ABSTRACT #1
SPEAKER: Dr. Badri Narayan  Resident Year 1  Department of Pediatrics

ENHANCING RESEARCH SKILLS FOR POST-GRADUATE PEDIATRIC TRAINEES: IMPLEMENTATION OF A PEDIATRIC RESEARCH CURRICULUM

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Objectives: Our purpose is to develop, implement and evaluate a research curriculum for pediatric trainees designed to improve research knowledge and skills. Background: Clinical Research is at the core of evidence-based practice. Health Services Research, Knowledge Transfer and Practice Audit are key features to establish and maintain good clinical practice. Pediatric residents and fellows must understand these features and become involved in research projects to acquire the knowledge, skills and competence to become better practitioners who are able to engage in their own research projects. Design/Methods: The Research Curriculum has been in place for 2 years: 2007-09. It is mandatory for all new paediatrics residents and offered to subspecialty residents and fellows. The curriculum includes the following components: 1) Formal Education (monthly) of clinical research /epidemiological fundamentals are presented by faculty members; each 3 hour session includes a lecture on health quality improvement/practice audit, followed by group discussion; 2) Journal Club (monthly) is structured to introduce and review key research methodologies and address important pediatric issues; 3) An Independent Research Project is a key component that should culminate in conference presentations and publications. At the midpoint of the research curriculum, trainees are solicited for feedback to assist with future planning and adjustments. Survey information collected from trainees identified their research background, attitudes towards research, baseline research knowledge, and areas of research interest. Results: All curriculum components were evaluated on an on-going basis. In Year 1 the new curriculum was well-accepted: 1) Formal Education [91% Good or Very Good]; 2) Journal Club [30% Excellent; 60% Very Good; 10% Good]. In Year 2 overall evaluation was similar to the first year: 1) Formal Education [7.5% Excellent; 87.5% Good or Very Good]; 2) Journal Club [12% Excellent; 59% Very Good, 29% Good]. Results are summarized in Figure 1.

Conclusions: The Pediatric Research Curriculum is part of a broader effort at our institution to develop excellence in pediatric practice through clinical research and practice audit while also developing interest in research and academic careers amongst pediatric trainees. The evaluation of the research curriculum shows improvement since implementation and feedback from trainees continues to be positive. Implementation of the research curriculum for our pediatric trainees addresses the need for strengthening the scientific foundations of clinical practice.

ABSTRACT #2
SPEAKER: Dr. Nina-Karen Bansal  Resident Year 4  Department of Pediatrics

CUTANEOUS POLYARTERITIS NODOSA IN CHILDHOOD: A CASE REPORT AND REVIEW OF THE LITERATURE

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Polycartieritis nodosa is a rare vasculitis of childhood. The cutaneous form is limited to the skin, muscles, joints and peripheral nerves. We describe a 7½ year old girl with cutaneous PAN (cPAN) presenting initially as massive cervical edema who later went on to develop more typical features, including subcutaneous nodules, livedo reticularis, myositis, arthritis, and mononeuritis multiplex. The use of systemic corticosteroids resulted in clinical improvement initially, but symptom recurrence has necessitated the use of DMARDs and biologic therapy. There have been approximately 140 reports of cPAN in the literature; clinical manifestations, laboratory measures, and treatment modalities are reviewed.

Conclusions: Therapeutic options are presented, including corticosteroids, DMARDs, and biologic therapy. Clinical manifestations, laboratory measures, and treatment modalities are reviewed.

ABSTRACT #3
SPEAKER: Dr. Mariana Deevska  Resident Year 3  Department of Pediatrics

THE IMPACT OF PROPHYLACTIC FRESH FROZEN PLASMA AND CRYOPRESENTATION ON THE INCIDENCE OF CNS THROMBOSIS AND HEMORRHAGE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA RECEIVING ASPARAGINASE

Mariana Deevska, L Abbott, C Fernandez, D Dix, V Price, H Wang, L Parker, M Yhap, C Fitzgerald, D Barnard, J Berman  Division Hem/Onc/BMT  UBC Department of Pediatrics /Dalhousie University/ IWK Health Centre

Introduction: Asparaginase (ASP) therapy is associated with depletion of antithrombin (AT) and fibrinogen (FG). Potential toxicities include CNS thrombosis (CNST) and hemorrhage. Historical practice at the IKW Health Centre (IWK) involves measuring AT and FG levels following ASP administration and transfusing fresh frozen plasma (FFP) or cryoprecipitate (CRY) to prevent thrombotic and hemorrhagic complications. Methodology: To determine if this practice reduced these complications in children with acute lymphoblastic leukemia (ALL) receiving ASP, incidence, outcome and clinical characteristics of ASP-related CNST in ALL patients at IWK were compared to a similarly treated cohort from B.C. Children’s Hospital (BCCH), where prophylaxis was not performed. Costs associated with preventative versus expectant management strategies were estimated. Results: From 1990-2005, 240 patients were treated at IWK and 479 at BCCH. Seven BCCH patients developed venous CNST (1.5%), compared with none at IWK. CNST occurred exclusively during induction. Six patients received anti-coagulation and continued ASP. The remaining patient discontinued ASP. All remain in remission. NCI high risk (HR) ALL predicted CNST risk (p=0.02), while gender, age, race, and BMI did not. Conclusions: Neither FFP nor CRY protected against CNST, suggesting prophylaxis is unnecessary for unselected ALL patients. However, prophylactic replacement for HR patients in induction may be appropriate and cost-effective.

Figure 1. Evaluation of Pediatric Research Curriculum Components 2007-2009

Year 1 (2007-08)  Year 2 (2008-09)
Formal Education (n=3)  Journal Club (n=3)  Formal Education (n=4)  Journal Club (n=7)

- Excellent
- Very Good
- Good
- Satisfactory
- Poor

- 100%
- 80%
- 60%
- 40%
- 20%
- 0%

Table 1. Evaluation of Pediatric Research Curriculum Components 2007-2009
positive skin tests or allergic reactions were seen in the patients receiving the H1N1 vaccine (n = 50). Three patients had a positive intradermal test to the vaccine given the vaccines in a split dose (10% of total dose, followed by 90% if no reaction after 30 minutes). Patients were observed for one hour. Skin prick testing and intradermal testing to vaccine prior to administration was done in a subset of the patients (n = 21). Individuals with negative skin prick tests for the seasonal influenza vaccine were not predictive of subsequent allergic reaction.

Summary:
Be safe without skin testing.

Background: "Moral distress" (Jameton, 1984), or the inability to complete one's perceived ethical obligation secondary to factors beyond one's control, has been extensively studied in Nursing literature. The most frequent culprit identified within that profession is working within a hierarchical system where challenges to staff opinion are discouraged. Being the attending physician, and thus ultimate decision-maker, however, presents its own challenges to "ethically appropriate" conduct, as physicians are often confronted with cases where intervention is of debatable utility, is not available, or is not desired (i.e. medically futile scenarios, limited resources, parental wishes, etc.). Residents are subjected to challenges both from their position within the hierarchy, and their responsibilities as physician-trainees; however, there is a paucity of literature on their experience of moral distress. The objective of this project, therefore, is to study: 1) Whether residents at the BCCH (in Pediatrics as well as other disciplines) experience moral distress? 2) How does this compare to that experienced by fellows and staff? 3) What are some specific examples of this? 4) What sorts of resources/support would help all levels of training deal with this experience? Methods: The design is that of a qualitative study, with a web-based questionnaire to be distributed via email to all residents/fellows/staff on-site in the month of April. The survey will include general and discipline-specific questions and will be partly developed through a focus group. General questions asked will include but not be limited to: demographic criteria (age, sex, number of children, formal ethics training, etc.), a definition of medical futility, a definition of moral distress, and an opportunity to provide examples. Discipline-specific questions are meant to assess resident/fellow/staff response to a particular scenario in which the physician/trainee would be expected to have special competence i.e. what is your threshold for continuing to treat with chemotherapeutic regimen in light of multiple-relapse ALL. All participants will be permitted two weeks to respond to the questionnaire; participation is voluntary and responses will be anonymous. Following closing of the survey, data will be organized in the context of demographic categories and reviewed by a statistician (Dr. Milner), in order to be analyzed by qualitative software. Completion of the project is anticipated by early July 2010.

Objective: The use of electrocorticographically (ECoG) – guided cortical resection in children with lesional epilepsy is controversial. Given the important developmental issues associated with seizures in children, we evaluated the effect of the decision to perform lesionectomy or ECoG-guided cortical resection on seizure outcome, seizure recurrence, and surgical morbidity in this population. Methods: We retrospectively analyzed seizure outcomes in 67 patients between the ages of three months and 16 years who underwent surgery for lesional epilepsy at British Columbia Children's Hospital. Thirty-four patients underwent ECoG and 33 patients had lesionectomy without ECoG. Results: One year post-operatively, approximately 80% of patients who had ECoG-guided cortical resection or lesionectomy were seizure free. However, there was a trend toward improved seizure freedom in patients who had ECoG at most recent follow-up (79% patients with ECoG seizure free, vs. 61% with lesionectomy only; mean follow-up time 5.8yrs, P = 0.078). There was no increase in neurological morbidity in patients who had ECoG-guided cortical resection, and these patients were less likely to experience repeat epilepsy surgery. Conclusion: Overall, using ECoG to guide additional cortical resection may lead to more robust seizure freedom in children with lesional epilepsy without increasing their risk of surgical morbidity.

Background: Since influenza vaccines are manufactured in eggs, there has been concern in the literature in the past about the risk for a significant allergic reaction in egg allergic individuals. As we continue to encourage vaccination against influenza, we must establish the safety of administering the H1N1 and seasonal influenza vaccines in egg allergic patients. Purpose: The publicity of the H1N1 pandemic increased the demand for flu vaccination including in the egg allergic. The MMR protocol has been safe but cumbersome. A simpler but less tried protocol with vaccines having < 1.2 μg/ml egg protein has been available. As current Canadian seasonal and H1N1 vaccines fulfill this criterion, we hypothesized either split or full administration should be safe without skin testing. Methods: Egg allergic individuals were administered the H1N1 (n = 50) and/or the seasonal influenza (n = 31) vaccines. Skin prick testing and intradermal testing to vaccine prior to administration was done in a subset of the patients (n = 21). Individuals with negative skin tests or those able to eat hidden egg received the full vaccine as a single shot. Those with positive skin tests or those unable to eat hidden egg were given the vaccines in a split dose (10% of total dose, followed by 90% if no reaction after 30 minutes). Patients were observed for one hour. Results: No positive skin tests or allergic reactions were seen in the patients receiving the H1N1 vaccine (n = 50). Three patients had a positive intradermal test to the seasonal influenza vaccine but no immunization reaction. Three patients (9.7%), had transient local reactions to the seasonal influenza vaccine. Summary: No significant reactions were seen in egg-allergic individuals receiving the H1N1 or seasonal influenza vaccines for a total of 81 vaccine events. Positive skin tests for the seasonal influenza vaccine were not predictive of subsequent allergic reaction.
Background: Hypoxic-ischemic encephalopathy (HIE) is characterized by decreased diffusivity (DAV), fractional anisotropy (FA), NAA/choline, and increased lactate/choline at 72 hours (hrs) in injured brain. However, early quantitative measures would be ideal since conventional MRI is so variable on the first day. We hypothesized that early quantitative diffusion tensor imaging (DTI) and proton MR spectroscopic imaging (MRSI) parameters are predictive of changes at 72 hrs. Objectives: To assess the relationship of DTI and MRSI findings at 24 hours of life with those at 72 hrs in a prospective cohort of term newborns with HIE. Design/Methods: 18 term newborns (median 39.6 weeks, range 36-41) with HIE were prospectively studied with MRI (standard imaging, DTI, MRSI) at both 24 and 72 (12) hrs. Standard images were scored according to previously published criteria. DAV and FA (brain microstructure), and NAA/choline and lactate/choline (metabolism) were determined separately in bilateral gray and white matter regions. Linear regression for repeated measures, adjusting for age at first scan (hour) and region of interest, was used to determine the relationship between values on day 1 and 3. The effect of systemic hypothermia was explored. Results: Standard imaging showed complex variations of findings between 24 and 72 hrs. In newborns who were not cooled (14/18), white matter DAV, FA, and NAA/cho at 24 hrs were strongly associated with values at 72 hrs (all P<0.001): decreased values at 24 hrs were associated with a greater reduction at 72 hrs. In gray matter, DAV and NAA/cho at 24 hrs were associated with values at 72 hrs (both P<0.04). Four newborns were treated with systemic hypothermia; their clinical features did not differ significantly from the normothermic group. However, cooling attenuated the relationship of values from 24 to 72 hrs: DAV in white (interaction P=0.04) and gray matter (interaction P=0.08), and gray matter lactate/cho (interaction P=0.01). Cooling was associated with higher NAA/cho in gray and white matter (both P<0.007) and white matter FA (F=0.008). Conclusions: In normothermic term newborns with HIE, quantitative MR values on the first day of life are strongly associated with those on the third day of life, providing an objective measure of injury before qualitative images. Systemic hypothermia attenuated the progression and severity of brain injury.

ABSTRACT #7  SPEAKER: Dr. Dawn Gano  Resident Year 3  RESIDENT PAPER #2

COMPARISON OF QUANTITATIVE DIFFUSION AND MRS PARAMETERS AT 24 AND 72 HOURS OF LIFE IN TERM NEWBORNS WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY

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ABSTRACT #8  SPEAKER: Dr. Joanne Yeung  Resident Year 3  RESIDENT PAPER #3

SERIAL MEASUREMENTS OF EXERCISE PERFORMANCE IN PEDIATRIC HEART TRANSPLANT RECIPIENTS

Joanne Yeung, JE Potts, GGS Sandor, DG Human  Division of Cardiology  UBC Dept Pediatrics

ABSTRACT #9  SPEAKER: Dr. Nina Rolf  Fellow  Division Hem/Onc/BMT  FELLOW PAPER 1

THERAPEUTIC POTENTIAL FOR TOLL-LIKE RECEPTOR 2 AGONISTS IN PEDIATRIC ACUTE LYMPHATIC LEUKEMIA (ALL):
INDUCTION OF APOPTOSIS AND ANTI-ALL IMMUNOGENICITY

Nina Rolf, A Karimnia, KR Schultz  Division of Hem/Onc/BMT  UBC Dept of Pediatrics/Child & Family Research Institute

Background: Despite overall high cure-rates for children with ALL, treatment options for relapsed or refractory ALL are limited and prognosis is poor. We previously showed that the Toll-like receptor (TLR) 9 agonist, CpG ODN, induces significant anti-tumor immune effects that may overcome the immune escape of ALL blasts that leads to relapse. Currently, this is being developed into a phase I clinical trial (TACL group). However, our recent research demonstrated that TLR2 receptors are more abundantly expressed on pre B-ALL cell-lines suggesting that TLR2 agonists potentially have better efficacy in generating anti-ALL immunity. Unlike other TLRs functionally active as homodimers, TLR2 forms heterodimers either with TLR1 or TLR6 to attain specificity. Objective: We tested the hypothesis that different synthetic TLR2 agonists (TLR2/6: Pam2CSK4=Pam2, TLR2/1: Pam3CSK4=Pam3) differ in their ability 1) to transduce specific signalling pathways, 2) to induce apoptosis in pre B-ALL cells, and 3) to augment pre B-ALL cell immunogenicity. Methods: Pre B-ALL cells pre-treated with each TLR2 agonist were compared to untreated samples using the following assays: 1) Signal transduction was studied by detecting phosphorylation of NFkB along with degradation of IkB by flow cytometry and time response curves were correlated with mRNA expression. 2) Apoptosis/necrosis of pre B-ALL cells was studied by flow cytometric detection of AnnexinV/7AAD. 3) Augmentation of immunogenicity in cell-culture was investigated by measuring induction of co-stimulatory molecules and increment of allogeneic T-cell proliferation. Results: Pam2 was a more rapid and potent inducer of NFkB signalling than Pam3. Induction of NFkB phosphorylation by Pam2 partially correlated with expression of TLR1 and TLR6 in pre B-ALL cell-lines. However, Pam3 induced significant apoptosis, while Pam2 did not. Both TLR2 agonists had similar impact on induction of co-stimulatory molecules (CD40, CD86), while Pam3 augmented immunogenicity of pre B-ALL cell-lines in T-cell allo-reactivity studies (Pam2 not yet tested). Conclusion: Both TLR2 agonists were able to alter ALL immunogenicity. However, only TLR2 agonist Pam3 (TLR2/1) potently induced apoptosis of pre B-ALL cells. This supports that TLR2 agonists, alone or in combination with TLR9 agonists, show promising efficacy in improving cure-rates for relapsed pre B-ALL. However, further investigations are required.
MI XED METHODS APPROACH TO DESIGNING AND IMPLEMENTING A SCHOOL-BASED NUTRITION INTERVENTION IN NEIGHBOURHOODS FACING FOOD INSECURITY

Kevin Harris, J Ng

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Background: Low fruit and vegetable (FV) intake is one component of poor diet and is more prevalent in food insecure children and adolescents. It is associated with adverse health outcomes including obesity, coronary heart disease, diabetes and reduced life span. The purpose of our study was to determine what factors influence FV intake in adolescents at risk for food insecurity and to implement an intervention to improve FV intake. Methods: We conducted focus groups, moderated by trained youth facilitators, in children 13-16 years old at risk for food insecurity to determine factors that influence FV intake. We then collaborated with Vancouver Coastal Health, the Vancouver School Board and Windermere Community School to implement an intervention to improve FV intake. The intervention was initiated by the school and student driven. It involved a media campaign, student participation, and altering the foods available on the school campus. We used a validated food frequency questionnaire to assess dietary intake before and after the intervention. We assessed the economic impact of the intervention on the school. Results: Twenty-one adolescents participated in the focus groups. They identified factors at home, school and personal attitudes that influenced diet. Important factors included parental food choices, taste preference, perceived cost of healthy foods, limited accessibility, and lack of understanding of the relationship between diet and health. Before and after the intervention we sampled 294 students in Grades 8 to 12. Food choices and frequency did not change over the course of the study period. The mean daily income from the intervention was $156.09 and the associated expenses were $131.73 corresponding to an annual surplus of $435. Conclusion: The main barriers to healthy diet in adolescents include financial limitations, limited accessible food sources and taste preference. These findings suggest that a school-based fruit and vegetable promotion programs should focus on improving availability and financial accessibility of these items. However in this short-term intervention, improving accessibility at school did not improve diet.

REDEFINING THE INCIDENCE AND OUTCOMES OF CNS ATYPICAL TERATOID RHABDOID TUMOURS AT BC CHILDREN’S HOSPITAL

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Background: Atypical Teratoid Rhabdoid Tumour (ATRT) of the central nervous system (CNS) is a rare type of highly malignant embryonal neoplasm. A specific antibody test to detect loss or mutation of the INI-1 tumour suppressor gene (hSNF5/SMARCB1) has been used at BC Children’s Hospital (BCCH) since 2007. Prior to the availability of this test, ATRT’s could be indistinguishable from other tumours by routine pathology, and therefore may have been under-diagnosed. Objectives: We applied the INI-1 test retrospectively to determine how many CNS embryonal tumours over the prior two decades would be classified as an ATRT. Identifying ‘cryptic’ ATRT’s allowed us to better describe the incidence and clinical outcomes for this unique tumour, which historically has been reported to have a dismal prognosis. Design/Method: With ethics approval, paraffin-embedded tissue was retrieved from storage for all BCCH patients from 1986 – 2006 who were diagnosed with a CNS embryonal tumour. Slides were prepared and re-stained with the anti-BAF47/INI-1 antibody, and histologic features were reviewed. Results: Ninety-four patient samples were available, and INI-1 staining showed loss of retention in 12 samples (including 2 previously reported as ATRT without INI-1 testing). Median age at presentation was 1.3 years (0.3 – 9 years), and there was a 9:3 female:male ratio. One patient was been treated with radiation, and 2 had metastatic disease. Median survival was only 14 months, but there were three long term survivors (4, 6, 8 years) without relapse. Revealing these ‘cryptic’ ATRT’s changes the incidence of ATRT from 4% (1/25) to 36% (9/25) of all <3 year old patients with embryonal tumours between 1986 - 2006. Conclusion: Previously there had been no reported survivors of ATRT at BCCH; by including our study findings, 25% of ATRT’s actually had a survival rate greater than 3 years. Two were young patients treated with intensive chemotherapy and no radiation, showing promise for this strategy. A better understanding of how many children have actually had ATRT’s and their corresponding survival rates is critical for designing more specific treatments in the future. Capturing ATRT as a separate entity inherently allows a more accurate reporting of survival rates for other CNS embryonal tumours.

LONG TERM PROGNOSIS OF EEG FINDINGS IN THE FIRST YEAR OF LIFE

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Objective: To determine how specific abnormal EEG findings found at 3 to 12 months correlate with clinical outcome on long term follow up. Material & method: This is a retrospective study of 358 term infants who had at least one EEG in the first year of life and subsequent clinical assessment between ages 4 to 16 years. Prognosis parameters included Epilepsy and Neurologic (intelligence, school performance, developmental milestones and neurological examination) outcomes. Long term prognosis was classified into “Normal” when patients had normal clinical outcome parameters, “Minor Sequelae” when patients had mild abnormalities in clinical outcome parameters, "Major Sequelae" when patients had moderate to severe abnormalities in clinical outcome parameters, and "Epilepsy" when patients had seizures and were on medication. Results: Preliminary results showed 66 had normal outcome, 39 had Minor Sequelae and 253 had Major Sequelae. 234 had Epilepsy on follow up and 106 had not. 117/358 had major abnormal EEG background of which 90% had Major Sequelae and 75% had Epilepsy. 98/358 had abnormal sleep potentials of which 91% had Major Sequelae and 80% had Epilepsy. 175/358 had epileptiform discharges of which 85% had Major Sequelae and 80% had Epilepsy. Conclusion: The presence of abnormal EEG findings during the first year of life may be predictive of unfavorable prognosis (Major Sequelae and Epilepsy). Abnormal EEG background and abnormal sleep potentials may not be predictive of Epilepsy outcome. Normal and mildly abnormal EEG findings were not correlated with definite outcome.
Chronic non-bacterial osteomyelitis (CNO) includes chronic recurrent multifocal osteomyelitis (CRMO) and SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis and osteitis), which are rare auto-inflammatory osteopathies affecting children. These syndromes are characterized by episodes of painful disease with risk of permanent bony deformities. No single agent has proven to be consistent in effectively treating these children. Therapies have included non-steroidal anti-inflammatories, corticosteroids, bisphosphonates, sulfasalazine, interferon-α, interferon-γ, and methotrexate. Unfortunately there are several cases that continue to be refractory to treatment. **Objective:** To report on a series of patients with refractory CNO disease who have been treated with biologic therapy (anti-tumor necrosis factor agents and anti-IL1 receptor antagonist (anakinra)). **Methods:** A retrospective, descriptive case series of four children with refractory CNO disease treated with biologic therapy. Set timepoints (T=0, T=6 weeks, T=12 months after initiating biologic therapy, and at latest follow-up) were used to measure disease activity as characterized by patient 10 cm pain visual analogue scale (VAS), physician VAS, radiologic findings, clinical examination, Childhood Health Assessment Questionnaire (CHAQ), and changes in inflammatory markers (CRP and ESR). **Results:** Three patients were treated with anti-TNF agents and one patient was treated with anakinra. All patients showed initial improvement in all parameters of disease activity, however one patient discontinued infliximab due to an (unconfirmed) fungal skin infection. The patient treated with anakinra had failed to sustain a good response at one year after initiating therapy. **Conclusion:** We present a descriptive report of the use of biologic therapy in refractory CNO disease which shows initial success in controlling disease activity. However, this response is not consistently sustained. Further studies will be helpful to determine the usefulness of these agents in treating refractory CNO disease.