UNSW AUSTRALIA

UNSW Paediatric Research Week 2016
Independent Learning Project (ILP) Awards

Never Stand Still | Medicine | Women's & Children's Health

Wednesday 16th November 2016
Sydney Children's Hospital

UNSW Paediatrics

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WELCOME

Welcome to the 4th Annual Independent Learning Project (ILP) Awards.

The Discipline of Paediatrics is delighted with the number of entries submitted this year; 28 abstracts were received, our highest number yet. Every one of them showcases the variety of research and innovative research collaborations that are being conducted across Paediatrics.

A big thank you to our committed supervisors who dedicate their time to lead and mentor these students, enabling them to undertake this wonderful opportunity as part of the undergraduate Medicine course at UNSW.

Thank you to all the ILP students who submitted abstracts this year and I would like to congratulate those presenting today. Please remember to vote for your favourite presentation. Two prizes will be awarded – Overall Winner and People's Choice. The winners will be announced at the end of the presentations.

Thank you also to our judges, who kindly scored all of the abstracts - a large feat! And to our oral judges who will be selecting our overall winner today.

It is also a pleasure to welcome our guest speaker, Monica Majumder, the recipient of the Margaret Dance Honours Prize for 2015.

I would like to thank Dr Sean Kennedy, Discipline of Paediatrics' Director of Education and Sam McFedries, Research Manager for organising this event.

If you would like further information about potentially supervising an ILP student in the future, please contact Samantha McFedries, Research Manager – s.mcfedries@unsw.edu.au

Enjoy the presentations,

Professor Adam Jaffe

John Beveridge Professor of Paediatrics
Head of Discipline of Paediatrics
School of Women's & Children's Health

Associate Director of Research
Sydney Children's Hospitals Network
(Randwick)

UNSW AUSTRALIA | Women's & Children's Health Medicine

The Sydney children's Hospitals Network
care, advocacy, research, education

WELCOME:

12:55PM Chair: Dr Sean Kennedy
Director of Education & Senior Lecturer
Discipline of Paediatrics, School of Women's & Children's Health, UNSW Medicine

FINALISTS PRESENTATIONS:

1:00PM Anna Camille Akon GASTROENTEROLOGY
Supervisors: Conjoint A/Prof Daniel Avi Lemberg; Dr Steven Leach
Project Title: *Haematological Proxy Measures and their Correlation with Thiopurines Metabolites in Paediatric Inflammatory Bowel Disease Patients*
Abstract: Page 9

1:15PM Georgina Dixson COMMUNITY CHILD HEALTH
Supervisors: Dr Sally Nathan; Conjoint A/Prof Susan Woolfenden
Project Title: *Characteristics and Drug Use Among Adolescents Admitted to Residential Treatment.*
Abstract: Page 14

1:30PM Jessica Ong EMERGENCY
Supervisors: Dr Susan Adams; Dr Arjun Rao
Project Title: *Helmet use in bicycles and other non-motorised recreational wheeled vehicles.*
Abstract: Page 27

1:45PM Rosie Sutherland GASTROENTEROLOGY
Supervisors: Dr Keith Ooi; Tamarah Katz
Project Title: *The changing nature of dietary intake in cystic fibrosis: an evaluation of energy-dense nutrient poor and nutrient-dense intake in Australian children with cystic fibrosis.*
Abstract: Page 33

GUEST SPEAKER: MARGARET DANCE HONOURS PRIZE WINNER 2015

2:00PM Monica Majumder ENDOCRINOLOGY
Supervisors: Prof Maria Craig; Prof William Rawlinson
Project Title: *Inflammation and enterovirus infection at the onset of type 1 diabetes*
Abstract: Page 41

AWARD PRESENTATIONS

2:15PM Presentation of the ILP Overall Winner; ILP People's Choice; and Margaret Dance Honours Prize 2015.

CONTENTS

In 2013, the Discipline of Paediatrics offered (for the first time) Independent Learning Project (ILP) students the opportunity to submit abstracts on the research they had been undertaking, competing to win one of two UNSW Paediatrics ILP Awards.

Since 2014, all UNSW Medicine students who were completing their ILP that year in the field of paediatrics were invited to enter. In 2016, The Discipline received 28 abstracts - the highest number yet, that were scored by a review panel. Four finalists were selected and will present their work at this special, Sydney Children's Hospital Grand Rounds.

Judges will decide the Overall Winner based on today's oral presentations.

The audience will cast their votes at the end of the presentations, which will determine the People's Choice Award.

The winners of both awards will be announced at the conclusion of the presentations.

WHAT ARE INDEPENDENT LEARNING PROJECTS (ILP)?

The Independent Learning Project (ILP) is intended to provide UNSW medical students with a period of in-depth study that engenders an approach to medicine that is constantly questioning and self-critical.

The ILP is undertaken in Phase 2 of the undergraduate medicine program at UNSW.

The ILP aims to promote lifelong learning patterns and skills which will enable students to approach future medical challenges in their careers with a rigour and depth not possible without a detailed knowledge of the formal processes of research, literature appraisal, data collection, analysis and presentation.

By the end of the ILP the students will be expected to achieve the following specific goals:

- An ability and inclination to question the basis of current scientific thinking in relation to medical and public health practice.
- To retrieve literature on a topic and demonstrate a familiarity with the use of medical databases.
- To evaluate current knowledge in a field and to provide a critical appraisal of that body of knowledge.
- To identify a problem in their chosen field and to understand and participate in the process of designing a scientific investigation of the problem.

- To be aware of the ethical issues involved in medical research as applied to their area of study.
- To critically evaluate data including the appropriate use and application of analytical procedures.

JUDGING CRITERIA

ILP abstracts submitted as entries for the awards were scored based on the following criteria:

- Is it well written with a clear and logical structure?
- Are the methods appropriate and adequately described?
- Are the results meaningful?
- Are the conclusions justified?
- Does there appear to be a significant amount of work in the study?
- Would it make an interesting oral presentation?

ACKNOWLEDGEMENTS

Thanks to Dr Sean Kennedy, Senior Lecturer and Director of Education, Discipline of Paediatrics who developed the concept of the ILP Awards.

Thanks also goes to our review panel who kindly scored all 28 written abstracts; and to those that will be judging the oral presentations today.

- Dr Hugh McCarthy
- Dr Nusrat Homaira
- Dr John Lawson
- Dr Sean Kennedy
- Prof Adam Jaffe
- Dr Rebecca Spicer

Thanks also to the students supported by their supervisors, who submitted abstracts for the awards.

DR MARGARET DANCE MBBS

Margaret Dance was one of 75 students in the first cohort attending UNSW's Medical School when it first opened in 1961. Margaret graduated the six-year MBBS programme, but sadly passed away during her residency. The Dance family bequested the Margaret Dance Prize in her memory which was administered by the late Professor John Beveridge in the early years, and UNSW.

Margaret had been plagued with ill-health throughout her academic studies and it is a true testament to her strength that she completed the course, even more remarkable that she was blind in one eye by final year, and both eyes during her residency. Margaret underwent two corneal grafts to restore her vision.

Margaret was treated by Fred Hollows and several of her professors, as her autoimmune disorder affected a number of her organs. Margaret's friend and peer, Sue Whereat (nee Mumford) noted that Margaret showed great courage and rarely complained, *she continued with such determination and grace despite her suffering...her illness robbed our society of a great doctor.'* [1]

[1]Pollitt, J., De Carle, D., & Whereat, S. (2015) And Now From The Beginning...The stories of the pioneer students of the UNSW School of Medicine.

MARGARET DANCE PRIZE

The Margaret Dance Prize is awarded annually by the Discipline of Paediatrics to the BSc Med (Hons) student with the highest mark for their honours research project. The prize is retrospective, therefore the 2015 prize will be awarded in 2016 and is only available for students who have been enrolled in the Discipline of Paediatrics.

The student who receives the Margaret Dance Prize is invited to present their research at this special, Sydney Children's Hospital Grand Rounds.

GASTROENTEROLOGY

Haematological Proxy Measures and their Correlation with Thiopurines Metabolites in Paediatric Inflammatory Bowel Disease Patients

Student: Anna Camille Akon

Supervisors: Conjoint A/Prof Daniel Avi Lemberg; Dr Steven Leach

Background: Thiopurine metabolite levels are used to monitor the safety and efficacy of thiopurine treatment in paediatric inflammatory bowel disease (IBD). However, thiopurine metabolite assays are expensive and not widely available. As an alternative, current haematological disease markers may be useful as proxy markers of thiopurine metabolite levels.

Aim: To establish the relationship between mean cell volume (MCV), lymphocyte count, 6-thioguanine nucleotide (6-TGN) levels and disease activity indexes in a population of paediatric IBD patients and assess the potential of these haematological markers as alternatives to thiopurine metabolite levels.

Methods: One hundred and ninety-nine paediatric IBD patients treated with thiopurines between 2008- 2015 who had 6-TGN measurements were retrospectively reviewed. Disease activity index and hematological markers were collected and compared to 6-TGN levels.

Results: Between 2008 to 2015, three different TGN assay methodologies were used with a significant difference in median TGN levels between methodologies. Data was subsequently analyzed separately by methodology epoch. There was a significant correlation between 6-TGN levels and both lymphocyte count and MCV. Using the previously established cutoff for minimum therapeutic concentration of 6-TGN of 235 pmol/8 x108 RBC, there was no significant difference in lymphocyte count for patients above and below this cutoff although there was a significant difference in MCV ($P < 0.01$).

Conclusion: Neither lymphocyte count nor MCV appear sufficiently robust to be used as a guide to optimise thiopurine dosing in paediatric IBD patients. A subsequent finding was that TGN levels significantly changed due to TGN testing methodologies. This finding indicated that TGN methodology should also be considered when using metabolite monitoring in clinical practice.

Clinical Experience and Parental Perspectives on the Ketogenic Diet for Children with Intractable Epilepsy: Factors Influencing Efficacy, Tolerability and Compliance

Student: Remi Banuelos

Supervisors: Dr Michael Cardamone; Dr Michelle Farrar

Objective: To evaluate the efficacy of the ketogenic diet (KD) in children with intractable epilepsy (IE) and understand parental perspectives on compliance and tolerability.

Study Design: Retrospective single centre study of 43 children with IE treated with the KD between 2012 and 2015. Parental perspectives were based upon 42 study questionnaires from 90 families whose children had commenced the KD.

Results: Seizure reduction was significantly associated with diet duration ($p<0.005$), and reduction in number of anti-epileptic medications ($p<0.005$). Reasons for diet discontinuation included no improvement in seizures (26%), poor compliance (9%), adverse effects (9%) and weight loss (9%). Side effects included hypercholesterolaemia (47%), hypertriglyceridaemia (42%), hypercalciuria (44%), constipation (42%) vomiting (28%) and diarrhoea (16%). Parental perceptions of seizure reduction were significantly correlated with their impressions of cognitive improvement, ($p<0.01$) and diet duration ($p<0.05$). Most parents felt satisfied, confident and supported during their experience with the KD. They reported difficulties with preparation and increased time required to administer the KD (31%), disruption of family dynamics (24%), compliance and understanding the network of care (19%), and food refusal (19%). Parents suggested further dietetic support, frequent KD follow-up clinics, and parent mentorship to help improve delivery.

Conclusions: The KD can effectively reduce seizures and medication. Parents reported improved cognition and valued its efficacy yet acknowledged the increased burden of care. Compliance is dependent upon seizure reduction.

Difficult toddler temperament – prevalence and associated factors at 18-month follow-up of a birth cohort.

Student: A'ishah Bhadelia

Supervisors: Conjoint A/Prof Susan Woolfenden; Prof Valsamma Eapen

Background: A difficult temperament, when coupled with other risk factors, may lead to behavioural and emotional adjustment issues during childhood, and beyond [1].

Aim: To investigate the prevalence of parental perception of difficult temperament in toddlers (mean age 21 months) in a population cohort and identify associated individual, family and socio-demographic risk factors.

Methods: Prevalence of parental perception of difficult temperament was derived from two questions from the 18-month follow-up questionnaire of the Watch Me Grow longitudinal birth cohort study. Data was available for 492 toddlers. The Short Temperament Scale for Toddlers (STST) was administered to a subset of 159 toddlers. Associated risk factors were identified using univariate and multivariable logistic regression.

Results: Parental perception of difficult temperament was found to be 7.3% (n= 36) in 492 children. STST identified 6.3% (n=10) of the159 toddlers with a difficult temperament. Unadjusted risk factors that were significantly associated with parental perception of difficult temperament were screen time >2 hours daily (OR = 2.32, 95% CI: 1.2, 4.6), child not being read to (OR = 3.37, 95% CI: 1.6, 7.1) and experiencing stressful life events within the past two years (OR = 2.05, 95% CI: 1.0, 4.1). Independent predictors of difficult temperament were screen time >2 hours daily (2.43, 95% CI: 1.2,4.9), child not being read to (3.92, 95% CI: 1.8, 8.5) and family history of mental health problems (2.69, 95% CI: 1.1, 6.5).

Conclusion: Parental perception of difficult temperament is 7.3% in this cohort. Toddlers with a difficult temperament were less likely to be exposed to stimulatory experiences and their families may be under greater stress, emphasizing the importance of parental education and support.

[1] Prior, M., Sanson, A., Smart, D., & Oberklaid, F. (2000). Pathways from infancy to adolescence. Australian temperament project.

PUBLIC HEALTH

How are parents who do not fully vaccinate their children framed by Australian newspaper media?

Student: Shefali Chaukra

Supervisors: Dr Niamh Stephenson; Dr Anita Heywood

Background: Will the 2016 “No Jab No Pay” policy on childhood immunisation raise immunisations rates, affect the public’s trust in public health and change social norms around vaccination? Parents’ decisions are shaped by social norms; and the media which both reflects and influences social norms has been selected as a tool to observe social norms in this paper, where we examine trends in newspaper framing of parents who do not fully vaccinate in two periods of major policy change (1997/98 and 2015/16).

Methods: Using Factiva, we collected 153 articles from 5 high circulating Australian newspapers in 1997-98 and 2015-16, which contained keywords: “children”, “parents” and “vaccinations”. A deductive coding was developed to identify 9 parental typologies.

Findings: In 2015/16 media focuses less over complacent attitudes, and more media attention is given to vaccine refusers through vilification and new characterisations (e.g. pro-choice). These changes in media representations can be seen to align with the shifting targets of the 97/98 and 2016 policies.

Discussion: The 2016 policy is associated with intensified discussion of “choice” and enabling media representations of anti-vaccination as “pro-choice”. The policy also raises a question over how clinical communications will facilitate genuine dialogue with concerned parents in the perceived absence of the ability to choose.

Conclusions: Media accounts of the policy appear to largely support the policy however there is potential for concern over the subtle shifts around parents’ view of the new policy’s effect on choice, and public health needs to be watchful of public attitudes and social norms in the future that may undermine public trust and confidence.

Demographic Changes and Outcomes of Very Premature Infants admitted to NICU in Australia and New Zealand

Student: Jacob Corlis

Supervisors: A/Prof Kei Lui; Dr Srinivas Bolisetty

Objective: To track outcomes of very preterm infants born between 1995 and 2013, cared for in Neonatal Intensive Care Units (NICU) in the Australia New Zealand Neonatal Network (ANZNN). Relative changes in the rates of mortality and major morbidities will be compared. Factors associated with the observed trends will be investigated.

Methods: A retrospective population based cohort study, of infants born before 32weeks gestational age cared for in NICUs in the ANZNN (n=62,654) over 18 years, was performed. Mortality, major morbidities and composite mortality or major morbidity rates were compared over three epochs (Epoch 1=1995-2000; Epoch 2=2001-2007; Epoch 3=2008-2013), using univariate and multivariate analysis. Clinical practices associated with outcome trends were examined. Outputs were stratified into three gestational age groups (<25 weeks, 25-27 weeks and 28-31 weeks) and total cohort.

Results: Data on 62,654 infants from the three epochs (Epoch 1, n=18372; Epoch 2, n=23241; Epoch 3, n=21041) was analysed. Crude and adjusted rates of mortality, major morbidity and composite death or major morbidity decreased across the study time period for all gestational age groups. Significant decreases were seen in neonatal infection, severe intraventricular haemorrhage and bronchopulmonary dysplasia, and in the eldest group in necrotising enterocolitis (NEC). NEC rates increased significantly in the youngest two gestational groups. Temperature management and antenatal corticosteroids were identified as factors significantly associated with improved outcomes. A concerning increase in outborn births was noted.

Conclusion: Severe neonatal adverse outcomes for the most part significantly decreased. Improving survival did not result in increased survival with major morbidities. Temperature management and antenatal corticosteroids were identified as factors associated with improved outcome trends, and a concerning increase in outborn births noted.

Characteristics and Drug Use Among Adolescents Admitted to Residential Treatment

Student: Georgina Dixson

Supervisors: Dr Sally Nathan; Dr Sue Woolfenden

Aims: To explore differences between adolescent males and females (aged 13-18 years) accessing residential rehabilitation for problematic alcohol and other drug (AOD) use; and to investigate risk factors for amphetamine-type stimulants (ATS) use in females.

Method: The study was a mixed-methods sequential design. Cross-sectional analysis of existing pre-treatment data for young people aged 13 – 18 years attending a rehabilitation program between 2009-2015 (n=954) was undertaken, followed by a focus group discussion and in-depth interviews with staff.

Results: There are significant differences between adolescent males and females in demographics and risk factors. Particularly, school disengagement (p=.016) and criminality (p=.000) were significantly higher in males than females and unstable accommodation was significantly higher in females than males (p=.008). Females were significantly more likely to be using ATS (p=.013), tobacco (p=.036) and opioids (p=.002). There were significantly higher rates of suicide attempts (p=.000) and self-harm (p=.000) reported by the females, as well as significantly more reports range of traumatic events. Cumulative trauma was the main predictor for female ATS use (OR=.009). Qualitative data provided context and depth to quantitative findings.

Conclusions: There are significant differences in adolescent males and females accessing residential rehabilitation for problematic AOD use. High levels of trauma and mental health problems in this population support the notion that traumatic childhood experiences are strongly associated with problematic AOD use at a young age. Increased attention to decreasing family violence, abuse and neglect is required. In clinical practice, a trauma-informed model of care is worthy of further investigation.

Does Ratio of Skin Prick Test Wheal Size Between a Primary Nut Causing Allergic Reactions and Other Nuts, Predict the Likelihood of Reacting to the Latter?

Student: Andrew Fong

Supervisors: Dr Brynn Wainstein; Prof Connie Katelaris

Background: Skin prick testing is commonly used for the diagnosis of food allergy but lacks specificity. It can therefore be difficult to predict the likelihood of reacting to foods on the basis of skin prick testing alone. There have as yet been no studies looking at whether adjusting for the ratio between the size of skin prick test allergen wheals, may be a better predictor than individual wheal size alone.

Methods: We identified patients at Sydney Children's Hospital who have had oral food challenges to both a nut known to have caused previous allergy (index nut) and a nut of unknown clinical significance identified by skin prick testing (secondary nut). Skin prick test wheal sizes for the two nuts performed on the same day were used to generate a ratio and an adjusted secondary nut skin prick test. ROC curves were generated to determine appropriate cut-off scores.

Results: An adjusted skin prick test wheal size of 0.365mm had 95% sensitivity but 15% specificity, whereas an adjusted skin prick test wheal size of 4.35mm had 95% specificity but 35% sensitivity. A secondary-index nut ratio of 0.185 had 95% sensitivity but 12% specificity, and a secondary-index nut ratio of 1.04 had 95% specificity but 29% sensitivity. ROC analysis showed that the area under the curve was equal for the two tests.

Conclusion: Adjusting for the ratio between the secondary nut and index nut may be clinically useful in predicting challenge outcome for nuts of unknown clinical significance.

PSYCHOLOGY | CANCER

The School and Educational Experiences of Siblings of Children with Chronic Illness: Australian Parents' Perceptions

Student: Lucy Gan

Supervisors: Dr Joanna Fardell; A/Prof Claire Wakefield

Siblings of children with chronic illness may experience difficulties at school, yet little is known about the impact of the ill child on siblings' school experiences. This study investigated parents' perceptions of school related difficulties and support that siblings of chronically ill children experienced. We conducted semi-structured telephone interviews with 35 parents of children with a chronic illness who had a school-aged sibling/siblings (4-25 years), representing the experiences of 43 siblings. Interviews were audio-recorded, transcribed and analysed using conceptual framework of Miles and Huberman. Twenty-six parents of 29 siblings identified school related difficulties, with 19 of these siblings' (65.52%) experiences found to be related to the ill child. We identified four themes that manifested in school; increased anxiety or stress at school, decreased attention from schools towards siblings in favour of the ill child, increased sibling-carer responsibilities that may translate into school behaviours and increased absenteeism due to the ill child's hospitalisation. Parent absences also impacted on the sibling's school functioning. Parents described general and psychological support from the school and the importance of monitoring the sibling at school and focusing on their unique needs. This highlights the important role of school psychologists and teachers in providing attention that the sibling may lack at home. School personnel may contribute to a family-school partnership that acts to normalise the daily functioning of siblings.

Relating newborn head circumference with Hirschsprung's disease

Student: Alexander Glyde

Supervisors: Dr Susan Adams; Dr Camille Wu

Background and Aims: Hirschsprung's disease (HSCR) is a congenital disorder, affecting 1:5000 neonates, characterised by aganglionsis of various lengths of intestines. HSCR is described as a complex, polygenetic, sex-modified disorder of neural crest cell (NCC) proliferation. Numerous genes are implicated in HSCR, but they have incomplete penetrance and are frequently associated with other disorders of NCC derived tissue. The extent of the relationship between HSCR and other disorders of neuro-proliferation, particularly in isolated disease, is largely unknown. We aim investigate a possible link between HSCR and broader neuropathy by relating newborn head circumference to aganglionic segment length.

Methods: Retrospective data was collected from Sydney Children's Hospital and compiled with data from the Royal Alexandria Hospital for Children and the Canberra Hospital over a 46-year period. Patients born at term, with known head circumference measurements at birth and aganglionic segment length were included. Syndromic patients and those with major CNS abnormalities were analysed separately. SPSS V23 was used for analysis.

Results: A total of 301 patients were included from baseline criteria. A further 64 (21.3%) were excluded due to syndromes or CNS abnormalities. 237 patients formed the main analysis. Newborn head circumference of non-syndromic boys with total colonic aganglionosis (TCA) was significantly smaller than non-syndromic boys with large bowel transitions ($p<0.05$). The observed trend was consistent across further sub-categories of aganglionosis, and appeared replicated in separate analysis of excluded cases. No clear trends were observed in girls.

Conclusions: Long-segment HSCR may be associated with broader neuro-proliferative dysfunction, even in isolated cases. Further research is needed to validate and quantify this finding.

CARDIOLOGY | PSYCHOLOGY

Quality of Life and Family Functioning after Diagnosis of a Cardiac Channelopathy: experiences of children and their families

Student: Stella Graham

Supervisors: A/Prof Nadine Kasparian; Dr Michelle McElduff

Background: The cardiac channelopathies are a rare group of inherited conditions, including Long QT Syndrome (LQTS), Short QT Syndrome (SQTS), Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) and Brugada Syndrome. Cardiac channelopathies can cause significant challenges for children and their families, including risk of sudden cardiac death, activity restrictions, potential surgery, and life-long medication. Despite this, there has been limited research investigating the impact of these conditions on Health Related Quality of Life (HRQOL), and family functioning, or on potential supportive interventions.

Methods: This study aimed to examine the psychological experiences of children with cardiac channelopathies and their families, with a focus on HRQOL and family functioning. Parents of children (aged 0-18 years) with a cardiac channelopathy attending a multi-disciplinary outpatient clinic completed self-report measures assessing their child's HRQOL, parental anxiety, depression and stress, family functioning, social support, and unmet needs.

Results: 61 parents participated (response rate: 62%). Based on parent report, children with cardiac channelopathies had poorer physical and psychosocial HRQOL, than normative samples. On average parents reported 14 unmet clinical care needs. Higher levels of parental psychological distress, and lower levels of perceived social support were associated with poorer parent reported HRQOL. Greater unmet needs, poorer social support, marital status, and increased parental age were associated poorer family functioning.

Conclusion: Parental distress and perceived support appear to be critical determinants of HRQOL and family functioning. There is a strong need for a multidisciplinary approach to the care of children with cardiac channelopathies. To address the determinants of HRQOL and family functioning, clinical care should integrate psychological support, social work and patient education. Such interventions must be assessed in future research.

Academic Achievement of Children with Cystic Fibrosis: What can we learn?

Student: Anida Hanxhiu

Supervisors: Conjoint A/Prof Davinder Singh-Grewal; Dr Dominic Fitzgerald

Objective: Children with Cystic Fibrosis are living longer, with an average life expectancy of 40 years, placing greater importance on academic achievement during childhood. This study investigated whether disease severity was linked to educational outcomes.

Methods: This is a retrospective cohort study/case series of 72 children with Cystic Fibrosis between the ages of 8 to 16 years in New South Wales and the Australian Capital Territory, Australia. Academic achievement was determined by NAPLAN and school report scores, including number of days absent in the previous semester.

Results: 56% (40/72) of participants who agreed to be involved in the study provided their NAPLAN results. Total SNOT score was associated with total absences and FEV1%. The average number of Pseudomonas Aeruginosa isolations was positively correlated with NAPLAN numeracy relative to the national average. There was no evidence to associate treatment burden, clinical status and school absence rates with academic achievement. There was no evidence to associate treatment burden, clinical status and school absence rates with academic achievement.

Conclusions: While this study was unable to observe a relationship between the burden of CF and academic achievement, it has provided an insight into some of the factors that could potentially be associated with poor school performance. Further research in this area, with a larger sample size, possibly involving multiple centres, would prove helpful in investigating the association between CF and academic performance.

Developmental outcomes in infants treated with propranolol for infantile haemangioma

Student: Georgia Heron

Supervisors: Conjoint A/Prof Orli Wargon; Dr Susan Adams

Recent publications and editorials have questioned the risks of using propranolol in the first year of life for infantile haemangioma, because this beta-blocker crosses the blood brain barrier. This study uses a developmental screening tool to assess children aged between 10 and 66 months who were treated with this medication in the first year of life at Sydney Children's Hospital Randwick and Great Ormond Street Hospital London. Over three years 162 developmental questionnaires were completed by parents using the validated screening tools, Ages and Stages Questionnaire 3rd Edition and Ages and Stages Questionnaire: Social and Emotional. 35 (21.6%) patients results required referral and an additional 10 (6.1%) were found to be in the monitoring zone. This data was analysed and compared to the normal population and showed that the gross motor scores were significantly lower than the normal population ($p=0.022$). When this data was categorised by age group, gross motor scores were significant lower in the first and second years of life ($p=0.003$ and $p=0.038$ respectively) and problem solving scores were significantly lower in the second year of life ($p=0.050$). 11 (7%) of ASQ:SE questionnaires required referral and there was no significant difference in scores when compared to the normal population ($p>0.05$). This larger study confirms developmental outcomes previously observed and introduces new data on social and emotional development.

The Identification of Novel Therapies in Diffuse Intrinsic Pontine Glioma (DIPG)

Student: Danielle Lapin

Supervisors: Dr David Ziegler; Dr Maria Tsoli

Diffuse intrinsic pontine glioma (DIPG) is a highly aggressive paediatric brainstem tumour, with a peak incidence in middle childhood and a median survival of less than 1 year in the majority of cases. The dismal prognosis associated with DIPG is exacerbated by the repeated failure of over 250 clinical trials to improve survival over standard radiotherapy. The conventional practise to not obtain biopsies in DIPG lead to a paucity in the availability of biological samples for laboratory experimentation and until recently greatly hindered therapeutic advancement. The discovery of critical oncogenic drivers including Histone H3, ACVR1 & TP53 include mutations not previously identified in other malignancies highlighting DIPG as a distinct biological entity. Our team has successfully completed a series of world-first High Throughput Screens, implementing a non-rational approach to identify pharmacological agents that may possibly become future therapies in DIPG. Promising candidates were selected for further investigation in vitro using cytotoxicity assays, colony formation assays, flow cytometry assessing apoptotic events and western blot to elucidate mechanisms of actions. The two calmidazolium based combinations demonstrated a synergistic reduction in DIPG cell viability at therapeutically relevant concentrations. Further, calmidazolium combinations significantly enhanced the anti-proliferative effect of radiation when administered together. The induction of apoptosis was successfully demonstrated in a time-dependent manner and incidentally corresponded to a reduction in CD90+ and CD133+ expressing DIPG cells. A reduction in key proteins in the calmodulin-calcineurin and PI3K signalling pathways represents both the discovery of a completely new and previously recognised pathway active in DIPG.

The Investigation of novel anti-inflammatory molecules and combinations to look for new treatments for IBD

Student: Wei Ting Elaine Lim

Supervisor: Dr Steven Leach; Conjoint A/Prof Daniel Avi Lemberg

Objective: Anti-inflammatory nutrients with reported anti-inflammatory properties have less severe side effects when compared to traditional pharmacological drugs. This makes anti-inflammatory nutrients attractive potential therapies Previous studies have shown that combining anti-inflammatory nutrients with similar activity, such as glutamine and arginine, can enhance efficacy and amplify their anti-inflammatory properties. The aim of this study was to investigate anti-inflammatory nutrient molecules, establish dose-response curves for the selected nutrient molecules and investigate synergistic associations between different combinations of nutrient molecules using an in-vitro model of intestinal inflammation.

Design: HT29 intestinal epithelial cells were incubated with a range of concentrations of histidine, cysteine, glycine and methionine, both individually and in combinations with glutamine and arginine. Following 6-hour exposure with tumour necrosis factor (TNF)-α to stimulate inflammatory response and the anti-inflammatory nutrient, cell counts, percentage viability and supernatant cytokine interleukin (IL)-8 levels were assessed.

Results: Glycine showed pro-inflammatory action with increased IL-8 production in a dose-dependent fashion. Histidine, cysteine and methionine showed anti-inflammatory action with suppressed IL-8 production in a dose-dependent fashion. Combinations of glutamine, arginine, histidine and cysteine did not show any synergism as these combinations did not further suppress IL-8 production compared to any of the amino acids alone ($p>0.05$).

Conclusion: This study provided further evidence that histidine, cysteine, methionine, glutamine and arginine have anti-inflammatory properties, however glycine has pro-inflammatory actions in the modelled used. Although these findings did not specifically identify useful anti-inflammatory combination, the findings contributed to knowledge of how anti-inflammatory synergies may work which may assist with the identification of successful synergies in future studies.

AYA Cancer Survivors' Experiences of the Healthcare System: A Qualitative Study

Student: Elizabeth May

Supervisors: A/Prof Claire Wakefield; Brittany McGill

Purpose: To qualitatively examine adolescent and young adult (AYA) cancer survivors' lived experiences of their diagnosis and treatment, and attitudes towards their ongoing healthcare, to determine barriers to healthcare engagement in early survivorship.

Methods: Forty-three participants were recruited between February 2013 and October 2015 as part of a larger Australia-wide randomized-controlled trial of a psychosocial intervention for recently off-treatment AYA cancer survivors called 'Recapture Life'. The current study analyzed baseline data in the form of the Psychosocial Adjustment to Illness Scale (PAIS), a semi-structured telephone interview. Interviews were audio recorded and transcribed verbatim, then coded-line by line. Data was analyzed for emergent themes using qualitative software NVivo.

Results: Most AYAs' (88%) expectations of the cancer trajectory did not align with the realities of their experience. Many participants did not demonstrate a good understanding of their cancer diagnosis (49%) or treatment (65%). However, participants expressed high levels of confidence in their healthcare teams, and demonstrated a conscientious approach to their ongoing cancer-specific and general healthcare.

Conclusions: The results further highlight the crucial role of healthcare professionals in ensuring AYA cancer patients have accurate expectations of diagnosis and treatment and develop a strong working knowledge of their disease that is maintained into survivorship. Although AYA cancer survivors may demonstrate a conscientious approach towards their health, they may require ongoing education and support to stay engaged with long-term follow-up care.

Implications and Contribution: Findings suggest AYA cancer survivors' expectations of the cancer trajectory may not align with the realities of their experience. However most have had positive experiences with healthcare practitioners and display conscientious attitudes towards their health, further indicating the crucial role of practitioners in keeping survivors engaged in long-term follow-up care.

Surgical Antibiotic Prophylaxis in Paediatrics: A study on adherence to optimise practice

Student: Zafar Ahamed Mohamed Rizvi

Supervisors: Dr Brendan McMullan; Conjoint A/Prof Pamela Palasanthiran

Background: Surgical antimicrobial prophylaxis (SAP) is an important measure to reduce infectious complications following surgery, but little is known about its performance and practice in Australian children.

Aims: This study aimed to review adherence to surgical antimicrobial prophylaxis in paediatrics, assess risk factors for non-adherence and investigate rate of early post-surgical infections.

Methods: A retrospective review was conducted of paediatric surgical cases at a tertiary children's hospital from April – May 2016. All patients between 0 to < 18 years old who had a surgical procedure were included. Patients undergoing non-invasive procedures, patients with non-penicillin antibiotic allergies, and patients who received antibiotics as therapy rather than prophylaxis were excluded. Data was collected on patient characteristics, surgical factors, antibiotic details and post-surgical infections. These were then evaluated against established hospital SAP guidelines for overall adherence, correct antibiotic choice, correct dosing (within +/- 10%), correct re-dosing, correct timing and duration. A multivariate regression analysis was then conducted to determine risk factors for non-adherence to SAP guidelines.

Results: Three hundred and twenty six cases met the inclusion criteria. SAP was indicated in 181 patients and not indicated in 145 patients. Overall adherence to the hospital guidelines was 39.6%. Adherence to the correct choice of antibiotic, dosage, timing and duration were: 81.2%, 59.2%, 85.6% and 77.6% respectively.

Risk factors for overall non-adherence related to incorrect wound classification by operator (OR: 2.795; p <0.001) and by surgical subspecialty. Ear, Nose and Throat (ENT) procedures were least likely (OR: 0.060; p<0.001) to be non-adherent. Incorrect antibiotic choice was more likely if the patient had a penicillin allergy (OR: 138.34; p=0.004) but was less likely to occur in emergency than elective cases (OR: 0.190; p=0.012). Incorrect antibiotic choices were least likely in orthopaedics and plastic surgery (OR: 0.038 and OR: 0.028 respectively). Incorrect dosing was

related to age groups, as dosing in adolescents was most likely to be non-adherent, compared to younger children. The presence of post-surgical devices were associated with decreased likelihood of incorrect dosage (p=0.022) but increased likelihood of incorrect timing and extended duration of SAP (p=0.030 and p=0.016 respectively).

There was insufficient data available for post-surgical infections at 7 days (31% of records with data available) and 30 days (19% of records with data available) Only 2 surgical infections were documented at follow up by 30 days.

Conclusions: Surgical antimicrobial prophylaxis, as measured by adherence to guidelines, is suboptimal in paediatric patients. Risk factors for non-adherence in various domains suggest areas of improvement for future interventions to optimise SAP adherence.

Models of care for long term survivors of childhood cancer: how do cognitive difficulties impact transitioning to adult care.

Student: Beeshman Nandakumar

Supervisors: Dr Joanna Fardell; A/Prof Claire Wakefield

Background: Paediatric cancer and its treatment leaves survivors prone to significant late effects which require ongoing medical care. As survivors become young adults they often transition from specialist paediatric care to adult-oriented or community-based healthcare. Cognitive difficulty is a late effect that may be a barrier to transition. The aims of this study are to (1) describe the attitudes of survivors and their families towards transition, and (2) investigate how perceived cognitive difficulties after cancer impact transition.

Procedure: Long-term survivors of childhood cancer and parents of survivors (less than 16 years) were recruited from 11 hospitals in Australia and New Zealand to participate in a semi-structured telephone interview regarding their transition experiences. Coding of transcribed interviews that formed overarching patterns were grouped into themes and content analysis was used to number the participants within themes.

Results: Of 33 participants (n=18 survivors, n=15 parents), 45% had transitioned. Participants described their attitudes towards transition as either positive (55%), neutral (15%), or negative (30%). Seventy-six percent of participants identified not experiencing cognitive difficulty. Amongst those with cognitive difficulty, 37.5% identified having positive attitudes towards transition, whilst 50% reported negative transition attitudes. Key barriers of transition emerged: over-dependence on paediatric carers, inadequate communication, a lack of confidence in general practitioners, and cognitive difficulty. Barriers and enablers shaped transition attitudes and who was identified as responsible for care.

Conclusion: Many survivors face cognitive late effects which can be a barrier to their transition out of paediatric care. Future research is needed to fully describe how survivors experience this barrier to transition.

Helmet use in bicycles and other non-motorised recreational wheeled vehicles.

Student: Jessica Ong

Supervisors: Dr Susan Adams; Dr Arjun Rao

Aim: The aim of this study was to describe patterns of helmet use, injury severity, and attitudes towards helmet use in children riding bicycles and other NMWRVs (non-motorised wheeled recreational vehicles).

Methods: This was a prospective cohort study recruiting children ages 0 to 16 involved in trauma secondary to bicycle and other NMWRVs, who presented to the emergency departments (ED) of two tertiary paediatric centres in the Sydney, Australia. Data on demographic, incident, injury severity/details, and attitudes towards helmet use (HU) and non-helmet use (NHU) were compared.

Results: 278 children presented to ED following bicycle or NMWRV accidents in the 6 month period. 41% were scooter riders, 39% were bicyclists, 18% were skateboarders and 2% were inline-skaters. Most injuries occurred among males (74%). The overall mean age was 9. HU was found to be significantly more likely in children riding bicycles and in specified recreational areas. Non-helmet users were more likely to be admitted to hospital. The majority of injuries were sustained to the upper limbs (44%) and the head (37%). The main influence for HU (74%) was found to be parental rules. The biggest factor influencing NHU was perceived low levels of danger.

Conclusion: This study proves that the lack of HU, especially in NMWRVs, is a current issue that needs to be attended to. A legislation mandating HU in NMWRVs is likely to promote its use whilst altering community norms and individual behaviours, ultimately reducing rate of injury.

NEPHROLOGY

Safety and Efficacy of Levamisole Use in Children with Frequently Relapsing and Steroid-Dependent Nephrotic Syndrome: A Retrospective Analysis

Student: Pasan Pannila

Supervisors: Dr Sean Kennedy; Dr Leah Krishock

Background: Levamisole is an antihelminthic medication which has been shown to be efficacious in preventing relapse in a proportion of children with idiopathic nephrotic syndrome. However, There is little evidence to inform clinicians regarding which children are more likely to respond to levamisole and the evidence on adverse drug effects is scant.

Objectives: To determine whether patient and disease characteristics can be used to discriminate levamisole responders from non-responders. To explore for risk factors for adverse events during levamisole therapy.

Methods: We retrospectively analysed all children who been prescribed levamisole for nephrotic syndrome at the Sydney Children's Hospital Randwick from 1/1/2000 to 1/1/2016.

Results: 53 children had received levamisole for the management of steroid dependent or frequently relapsing nephrotic syndrome. 78% responded to levamisole and experienced a reduction in their relapse rate. Responders achieved an 83.9% decrease in relapsest. Those who responded to levamisole were not different to those who didn't in terms of either baseline patient characteristics or pattern of nephrotic syndrome. 36.4% experienced one or more side effects including 6 children with anti-neutrophil cytoplasmic antibody (ANCA) positivity, 2 of whom developed an ANCA-associated vasculitis. The risk of side effects was not associated with patient characteristics, drug dose or duration of therapy.

Conclusion: Levamisole is an effective steroid-sparing agent for frequently relapsing and steroid-dependent NS. It is not possible to predict responsiveness prior to therapy. Adverse events are relatively common and can be severe, therefore monitoring including measurement of serum ANCA is warranted.

Medical management of neonatal abstinence syndrome: A survey of current practices and attitudes

Student: Cecile Pham

Supervisors: Conjoint A/Prof Julee Oei

Aim: To determine current clinical practices regarding medical management of neonatal abstinence syndrome (NAS) and to examine the strengths of medications used in Australia, New Zealand, the United States of America (USA) and the United Kingdom (UK).

Methods: Between June and September 2016, an online questionnaire was sent to healthcare workers involved in the care of infants with NAS.

Results: Of the 124 respondents (85% neonatologists), Australian respondents were the largest proportion (55%) with participation from each state and territory. Meanwhile, the USA, New Zealand and the UK made up 23%, 15% and 7%, respectively. The majority (114, 94%) used morphine as first-line medication, whilst the other 6% used methadone. There was much wider variation in the range of second-line medications used, primarily phenobarbitone (73, 59%) and clonidine (21, 17%). Many respondents who use morphine and phenobarbitone did not know the strength of the solution used at their hospital, 35% and 56% respectively. Of those who did know the strength, there was great variation by twenty-fold and ten-fold, respectively. The most frequent concentrations used were 1.0mg/mL and 10.0mg/mL, respectively. The most frequent dosing intervals used were six-hourly and twice-daily respectively.

Conclusion: There is wide variation in the medical management of NAS. Variations in medication strength may result in significant medication errors. We propose the implementation of standard, commercial-manufactured concentrations to eliminate these risks.

Quality of life in children who have had a fundoplication surgery for the treatment of gastroesophageal reflux disease

Student: Shravya Pilli

Supervisors: Dr Usha Krishnan; Dr Ashish Jiwane

Background: Evidence on quality of life (QOL) outcomes in children post-fundoplication surgery are limited. Previous studies lack the use of paediatric-specific instruments and fail to provide a child's perspective when possible.

Objective: To explore and understand QOL outcomes in children who have had a fundoplication surgery for the treatment of GORD using post-operative results of GORD-specific and paediatric-specific questionnaires.

Methods: In this monocentric exploratory study, 115 patients who underwent fundoplication between 2006 and 2013 were contacted for recruitment and provided with parent and child reports of three questionnaires – GERD-HRQL, PEDS-QL Gastrointestinal Symptoms Module and PEDS-QL Generic Core Scales. Data analysis on QOL outcomes were based on these responses.

Results: A total of 29 patients responded, with variation in distribution of responses by questionnaire. The mean age was 11.26 years, 55.2% were male and 20.7% were neurologically impaired. Significant relationships ($p<0.05$) were found between QOL and the variables – gender, neurological impairment, concurrent gastrostomy and current medications. Males, neurologically normal children, children who had a concurrent gastrostomy and those currently not on medications reported a better QOL than their counterparts. Significant positive correlation ($p<0.05$) was found between symptom-based QOL and general QOL. While QOL appeared to be primarily better in the medium-term group compared to the short-term group and in accordance to child perception compared to parental perception, statistical significance was not found.

Conclusion: Post-surgical QOL outcomes have multiple influential factors. Developing research models which will permit assessment of QOL by comparing not only pre-surgical and post-surgical patients, but also children who are being treated with lifestyle medication and children who are on anti-reflux medications in both the short- and long- term, may validate the current high trend in paediatric fundoplication surgeries.

Outcomes of Children Treated as Outpatients for Intra-Uterine Drug Exposure – An 18 year follow up

Student: Raqeeb Rasul

Supervisors: Conjoint A/Prof Julee Oei

Backgroud: The practice of managing children exposed to intra-uterine drugs, especially those with neonatal abstinence syndrome (NAS), is limited is due to resource difficulties and concerns about child safety.

Aims: To demonstrate the safety and outcomes of an outpatient model of care in the management of mothers and infants affected by drug-use disorder.

Methods: Retrospective chart review of 774 inborn infants managed by the Chemical Use in Pregnancy Service (CUPS) team between 1998 to 2007 (epoch 1) and 2007-2016 (epoch 2).

Results: Attendance rate in the clinic was >90%. There were 404 and 370 mother-infant dyads in epoch 1 and 2, respectively. In epoch 2, opioid use decreased (OR 0.3) and amphetamine use increased (OR 1.7). Mothers had antenatal care earlier (16 v 19 weeks) and better infant gestation (37.9 v 37.6 weeks) and birth weight (2937 v 2832 grams). Fewer children were involved with child protection services (OR 0.6) but reports were more likely to be made before birth (OR 7.4). Hospitalization was shorter (9 v 7.5 days) and fewer opioid-exposed babies were medicated for NAS (OR 0.3). Overall, 199 infants were discharged on NAS medication with 3 medication errors occurring (none led to permanent sequelae). There were 5 deaths (SIDS=4, drowning in bathtub=1) – none occurred in infants concurrently medicated for NAS.

Conclusion: Results show that with adequate multidisciplinary support, outpatient follow-up of infants exposed to intra-uterine drugs is feasible and well attended by the families. It decreases infant hospitalization with low rates of medication errors.

NEUROSCIENCE

Expression of Vascular Endothelial Growth Factor Receptor 3 (VEGFR-3) Following Hypoxia in the Developing Retina

Student: Gracia Sasongko

Supervisors: Dr Meredith Ward; Dr Nicole Jones

The vascular endothelial growth factor (VEGF) family consists of a group of isomers that work through tyrosine receptor-binding. Originally known for their role in angiogenesis, more recently they have been found to have mitogenic and regulatory effects seen in non-vascular tissue. VEGFR-3, specifically known for its critical function in lymphangiogenesis (Tammela & Alitalo, 2010), has also recently been identified in the nervous system, including neurogenic regions of the brain and the eye (Choi et al., 2010; Hou et al., 2011; Jenny et al., 2006; Ward & Cunningham, 2015). The expression pattern of VEGFR-3 and its cellular associations in the eye, however, has not yet been comprehensively reported. We describe the retinal expression of VEGFR3 and changes seen following hypoxia-ischaemic (HI) injury alone, and HI injury with administration of VEGFC ligand, determined by double-labelling immunohistochemistry in rodents from postnatal day (P)10 to P21. We found high expression of VEGFR-3 across age and intervention groups in the retina, associated with neural progenitor cells, astrocytes, and mature neurons. Earlier recovery of the injured ganglion cell layer (GCL) and retinal pigmented epitheium (RPE), along with preservation of mature neurons was observed following HI VEGF-C treatment. Our finding also confirmed the previously known role of VEGF-C in angiogenesis and identified the novel neurogenic and protective role of VEGF-C in the developing eye after HI injury.

The changing nature of dietary intake in cystic fibrosis: an evaluation of energy-dense nutrient poor and nutrient-dense intake in Australian children with cystic fibrosis

Student: Rosie Sutherland

Supervisors: Dr Keith Ooi; Tamarah Katz

Background: Advancements in CF management have engendered considerable improvements in survival and prognosis. However, as most children with the disease now survive into adulthood, the prevalence of chronic diseases related to dietary intake has correspondingly increased. Much of the burden associated with diet-related chronic disease (DRCD) is attributable to the overconsumption of foods which are energy-dense, but nutrient-poor (EDNP). While many studies have investigated these variables in healthy children, little information exists among children with CF.

Objective: To evaluate ND and EDNP intake in children with CF, and the role for socioeconomic factors in identifying patients predisposed to high EDNP intake.

Design: This is a prospective, cross-sectional study of children with CF aged 2-18 years (37 male; mean age 9.7 years) and age- and-sex-matched controls. Dietary intake data was obtained using the Australian Child and Adolescent Eating Survey (ACAES).

Results: Children with CF (n=80) consumed more EDNP food sources compared to control children in terms of both total energy intake [5439 (3524-7776) vs. 2869 (2006-4313) kJ/day; $p<0.0001$], and as a proportion of energy intake (43.2 ± 12.3 vs. 34.0 ± 13.7%En; $p<0.0001$). This difference was significant across all gender and age comparisons. Although children with CF had greater energy intakes [12812 (10500-15751) vs. 9357 (6914-12445) kJ/day; $p<0.0001$] than controls, this was largely derived from EDNP sources. High EDNP intakes (>10 serves/day) were associated with greater socioeconomic disadvantage ($p<0.0001$) and rural residential location ($p=0.03$).

Conclusions: Marked improvements in survival have seen the emergence of CF as a chronic disease of adulthood. While a high-fat, high-calorie diet has been invaluable for these improvements, contemporary changes in dietary sources and patterns may lend to the CF diet becoming a junk food diet.

GASTROENTEROLOGY

Exhaled breath condensate & salivary pepsin as non-invasive markers of reflux aspiration in children with oesophageal atresia and tracheo-oesophageal fistula

Student: Yadhavan Upendran

Supervisors: Dr Usha Krishnan; Dr Steven Leach

Introduction: Children with Oesophageal Atresia and Tracheo-oesophageal Fistula (OA-TOF) may suffer from reflux aspiration secondary to gastro-oesophageal reflux disease (GORD). There are currently no non-invasive tests for the diagnosis of reflux aspiration in children. We hypothesised that exhaled breath condensate (EBC) and salivary pepsin are potential non-invasive markers of reflux aspiration.

Aim: To measure pepsin in EBC and saliva and to correlate the presence of pepsin with:

- Objective measures of GORD and pulmonary function
- Validated gastrointestinal and respiratory symptom questionnaires.

Method: EBC and saliva was collected from children aged between 5 and 18 years attending the OA-TOF clinic. EBC was obtained using a refrigerated circuit (EcoScreen) as per ATS/ERS recommendations. Samples collected were analysed using two specific monoclonal antibodies against human pepsin A (Peptest). These results were correlated with:

A. Parent/child completed gastrointestinal paediatric quality of life questionnaire (PedsQL)

B. Parent completed Liverpool respiratory symptom questionnaire (LRSQ)

C. Results of pH-impedance monitoring and endoscopy where performed

D. Pulmonary function testing (PFT) results

Results: EBC was collected from 14 OA-TOF children, 11/14 also provided salivary samples. Pepsin levels in all EBC samples were below the level of detection (>16ng/mL). However, pepsin was detected in 4 (36%) of the salivary samples. The mean levels of pepsin were higher in children with reflux symptoms [171.8 ng/mL (SD=143.6)] than those without (7.9 ng/mL (SD=20.8)] (p=0.01). Pepsin levels also significantly correlated with overall child (r2=0.68) (p=0.01) and parent (r2=0.50) (p=0.02) gastrointestinal PedsQL scores as well as LRSQ scores (r2=0.40) (p=0.04).

The presence of salivary pepsin did not significantly correlate with objective measures of pulmonary function and GORD.

Conclusion: Salivary pepsin was detected in over a third (36%) of children with OA-TOF in this study. It's role as a potential non-invasive marker of reflux aspiration needs to be validated with further studies in larger populations using a more sensitive assay than the Peptest.

The Effect of Cross-Chest Clip Use on Injury Outcomes in Young Children during Motor Vehicle Crashes

Student: Evangeline Woodford

Supervisors: Prof Lynne Bilston

Introduction: Traffic crashes have high mortality and morbidity for young children. While it has been established that many specialised child restraint systems improve injury outcomes, no large-scale studies have investigated the role of the cross-chest clip during a crash.

Aim: To investigate the relationship between cross-chest clip use on injury outcomes in children between 0-4 years of age during a crash, with particular focus on neck injury occurrence.

Method: The Crashworthiness Data System (CDS) of the US National Automotive Sampling System (NASS) was analysed to identify a population of cases between 0-4 years with restraint use analogous to Australian legislative requirements. Multiple regression analysis within the software SAS 9.4 (SAS Institute Inc., Cary, NC, USA) was used to model injury outcomes while controlling potentially influential variables such as age, crash severity, crash direction and restraint type. Outcomes for children <12 months were considered separately to children aged 1-4 years.

Results: In children <12months old some association existed between correct chest-clip use and decreased moderate to severe injury occurrence ($p=0.0054$). Neck injury for this age group only occurred in children correctly using the cross-chest clip. For 1-4 year old children, use of the cross-chest clip had no identifiable influence on the occurrence of moderate to severe injury within the crash. However, for the same age group, correct cross-chest clip use significantly decreased the odds of neck injury (OR = 0.49; 95%CI 0.27-0.87) compared to incorrect or absent cross-chest clips.

Conclusion: Correct cross-chest clip use appeared to decrease neck injury occurrence in children aged 1-4 years old using harnessed child restraints, but had no effect on overall injury severity. Further investigation of the cross-chest clip for children <12 months old is required to determine their impact in this age group.

A Prospective, Multi-centre Randomised Controlled Trial of Efficacy and Safety of Non-Operative Management of Acute Appendicitis in Children

Student: Jane Xu

Supervisors: Dr Susan Adams; Dr Guy Henry

Background: The gold standard treatment for appendicitis in children is operative management (OM) by means of appendicectomy. Non-operative management (NOM) for acute uncomplicated appendicitis (AUA) may be safe and effective. We present interim results of this clinical trial designed to investigate the safety and efficacy of NOM alone for AUA in the paediatric population.

Methods: A prospective randomised clinical trial of children aged 5-16 years with AUA comparing NOM with OM commenced on June 11, 2016 at two Australian tertiary paediatric hospitals. The primary objective is to determine the safety and efficacy of NOM (antibiotics alone) for AUA in children.

Results: As of October 2, 2016, there are 41 patients enrolled; 16 OM and 25 NOM respectively. Baseline characteristics between the groups are comparable. The success rate of NOM is 72% (18/25) at hospital discharge, and 68% (17/25) were operation-free at a two-week follow-up phone call. There have been 10 cross-overs from antibiotic management to operative. Of these, seven had failed initial NOM, and three re-presented for ongoing pain (at 1 day, 6 days, and 1 month). At appendicectomy, seven of the 10 cross-over patients were found to have complicated appendicitis, three with a normal appendix and two with AUA. The mean length of stay in hospital is 2.3 days (0.6-7.9) for OM and 2.6 days (0.8-8.5) for NOM (p=0.54) accounting for cross-overs, and return to school 6.8 days versus 7.1 days (p=0.91).

Conclusions: These preliminary results suggest management of AUA in children with NOM may be a reasonable first-line therapy. Additional follow-up and continuation of this trial with a large sample size is warranted for determination of longer-term success rate, efficacy and safety.

Paediatric venous malformations and the risk of coagulation profile abnormalities with growing venous malformations

Student: Kevin Zhou

Supervisors: Dr Susan Adams; Conjoint A/Prof Orli Wargon

Background: Venous malformations are slow-flow congenital vascular malformations that enlarge with age and may be associated with Localised Intravascular Coagulopathy, characterised by elevated D-dimer and decreased fibrinogen levels. This coagulopathy may be complicated by thromboembolic events due to progression to systemic Disseminated Intravascular Coagulopathy, particularly as a result of interventions. As such, the appropriate administration of anti-coagulation prophylaxis to patients is vital in preventing such complications.

Objectives: The aim of this work is to determine the incidence of Localised Intravascular Coagulopathy and its complications in children with venous malformations. We hypothesised that the presence and severity of Localised Intravascular Coagulopathy is associated with lesion size and position. We also hypothesise that as children age, Localised Intravascular Coagulopathy is more likely to become a complication, however therapy that reduces the capacitance of venous malformations would reduce the severity of Localised Intravascular Coagulopathy.

Method: A prospective cohort analysis was performed on the paediatric venous malformation patients at Sydney Children's Hospital from 2011-2016. Patients were assessed for the presence of Localised Intravascular Coagulopathy, (D-dimer >0.5μg/mL and/or fibrinogen <1.62mg/mL). The volume, margins and tissue involvement of each lesion were assessed with medical imaging (either ultrasound or magnetic resonance imaging). Univariable regression analyses assessed the associations between patient and lesion features with the presence of Localised Intravascular Coagulopathy and D-dimer levels. Hierarchal stepwise regression was applied to assess the significance of these findings. Non-parametric analysis was performed to assess the efficacy of sclerotherapy on reducing D-dimer levels.

Results: 133 patients were included in this study. An earlier age of presentation was associated with the presence of associated vascular malformations and poorly circumscribed lesions ($P<0.05$). Poorly circumscribed lesions were also found to be associated with lesions involving the lower limb ($P<0.001$). 40 of 94 patients (42.6%)

with recorded D-dimer/fibrinogen levels had Localised Intravascular Coagulopathy prior to any treatment. Elevated D-dimer levels were associated with larger lesion volumes ($P<0.001$), multifocal lesions ($P<0.01$) and having lesions not affecting the lower limbs ($P<0.05$), whilst the presence of Localised Intravascular Coagulopathy was associated with larger lesion volumes ($P<0.01$). Pain was associated with higher D-dimer levels ($P<0.01$) and the presence of LIC ($P<0.05$), whilst lesions affecting the head, face or neck were least likely to be associated with pain ($P<0.001$).

Conclusion: Elevated D-dimer levels are correlated with larger lesion volume and greater lesion number and each paediatric patient with a venous malformation should have their D-dimer levels assessed to assess the extent and number of their malformations (some of which may not be clinically apparent). This allows identification of occult lesions and adequate anti-coagulation prophylaxis to be administered to prevent the progression of Localised Intravascular Coagulopathy and its complications.

ENDOCRINOLOGY

Cytokine Profiles as Biomarkers for Type 1 Diabetes and Enterovirus Infection

Student: Monica Majumder

Supervisors: Prof Maria Craig; Prof William Rawlinson

Substantial evidence suggests enterovirus infection contributes to the development of type 1 diabetes, potentially involving aberrant cytokine responses. This population based case-control study of 156 children at diabetes onset and 162 controls examined the relationship between enterovirus infection, inflammation and type 1 diabetes. Serum levels of 50 cytokines, chemokines and growth factors were measured using Luminex XMAP technology. Children with diabetes demonstrated a distinct inflammatory profile: 17 pro-inflammatory (IL-1β, IL-6, IL-15, IL-23, IL-33, sCD40L, TNF-β, TRAIL, CCL2, CCL4, CCL8, CCL17, CXCL1, CXCL5,EGF, TGF-α, TPO) and three anti-inflammatory cytokines (IL-2, IL-10, IL-13) were significantly higher, and seven (IFN-α, IFN-γ IL-7, CCL14, CCL21, PDGF-AA) significantly lower in cases compared with controls. Using random forest analysis, 15 cytokines (CCL21, sCD40L, PDGFAA, IL-15, IL-7, TGF-α, TNF-β, IFN-α, CCL17, EGF, IL-2, TRAIL, CXCL5, IL-1β and CXCL1) distinguished cases and controls with 95% accuracy. Enterovirus infection, detected by qRT-PCR, was threefold more common in cases versus controls. TNF-β, sCD40L, CCL17, CCL22 and CXCL13, were significantly lower in enterovirus positive type 1 diabetes cases compared to enterovirus negative cases while CCL14, sIL-2Ra and PDGF-AA were significantly lower in both controls and cases positive for infection compared to those without. These findings indicate a largely pro-inflammatory milieu at type 1 diabetes presentation and that enterovirus infection contributes to dysregulated cytokine responses.

Evolution of Glucose Tolerance in Children with Cystic Fibrosis

Student: Avinesh Chelliah

Supervisors: Dr John Widger; Dr Keith Ooi

Background: Cystic fibrosis-related diabetes (CFRD) is the end-point of a spectrum of abnormal glucose tolerance, with significant impact on lung function, nutrition and mortality. The current gold standard for screening and diagnosis is the two-hour oral glucose tolerance test (OGTT). However, this test has been shown to have poor sensitivity and reproducibility. Glucose tolerance is known to vary over time in children with CF. The aim of this study was to evaluate the longitudinal progression of glucose tolerance in children with CF using a 30-minutely sampled OGTT and compare two-hour glucose tolerance categories with peak glucose categories.

Aim: Eight years of OGTT results were collated for children aged 10 and over at the Sydney Children's Hospital.

Methods: One hundred and ninety-nine paediatric IBD patients treated with thiopurines between 2008- 2015 who had 6-TGN measurements were retrospectively reviewed. Disease activity index and hematological markers were collected and compared to 6-TGN levels.

Results: A total of 162 OGTTs were analysed in 51 patients. Glucose levels fluctuated greatly according to two-hour glucose, peak glucose and area under the curve (AUC) across five time-points. Mean variance between tests for two-hour glucose was 4.65 mmol/L, and 3.72 mmol/L for peak glucose. Established criteria classified 84% of all tests as normal glucose tolerance (NGT). Of these, proposed criteria classified 66% as abnormal. During the two-hour OGTT, tests classified as NGT had a median glucose significantly different to those classified as impaired glucose tolerance (IGT) and CFRD.

Conclusion: Glucose levels on OGTT were variable across all measures, although peak glucose was slightly more reproducible. Peak glucose identified early levels of glucose intolerance in patients considered normal by two-hour glucose. A one-hour OGTT may be sufficient in distinguishing between normal and abnormal glucose tolerance.

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