 5 minutes of HUT. Several therapies were attempted in each patient, with lifestyle changes being the most common. Pharmacological therapies included plasma volume expansion, increased peripheral vascular resistance and prevention of excessive tachycardia amongst others.

Conclusions: Pediatric or adolescent POTS and adolescent autonomic dysfunction are increasingly being recognized as common disorders of youth. They can be challenging to treat and diagnose. An awareness of dysautonomia syndromes is important when faced with a multitude of symptoms in the adolescent.

ABSTRACT #15

SPEAKER: Dr. Amitava Sur

Division of Neonatology

Fellow Research Project

Palivizumab Study- Research in ProgressAmitava Sur, A Solimano, N Marr, S Turvey, P Lavoie, E Kwan, A Callejas [Division of Neonatology]

Background: RSV infection is responsible for most of the approximately 12,000 hospitalizations for respiratory illness per year in children younger than 2 years of age in Canada. PVZ has been approved for use in Canada since 2002 for the prevention of RSV-associated hospitalizations in high-risk infants who are at risk of severe RSV disease. Our research teams works to determine if the current modification in the passive immunization schedule (changed from previously 5 doses to 3 or 4 doses) provides adequate protection in this population. For this purpose, we will determine the serum PVZ levels using a novel enzyme-linked immunosorbent assay. Human data regarding pharmacokinetic properties of PVZ are lacking. Protective levels of PVZ against RSV are essentially based on animal data, and current protective levels of >40 ug/mL have been arbitrarily defined as "protective" despite the fact that lower concentrations (between 25 and 30 ug/mL) have been shown to provide the same 99% reduction of RSV viral loads in cotton rat model of RSV infection. The BC RSV program now recommends a 3-4 dose schedule instead of the 5 dose schedule practiced previously. But this has been deemed "unsafe" by a recent study sponsored by Mediimmune (manufacturer of PVZ). We aim to establish that the end of season serum levels of PVZ with the 3-4 dose schedule are above the accepted protective norms.

Objectives: 1) Validation of an assay developed to directly measure PVZ levels in children. 2) Determine therapeutic levels of PVZ (and clinical outcomes) at the end of the RSV season in infants receiving 3 versus 4 doses of PVZ during the 2013/2014 season.

Methodology: Infants who are already eligible to receive the full 3 or 4 dose PVZ regimes according to BC RSV prophylaxis guidelines for the RSV season 2013/2014 will be asked to participate. Patients will be recruited at the beginning of the RSV season while they are still admitted in the NICU prior to their discharge, or when they come to their first visit to the RSV prophylaxis clinic. Infants who are enrolled in NICU will have a total of three blood samples taken, one before the first dose of PVZ (control samples), one 24h to 5 days after the first dose (to measure PVZ peak levels), and a third sample at the end of the season (to measure PVZ trough levels). Along with PVZ levels, we also plan to assess RIG-I (retinoic acid inducible gene 1) receptor function.