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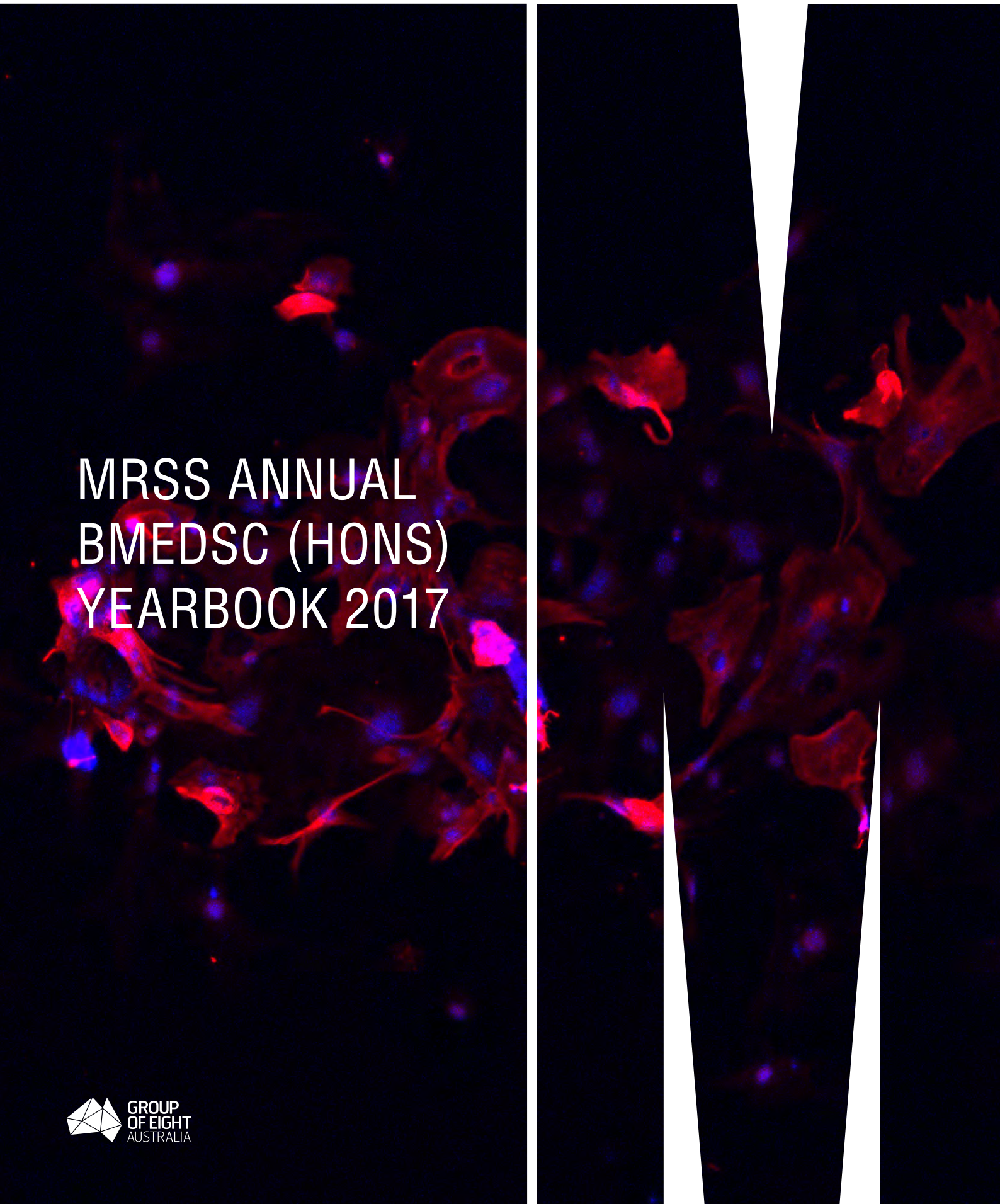
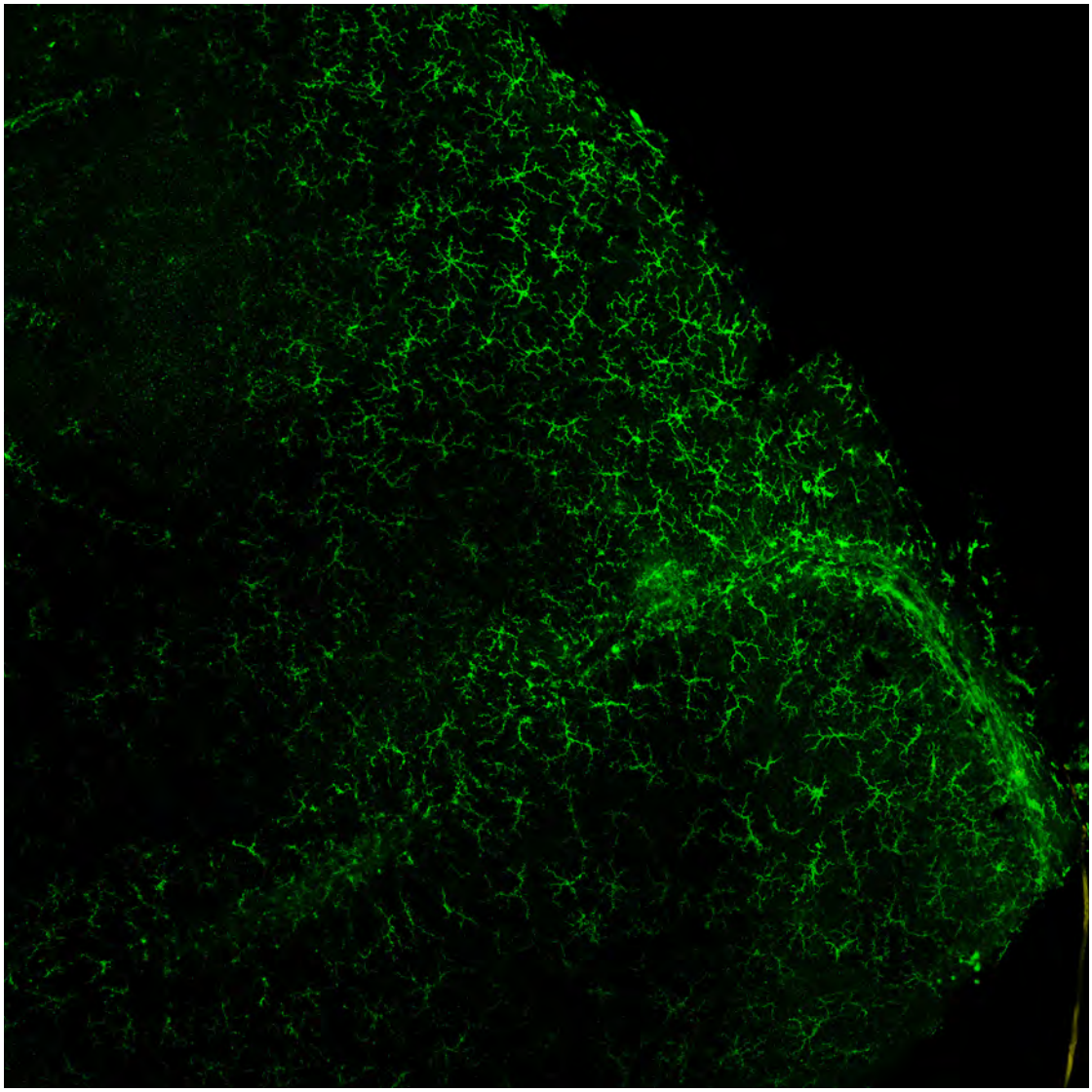
MEDICINE,
NURSING AND
HEALTH SCIENCES



MRSS ANNUAL BMEDSC (HONS) YEARBOOK 2017

GROUP OF EIGHT AUSTRALIA



Front Cover

Jessica Stark "Dancing Astrocytes"

Immunocytochemistry staining of primary astrocyte cultures with Glial Fibrillary Acidic Protein (GFAP) and DAPI. GFAP is expressed by astrocytes and is upregulated when astrocytes become reactive in response to inflammation, it is considered a hallmark of inflammation in the brain

Inside Front Cover

Danica Joseph "Well-Intentioned Defenders"

Iba-1+ microglia seen in diseased retinas of P45 HELxTCR mice with spontaneous experimental autoimmune uveitis. As the resident immune cell of the retina, microglia are usually found in its superficial layers and to an extent in the outer plexiform layer. In diseased states these cells are activated, retracting their processes for a more amoeboid morphology, accumulating around areas of vasculitis and the outer retina. Here the microglia are seen around the optic nerve, and in higher concentrations around vessels.

Message from the BMedSc(Hons) Course Management Committee

Dear BMedSc(Hons) Students,

Congratulations on completing your BMedSc(Hons) degree! It is a VERY significant achievement, well done.

The Course Management Committee would like to thank each and every one of you for undertaking BMedSc(Hons). We hope that the BMedSc(Hons) year has challenged you both personally and academically. It's a year that is meant to give you a new appreciation of how much more there still is to learn about medicine, about how new knowledge is created, how medical research is translated into changes in clinical practice and how important evidence-based medicine is for ensuring that changes to practice are justified. By the end of the year most students will feel like they have undergone an exponential learning curve, not just in their research area, but also in their confidence to critically evaluate new research findings, to communicate in written and oral formats and in their ability to work independently, as well as a member of a team. We hope that your Honours year has equipped you with all of these skills and many more.

We would like to express our thanks to your supervisors and to the large number of unsung heroes who have devoted their time this year to help you learn. The Course would not be possible without them. We are also very grateful to the large number of examiners who willingly volunteer their time every year to assess the oral and poster presentations, literature reviews and theses. Thank you also to the MRSS committee, particularly your BMedSc(Hons) Chairperson Dinesh Giritharan. Together they have worked hard to organize information nights and to feed back your questions and comments, helping to improve your own experience as well as that of future cohorts.

On behalf of the BMedSc(Hons) Course Management Committee, we wish you all the very best for a bright future.

Dr Megan Wallace, Director of Medical Student Research
Chair: BMedSc(Hons) Course Management Committee

Message from MRSS

And just like that, we have come to the end of an amazing year!

As is often said, "it's about the journey, not the destination" and I don't think that could be better exemplified than through the BMedSc(Hons) experience. While we might all be graduating with the same degree, I think it's fair to say that what has made this year so memorable are our individual experiences – whether that be through successful/failed experiments, the triumph/struggle of patient recruitment or the inspired/procrastination-filled periods of thesis writing.

This yearbook is a testament to all of those experiences, a small token of the incredible feats you have achieved over this year, something that you will be able to look back on with pride and nostalgia in the future.

I hope that the year has broadened your horizons and has left you with a desire to ask more questions in the hope of finding more answers, and in turn, help shape a better world. I can't wait to hear of all your successes in the years to come!

Dinesh Giritharan
Deputy Chair and BMedSc(Hons) Representative,
Medical Research Students' Society

Donna Almira

The Role of the AT2 Receptor in Experimental Diabetic Nephropathy

A/Prof Terri Allen and Dr Bryna Chow, Department of Diabetes, Central Clinical School

Hi I am Donna. I'm currently on my fourth year of medical course in Universitas Indonesia. There are several reasons why I chose this project. First, from the project description, it showed that the project was feasible to be done in an Honours year. Second, I am interested in learning about laboratory techniques, and this project offered me several interesting techniques, including gene and protein analysis, which really useful for those who wants to get a better understanding about laboratory-based research. Third, I wanted to fulfill my curiosity about diabetes. And with this project, I was able to prove and got a better idea on how diabetes occurs, and tested a drug in a diabetic mouse, which mimics human diabetes. My critical analysis skill was honed by this project, which makes it more interesting to figure out something new by your own. Finally, I should say that I am very lucky to have such helpful and friendly laboratory fellows for the support and unforgettable memories during my Honours year. For future students, just enjoy your research cause you will be amazed with what you have done eventually. Feel free to contact me at donnalmira19@gmail.com for more information about my department.

Abstract

Background: Diabetic nephropathy is one of the most common diabetic complications, in both type 1 and type 2 diabetes. There are several mechanisms proposed for the cause of diabetic nephropathy, and one of the most dominant and well understood is the Renin Angiotensin Aldosterone System (RAAS). Angiotensin II is its main effector peptide, and it has two well-known receptors. AT1R is one of the receptors believed to have more harmful than beneficial effect to the body. Whereas AT2R is another angiotensin II receptor, that shows some opposite effects, which counteract the action of AT1R. Until now, the role of AT2R in disease, especially diabetes, remains controversial. It has been postulated from previous studies that the activation of AT2R may improve the inflammation, fibrosis, as well as oxidative stress, which may lead to kidney failure in the diabetic mouse. However, other studies have also suggested that instead of counteracting the AT1R, the AT2R may even support the detrimental action produced by the AT1R, and worsen the diabetic condition. Based on these findings above, the aims of this study were to investigate the role of the AT2R agonist, C21, in a more severe, stable, model of experimental diabetic nephropathy, the Akita mouse.

Method: In vivo experiments using 6–week-old male wild type and diabetic (Akita) mice on a FVB/N background were used in this study. Both control and Akita mice were treated with either a vehicle (0,1mol/L water) and served as controls or Compound 21 (C21) (1mg/kg/day) via daily gavage, over a 16-week period. Gene and protein analysis were done through qRTPCR and western blot respectively. Immunohistochemistry and PAS staining were used to look for extracellular matrix deposition indicating renal injury.

Results: C21 did not affect glycaemic control and blood pressure in either treatment group. Albuminuria was assessed at the 10-week time point. C21 treatment in the diabetic group did not reduce albuminuria when compared to the untreated diabetic group. There were no changes observed in the mesangial injury in control and diabetic group with or without treatment. Several pathological processes markers were tested. MCP-1, TNF-α, p47phox, and fibronectin were increased in diabetic mice and surprisingly C21-treated diabetic group demonstrated a significant increase at gene expression, and protein level for MCP-1 in particular. Diabetes was associated with increased extracellular matrix deposition as assessed by collagen III and collagen IV immunohistochemical staining in the kidney cortex, which was further increased with C21 treatment. There was no change detected in the AT1R gene expression, however AT2R was found to be significantly increased in diabetic mice and was not affected by C21.

Conclusions: AT2R activation, through its agonist, C21, in a severe model of diabetic nephropathy, the Akita mice, showed a pro-inflammatory, pro-fibrotic, and pro-oxidative stress effect. Along with this, there was unchanged or increased expression of several markers at the gene and protein levels, unchanged structure and function of the kidney, as well as increased extracellular matrix deposition. These findings could potentially become a consideration in determining the role of AT2R in the context of clinical diabetes complication.

Benjamin Amberg

The Impact of Partial Amniotic Carbon Dioxide Insufflation on the Fetus

Ryan Hodges, Stuart Hooper, Kelly Crossley, The Ritchie Centre, Hudson Institute of Medical Research, Clayton, Australia
Department of Obstetrics and Gynacology, Monash Medical Centre, Clayton, Australia,

Developing a passion for science, using PubMed, searching the literature, data analysis and scientific writing. These are pretty standard personal developments for med students finishing a BMedSci however the biggest thing I have learnt this year is how to be wrong! How to be 100% confident that you're right, for it all to mess up and for you to be wrong again. When studying medicine being wrong is often considered something negative, a mistake or a poor outcome. At the start of the year I was guilty of this mentality. Although it has taken a while, this year has taught me that science is different. Being wrong is how you move forward, how you improve your histology protocol and learn what the answer to your question isn't. I've learnt that the results of your thesis don't have to match up with your hypothesis and that it's actually more fun to think about why you were wrong than to celebrate that you were right. I think this appreciation for the art of 'stuffing up' has applications well beyond medicine or science and will only benefit me in the future.

Abstract

Background: Partial amniotic carbon dioxide insufflation (PACI) with cold/dry carbon dioxide (CO2) gas is currently used in several major fetal surgery centres internationally to improve visualisation and to facilitate fetoscopic rather than open myelomeningocele repair. Studies in a sheep model of PACI at lower pressures and shorter durations than are currently used in humans demonstrate that CO2 readily diffuses from the amniotic cavity into the fetal vasculature causing fetal hypercapnia and acidosis. Furthermore, high rates of preterm premature rupture of membranes occur after fetoscopic surgery and little is known about the causative role of cold/dry PACI or the potential benefit of heating and humidifying the CO2. Our study aimed to investigate the acid/base and haemodynamic effects of cold/dry PACI in the sheep fetus at clinical insufflation parameters. We also aimed to assess and compare the effect of PACI with cold/dry versus heated/humidified CO2 on fetal membrane inflammation, a marker of early membrane rupture.

Methods: We instrumented the fetal and maternal circulation of ewes at 105 days' gestation (term 145 days). Seven ewes underwent PACI with standard cold (22oC) dry (0-5% humidity) CO2 and five with heated (40oC) humidified (100% humidity) CO2 at 15mmHg for 180 minutes. Seven non-insufflated controls were sourced from a previous experiment. We continuously monitored the haemodynamic status of the mother and fetus and measured the blood gas status of each intermittently. Fetal membranes were collected for histological analysis. Data are presented as mean ±SEM.

Results: Compared to non-insufflated controls at 90 minutes, fetuses insufflated with cold/dry CO2 became severely acidotic (pH: 6.86 ±0.08 vs. 7.24 ±0.04, p<0.01) and had marked increases in the arterial partial pressure of CO2 (145.3 ±25.5 vs. 54.9 ±2.5mmHg, p<0.01) and serum lactate (7.4 ±1.1 vs. 3.4 ±0.4, p<0.01). These changes correlated with significant reductions in fetal carotid artery pressure (25.5 ±8.7 vs. 41.3 ±3.3mmHg p=0.02) and carotid artery blood flow (8.5 ±5.9 vs. 34.0 ±4.6 ml/kg/hr, p=0.02) compared to non-insufflated controls ultimately limiting fetal survival (0% by 139 minutes). Interestingly, acid base and haemodynamic disturbances were considerably less when the CO2 was heated and humidified and this was reflected in fetal survival (60% at 180 minutes). Standard cold/dry CO2 significantly increased the number of immune cells in the amnion compared to non-insufflated controls (2.7 ±0.7 vs. 0.7 ±0.3 cells per field of view, p=0.03) and the heated/humidified group (2.7 ±0.7 vs. 0.3 ±0.1 cells per field of view, p=0.03).

Conclusions: We observed significant acid base and haemodynamic disturbances when fetal sheep were insufflated with cold/dry CO¬2 at 15mmHg for 180 minutes raising safety concerns about the potential implications in humans. Standard cold/dry CO2 also resulted in fetal membrane inflammation which may explain high rates of PPROM following PACI in humans. These physiological and membrane changes were partially mitigated by heating and humidifying the CO2 suggesting that this technique may improve clinical outcomes of human fetuses undergoing fetoscopic myelomeningocele repair.

Avicenna Akbar Anwar

Deciphering the Synergistic Killing of Polymyxin-Minocycline Combination against Multidrug-resistant Acinetobacter baumannii using Metabolomics

Professor Jian Li

I was doing my honours project from July 2016 until May 2017. This project gave me a whole new experience regarding biomedical and experimental work. I choose a search regarding antibiotics drug development because I had saw how antibiotics abuse have become a bad habit in my home country, Indonesia. This antibiotics abuse caused a lot of new MDR bacteria and I hoped by doing research regarding antibiotics to fight against superbugs, It would give beneficial knowledge for me when I came back to Indonesia. It started when my supervisors asked me to design my project and finished when I submitted my thesis. It was not an easy journey, but it was fun. For future student, make sure you choose a research in accordance with your interest, so that you can enjoy what you are doing.

Abstract

Background: Multidrug resistant Gram-negative bacteria have become a global health problem. And according to WHO, Acinetobacter baumannii tops the list of bacteria for which new antibiotics are urgently needed. Combination therapy is the current alternative to treat multidrug-resistant Acinetobacter baumannii, that has become resistant to polymyxins. Previous study shown that polymyxins and minocycline combination have synergistic effect. Additionally, minocycline has anti-inflammatory potential that might reduce toxicity caused by polymyxin. However, the detailed mechanism of action is still unknown. This is the first study to elucidate the synergistic effect of polymyxin B-minocycline combination on the metabolome of A. baumannii.

Method: The metabolomics sample of polymyxins-susceptible Ab 03-149.1 and polymyxin-resistant Ab 03-149.2 were taken following treatment with polymyxin B (2 mg/L) or minocycline (2 mg/L) alone, and their combination at 1 hour, 4 hours and 24 hours. Quick quenching using ethanol and dry ice was done directly after samples taken each time point to fixate the metabolites. Each sample was diluted using CAMHB to reach the OD600nm ~0.5 for normalization. Then, medium components and extracellular metabolites were removed by washing cell pellets twice with 0.5 mL of 0.9% NaCl (4 °C) and centrifugate at 3,220 × g at 4 °C for 10 min. Then, the cell pellets were extracted using chloroform:methanol:water (1:3:1, C:M:W). The supernatant was centrifuge at 14,000 × g at 4 °C and measured using LC-MS.

Results: Polymyxin and minocycline shows similar metabolites perturbation. Polymyxin and minocycline alone or in combination treatment caused disruption of the bacterial outer membrane and cell wall, as demonstrated by perturbation of glycerophospholipids and fatty acids in all time points. Decrease of arginine metabolism was also observed in monotherapy or combination therapy, especially in N2-succynil-L-arginine, N2-succynil-L-ornithine, and N2-succynil-L-glutamate which are part of arginine degradation pathway. Arginine pathway are closely related to oxidative stress and TCA cycle that plays a role in bacterial energy metabolism. Down-regulation of nucleotide metabolism via 5-phospho-D-ribose α-1-pyrophosphate (PRPP) was associated with perturbations in the pentose phosphate pathway mostly in combination treatment at 24 hours. In polymyxin-resistant Ab 03.149.2 down regulation of cell wall biosynthesis via D-sedoheptulose 7-phosphate that was also associated with pentose phosphate pathway was observed in 24 hours. However, in polymyxin resistant Ab 03-149.1 this D-sedoheptulose-7-phosphate downregulation was only observed in 4 hours after minocycline single treatment. D-sedoheptulose 7-phosphate plays a big role in cell wall biosynthesis.

Conclusions: In general, polymyxin-minocycline combination treatment shows more significant metabolites changes compared to either monotherapy. We discovered that the combination synergistically killed A. baumannii by enhancing the perturbation of amino acid, lipid, carbohydrate, and nucleotides metabolism.

Joash Arnold

Utility of CT brain imaging in patients presenting to the emergency department with an altered mental state resulting from overdose or intoxication

Professor Andis Graudins, Monash Emergency Research Collaborative, Associate Professor Rob Meek, Monash Emergency Research Collaborative

I'm a fourth-year medical student who completed a toxicology project at the Dandenong Emergency Department. This year has been a great experience in learning how to undertake a research project by myself. Whilst the BMedSc year is self-directed I could not have completed this year without my supervisors. I would like to thank my supervisors for all their support this year in the writing of assessments and for even visiting me in hospital when I had appendicitis! I would highly recommend them to future students, and would recommend ED research for anyone interested in Emergency Medicine or General Medicine. I would be happy to be contacted by future students regarding ED research at jkaru1@student.monash.edu.

Abstract

Background: Poisoning is a common presentation encountered in the emergency department (ED). Often patients can present with an altered mental state (AMS) after overdose/intoxication. Because of the varied aetiology of AMS, clinicians may order a cranial CT (CTB) scan to rule out underlying intracranial pathology. Previous studies have shown there is low incidence of acute intracranial pathology on CTB in patients with undifferentiated AMS when head trauma is not present. A small body of evidence suggests that scanning a poisoned population also returns a low incidence. Repetitive scanning of patients can increase the chance of developing a fatal cancer and therefore unnecessary scans should be avoided.

Aims and Hypotheses: Aim 1: Describe the incidence of acute intracranial pathology on CTB in a poisoned population presenting with AMS. We expect that the incidence will be low.

Aim 2: Compare the incidence of acute intracranial pathology on CTB in patients with known and suspected poisoning. We expect that incidence will be higher in suspected poisoning.

Aim 3: Identify clinical factors that may be associated with the presence of acute intracranial pathology on CTB. We expect that focal neurological changes, pupillary changes and head trauma will be associated with a positive CTB.

Aim 4: Describe the cumulative radiation risk as expressed by the number of CTB scans that patients received in the past. We expect that many patients presenting with recurrent poisoning will have received multiple CTB scans.

Method: A retrospective audit was performed of all three Monash Health sites between Jan 2014 and Dec 2016. Patients with a CTB performed and an ED discharge diagnosis of overdose/intoxication were elicited from Symphony, the ED electronic medical record (EMR). Data variables were subsequently extracted from the Symphony EMR, hospital scanned medical records and an online radiology system. This included demographic data, clinical findings, features of poisoning, disposition and CTB findings. Data were analysed using Graph Pad InStat.

Results: There were 980 presentations in this study after performing the search strategy and excluding patients with incorrect diagnoses. The median age was 44 years (IQR:33-56) and 67% were male. The median GCS on presentation was 14 (IQR:9-15). Of all patients in the cohort, 195 (20%) were admitted to the ICU and 180 (18%) were intubated. A total of 463 (47%) patients were suspected of having a head injury. Five patients (0.5%) had a positive CTB (acute intracranial injury) and 34 (3.5%) had an acute extracranial injury. All patients with positive CTB findings had a suspicion of head trauma.

Conclusions: The incidence of a positive CTB was demonstrated to be extremely low in a poisoned population. There was no distinction in CTB outcomes between known or suspected poisoning, and the incidence in both groups was also extremely low. No clinical features such as neurological findings were associated with a positive CTB. Many patients in this study received multiple CTB scans on previous presentations for repeated pharmaceutical overdose. This study suggests that we are currently over-utilising CTB in patients with overdose and no suspicion of head trauma.

Damian Azzollini

Mapping the neural circuitry of cough using the inhalation of capsaicin and adenosine tri-phosphate.

A/Prof Michael Farrell – Department of Medical Imaging and Radiation Sciences • Prof Gary Egan – Monash Biomedical Imaging

I decided to undertake this neuroimaging project as it is a perfect mix of neuroscience and medical imaging. I've long been fascinated both by the inner workings of our most complex organ, and the incredible technology used to construct images of our bodies, so this project was a perfect fit for me.

I learned an enormous amount, not just about the neurology of the human cough mechanism, but also about the technology that allows us to create anatomical and functional images of the brain. I also learned a lot about process of conducting scientific research, which will be very useful in my pursuit of a successful career as a clinician-scientist.

Abstract

Background: Cough Hypersensitivity Syndrome (also known as chronic cough) is a disorder of sensory processing that results in long-term excessive coughing. It represents a substantial challenge for clinicians, having a high global prevalence and causing considerable detriment to sufferers' lives. Despite this, no effective therapies exist due to a lack of understanding of the neurology behind cough.

Recent research into the neurology of cough in rodents has identified two anatomically discernible afferent neural pathways from the airways – one of a somatic phenotype and the other of a visceral phenotype. The pathways' receptor profiles are such that capsaicin stimulates both of them while adenosine tri-phosphate (ATP) only stimulates the visceral pathway. This finding in rodents has led to the proposition that humans possess homologues of these pathways, and that they connect to different sets of cortical regions. This could have important implications for the study of Cough Hypersensitivity Syndrome.

This study aimed to determine if there are brain regions that activate significantly more to the inhalation of nebulised capsaicin than ATP.

Method: Twenty healthy participants inhaled nebulised capsaicin and ATP while undergoing psychophysical testing and functional magnetic resonance imaging (fMRI).

Participants first underwent psychophysical testing involving the inhalation of capsaicin and ATP at various doses. This was both to characterise the responses elicited by the two substances, and to choose appropriate doses to inhale during scanning. Once these doses were chosen, participants underwent the fMRI scanning protocol where they inhaled each substance in pseudorandom sequence whilst functional images were acquired. The functional images were processed and analysed to determine which regions of the cortex activated, and to what extent, during the inhalation of each substance.

Results: Capsaicin elicited more frequent coughing than ATP at higher doses ($F(4,76)=15.2$, $p<0.001$). The imaging results showed that both capsaicin and ATP inhalation activated widely distributed cortical networks. Regions showing significantly more activation to capsaicin than ATP included the bilateral primary somatosensory cortices, cerebellum, supplementary motor area, and left anterior insula (voxel inclusion threshold $Z=2.3$, cluster threshold $p<0.05$).

Conclusion: The identification of these differences supports the proposition that humans possess two afferent cough pathways that connect to different sets of cortical regions, and that they mediate differing psychophysical responses.

The inclusion of the primary somatosensory cortex as one of these regions further suggests that these pathways follow a somatosensory-viscerosensory dichotomy. It is, however, important to note that there is no known substance that uniquely stimulates the somatic pathway, meaning this study does not provide a complete picture of both human cough circuits.

This study's findings add to our knowledge of cough neurology, supporting a previously unknown concept of humans having two cough circuits. This new evidence serves as a springboard from which further investigation can be conducted on the circuitry and characteristics of these pathways, as well as the way in which they are altered in Cough Hypersensitivity Syndrome.

Michael Barclay

Defining the 'Teachable Moment': a qualitative phenomenological analysis of the impact of emotional and cognitive reactions to acute emergency presentation on motivation to change future alcohol-related behaviour.

Associate Professor Diana Egerton-Warburton (Monash Health), Professor Andis Graudins (Monash Health), Professor Steve Allsop (Curtin University), Doctor Jennie Hutton (St Vincent's Health)

I'll be going into final year in 2018 and hope to combine my three medical interests of emergency medicine, paediatrics and public health into a career. My passion for public health and emergency medicine helped guide me towards potential supervisors. When I spoke to my supervisor about potential projects she told about a particular passion of hers: the, often dismissed, harms from alcohol consumption. After doing some research myself and looking at the work she had done I was both impressed and inspired. She was also keen to keep me in touch with clinical medicine by organising regular shifts in the emergency department so I jumped on the opportunity. What I've learned this year is how to apply a critical, scientific perspective to research and I've gained an appreciation for just how much work goes into that journal article you read the abstract of in preparation for a class. There are highs and lows in anything we do but my advice to prospective students is a) find a supervisor who inspires you and b) find a project you can be proud of because these are the things that help you through the lows and help you celebrate the highs.

Abstract

Background: Alcohol-related harm (AH) has a profound impact across biological, psychological, injury-related and broader economic domains. Australia's alcohol consumption ranks highly compared to other similar countries and is responsible for a significant public health burden. It has been suggested that alcohol-related presentations to the emergency department (ED) may create an opportunity to capitalise on the 'Teachable Moment' (TM). Brief interventions (BI) attempt to harness this potential for significant health behaviour change by targeting interventions to the immediate ED setting. Evidence suggests that BI have small and varied effect sizes with little effect on long-term behaviour. However, there is little qualitative evidence on how patients react to the concept of the TM and what influences their motivation to change future behaviour.

The aim of this study is to investigate patients' emotional responses to emergency presentation for AH and to explore the determinants which influence any change in alcohol-related behaviours. This will be used to develop a new model of the TM and inform future research of BI effectiveness.

Method: This is a qualitative phenomenological study which recruited patients aged over eighteen years based on presentation to ED for alcohol-related reasons. Exclusion criteria included: dependence; recreational drug taking; critical illness; or, mental incapacity. Semi-structured interviews with these participants involved questions regarding: the events of the presentation; their emotions; their usual drinking habits; changes to their perception of the risks of alcohol; motivation to change their habits; and, their thoughts on the TM and understanding of it. Interviews were recorded then transcribed and analysed using NVivo 11 software to identify common themes. Patients were recruited until saturation of results.

Results: Ten patients were recruited. Three major themes were identified and were: perception of their alcohol habits; perception of the event; and, influence on future behaviour. The most common reason to drink was identified as social enhancement or pressure. The most common emotions regarding presentation were shock, indifference, acceptance, embarrassment and inconvenience with varying degrees of intensity. While all participants agreed with the concept of the TM there was a split between those who were motivated to change their drinking habits (six participants) and those who were not (four participants).

Conclusions: This study suggests that not all patients presenting to the emergency department with AH may be strongly influenced, at the time, to make changes to the drinking habits based on their emotional and cognitive response to the presentation. This may assist in explaining research that suggests ED-based BI do not have large, sustained influence on individuals' future alcohol-related behaviour. In contrast to the traditional understanding of the TM, our research in AH suggests a model where, simply connecting the injury or harm to the consumption of alcohol may be as effective as a more intensive intervention while significantly reducing the time and resources required to perform it. This is likely to make BI more feasible in an ED setting and allow broader utilisation, further enhancing the potential for significant population benefit.

Windy Cendrick

The relationship between knee muscle and its structure in osteoarthritis population

A.Prof Anita Wluka, Dr Monira Hussain and Dr Yuanyuan Wang. School of Public Health and Preventive Medicine

Hi, I am Windy Cendrick, third year medical student at Faculty of Medicine University of Indonesia. I had my honours project in School of Public Health and Preventive Medicine, under the supervision of a marvellous team; A.Prof Anita Wluka, Dr Monira Hussain and Dr Yuanyuan Wang. Don't be scared to learn as the beginning is always hard and harsh, but enjoy the journey of learning.

Abstract

BACKGROUND & AIM: Osteoarthritis (OA) is the common and the economic burden of OA is high in Australia. knee OA is the most common type of OA. There are few evidences showing that knee muscle is associated with knee structure in OA., However the current evidences of a relationship are limited and some are contradicting to each other. Therefore, the aim of the study is to examine the relationship of knee muscle and knee structures in knee OA in symptomatic OA population

DESIGN: double blind placebo-controlled randomized clinical trial (cohort study).

METHOD: 410 participants were recruited at baseline, with symptomatic knee OA with no end-stage OA, trauma, or disabilities, were recruited and randomized to be included in the study. Each participant had MRI of the affected knee on baseline and follow-up (around 24 months later). Exposure measures: knee muscle strength and size be measured twice (at baseline and follow-up), from dynamometer measurement for strength and MRI images for muscle size. Outcome measures: cartilage volume, cartilage defects and bone marrow lesions, were measured twice, baseline and follow-up, from the MRI images. Results were analysed using the univariate linear regression and multivariate linear regression adjusting for confounders.

RESULTS: Among the 413 participants included in the study; 363 (87.9%) had 2-year follow up knee MRI; 227 (62.5%), among those who did follow up MRI, had follow up leg strength measurement. Stronger muscle was associated with the larger cartilage volume in lateral patellofemoral joint, p=0.01. Moreover, larger muscle was associated with the larger cartilage volume and lower BML score in lateral tibiofemoral and patellofemoral joint, p<0.05.

CONCLUSION: The main findings of the study demonstrate that the stronger and increased muscle size was associated with the larger cartilage volume and higher BML score at the lateral tibiofemoral joint. In addition, larger muscle size was associated with larger cartilage volume and lower BML score at the lateral tibiofemoral joint and patellofemoral joint.

Although these findings will need to be tested in other study population, in general, muscle strength and size were protective in symptomatic OA population.

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Jacinta Cheng

Complex Trauma Disorder and the effect of early life trauma on cognition and emotion regulation

Professor Jayashri Kulkarni, Dr Caroline Gurvich, Dr Natalie Thomas, Dr Abdul-Rahman Hudaib
Monash Alfred Psychiatry Research Centre, Central Clinical School, Faculty of Medicine, Monash University and the Alfred Hospital, Melbourne, Australia

I completed my project at the Monash Alfred Psychiatry Research Centre with the Women's Mental Health Team. I chose my project as I have a strong passion for women's health – whether mental, reproductive, or physical – so this seemed like the perfect way to combine my interests! My project was clinically focused and allowed me to have a lot of patient contact throughout the year, something that I enjoyed immensely.

I chose to undertake a BMedSc in order to gain a taste of medical research and to experience the other side of clinical practice. Although challenging at times, this year was extremely fulfilling and taught me so many things – how to run a clinical study, how to write a scientific paper, how to be independent; the list goes on!

I am incredibly grateful to everyone at MAPrc, in particular my supervisors who supported me every step of the way, from developing the study to writing my thesis. I have made so many wonderful friends along the way, which made the year all the more rewarding. I would highly recommend doing a BMedSc to anyone considering it!

Abstract

Background: Complex Trauma Disorder (CTD), which includes Borderline Personality Disorder and other symptomatology along this spectrum, is a debilitating psychiatric disorder characterised by pervasive interpersonal and behavioural difficulties. Impaired cognitive and emotional functioning have been identified as key components of CTD and underlie many of the symptoms. Additionally, neuroimaging studies have revealed evidence of dysfunctional neuronal networks which may mediate these deficits. A history of trauma is extremely prevalent in this population, with up to 90% of individuals with CTD reporting some form of early life trauma. Research investigating the potential effects of childhood maltreatment on brain development and neuroendocrine changes is rapidly progressing, and it has recently been reported that the long-term effect of trauma may depend on the stage of neurodevelopmental period at which it transpires.

Aims: 1. To identify if there are differences in the experience of early life trauma between people with and without CTD

2. To identify which aspects of cognitive and emotional function differ between people with and without CTD

3. To explore whether specific types and timings of trauma, in people with CTD, predict for cognitive and emotional impairments in adulthood

Method: Twelve adults with CTD and sixteen controls were administered a series of measures over two sessions. CTD symptom severity was determined using the Diagnostic Interview for Borderline Personality Disorder, Borderline Personality Disorder Severity Index, and Borderline Estimation Severity Over Time scale. Participants also completed a retrospective self-report measure exploring their early life experience of potentially traumatic events: the Maltreatment and Abuse Chronology of Exposure Scale. Emotional function in adulthood was measured with the self-reported Difficulties in Emotion Regulation Scale as well as a computer-administered empathy task (Multifaceted Empathy Test). Cognitive function was assessed using a battery of computer-administered tasks (Cogstate), a modified Stroop task and an antisaccadic eye movement tracking task.

Results: We found that when compared to controls, people with CTD experienced an increased frequency and duration of early life trauma. They also displayed impairments in executive functioning, cognitive empathy (identifying emotions) and emotion regulation. There was no significant difference in the domains of basic processing. Lastly, we found a significant association between some types and timings of trauma and performance on the antisaccade, Stroop and cognitive empathy tasks. We hypothesise that middle childhood (ages 6 – 10) and adolescence (ages 11 – 18) are likely to be stress-sensitive periods in the development of executive functioning.

Conclusions: This study confirms the presence of cognitive and emotional impairments in CTD. It is necessary to accurately quantify these deficits so that future research directions can be identified and novel treatment pathways investigated. Furthermore, this study provides support for the presence of stress-sensitive periods of neuropsychological development, specifically in the domains of executive functioning and cognitive empathy. Therefore, by increasing our awareness of the role that early life trauma plays in CTD and the enduring effects it has in adulthood, we may be able to identify populations at risk of developing psychopathology in adulthood, allowing for early intervention.

Zelia Chiu

Vitamin D Status in Uveitis Patients

A/Prof Anthony Hall: Department of Ophthalmology, The Alfred Hospital, Prahran, Victoria
A/Prof Lyndell Lim: Clinical Trials Research Centre, Centre for Eye Research Australia, East Melbourne, Victoria; Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria

I chose to undertake a BMedSc(Hons) after my fourth year. After reaching out to several potential supervisors, I met my supervisor, who was incredibly kind and supportive. While admittedly the project was a bit risky (prospective studies are much riskier than retrospective studies), I heard from past students that the choice of supervisor is, in many ways, more important than the project itself. It was the best decision I could have made (my nugget of wisdom: supervisor first, project second!).

While based at the Alfred Hospital, I spent time recruiting at the RVEEH and a private ophthalmic practice. It turned out to be an incredibly interesting and rewarding project, with great overseas/local travel opportunities and conference presentations. Feel free to contact me if you have any questions!

Abstract

Background: There are links between autoimmunity and vitamin D deficiency. Vitamin D supplementation is being trialled as preventative management for some auto-immune diseases. Animal studies have demonstrated that calcitriol inhibits the development of experimental autoimmune uveitis (EAU), and has potential to reverse already-developed EAU. While few clinical studies have been performed, and none investigated the effect of vitamin D levels on activity, all studies thus far have demonstrated an association between vitamin D deficiency and uveitis. We investigated the relationship between serum vitamin D levels and uveitis activity, and the relationship between forms of vitamin D supplementation and uveitis activity.

Methods: An observational case-control study recruiting patients with active and inactive non-infectious uveitis from two Victorian tertiary hospitals and a private ophthalmic practice was performed. Patients were recruited between February and August 2017. All patients had a serum 25-hydroxyvitamin-D measurement, and completed a questionnaire regarding vitamin D intake and UV exposure. Analysis of serum vitamin D levels was performed between active and inactive groups, and demographically-matched data from the ABS Nutrition Survey 2011-2012. The results of the questionnaire were compared between active and inactive groups to explore this relationship.

Results: 75 patients with active non-infectious uveitis and 77 patients with inactive non-infectious uveitis were identified, with a median age of 45. The median (IQR) level of serum vitamin D in active uveitis was 47nmol/L (29,70), significantly lower than the inactive control group at 64nmol/L (52,79) ($p<0.001$). The active uveitis group was found to have lower serum vitamin D levels than ABS controls, who had a median (IQR) of 62nmol/L (46,77). In our questionnaire analysis, vitamin D supplementation was demonstrated to be significantly related to decreased uveitis activity ($p=0.022$). When we sub-analysed only vitamin D deficient participants, sun exposure was significantly related to decreased uveitis activity ($p=0.0153$ and $p=0.0200$ for weekday and weekend analyses respectively).

Conclusion: Participants with active uveitis had lower serum vitamin D levels than inactive controls, with significantly lower medians reported in active uveitis when compared to inactive uveitis and ABS controls. Furthermore, vitamin D supplementation and sun exposure were found to be associated with decreased uveitis activity, thereby indicating the potential for vitamin D supplementation as a preventative management option. Further studies are recommended to determine the efficacy of vitamin D supplementation in decreasing relapses of uveitis.

Erin Clarke

How useful is an early pregnancy oral glucose tolerance test in women at high risk for gestational diabetes?

Professor Shaun Brennecke, Dr Tom Cade. Department of Maternal-Fetal Medicine, Royal Women's Hospital, Parkville. University of Melbourne.

Hello! I'm a final year med student but I actually hail from Notre Dame in Perth. I enrolled in the BMedSc so I could move to Melbs and work at the Women's. I chose this project as I wanted to do clinical research and get extra clinical experience in O&G. Honours was a great year and I absolutely loved it. Should you do a BMedSc? Yes. Absolutely.

However, there will be many steep learning curves, so be clear about your goals for the year. My word of advice is to not take the first project or supervisor that presents itself, despite this being the easy option. Choose a project, supervisor and lab environment that resonate with you. This will keep you sane throughout the hard times and make it all worth it.

I'm very happy to chat about my project or O&G research in general on erin.clarke@live.com.au :)

Abstract

Background: Gestational diabetes mellitus (GDM) is glucose intolerance first detected during pregnancy. Adverse outcomes of GDM include macrosomia, preterm birth, caesarean section and pre-eclampsia. Australia conducts universal screening for GDM between 24 – 28 weeks gestation, using a 75g 2 hour oral glucose tolerance test (OGTT). High-risk women (such as those with previous GDM, obesity, or advanced age) undergo early screening before 24 weeks. The rationale is that earlier diagnosis provides more time for treatment, with a view to minimising adverse outcomes. It is assumed that the longer GDM is undiagnosed and untreated, the more adverse the outcomes. However, there is a paucity of evidence examining the adverse outcomes of early-diagnosed, high-risk women using current diagnostic criteria. Furthermore, current criteria are based on the associations between hyperglycemia and adverse outcomes in women >24 weeks gestation. These criteria are used in early screening despite a lack of evidence to support this. Evidence is needed that examines how early pregnancy hyperglycemia is associated with adverse outcomes.

Method: A retrospective audit was conducted on women diagnosed with GDM using a 75g 2 hour OGTT. The audit was conducted between April 2015 and January 2017 to coincide with the adoption of current diagnostic criteria formulated by the International Association of the Diabetes and Pregnancy Study Groups. All women were treated with diet or insulin to achieve standard glycemic targets. Pregnancy outcomes were compared between 'Early GDM' diagnosed <24 weeks (n=133) and 'Late GDM' diagnosed >24 weeks (n=636). Associations between OGTT values and adverse outcomes were examined for Early GDM.

Results: Early GDM had a lower frequency of newborn composite outcome compared to Late GDM (20.3% vs. 30.0%, p=0.02). The frequencies of primary caesarean, hypertensive disorders, postpartum haemorrhage, birthweight >90th percentile and preterm birth were similar between groups. The fasting plasma glucose in Early GDM was associated with birthweight >90th percentile (OR 3.50, 95%CI 1.05 – 11.64, p=0.04). The fasting glucose showed linear associations with the remaining outcomes. The 2 hour plasma glucose was associated with preterm birth (OR 1.84, 95%CI 1.02 – 3.30, p=0.04). No other trends were seen for post-load values.

Conclusions: Early diagnosis was associated with a reduction in newborn morbidity. Other adverse outcomes were similar between groups. Frequencies may have been higher in the absence of early diagnosis and treatment. Therefore, early screening may be justified. However, despite early treatment, linear associations were seen between fasting glucose and outcomes, notably birthweight >90th percentile. Early treatment may be beneficial in ameliorating the risk associations for post-load values but not for the fasting glucose. Future prospective studies examining the effect of early and routine diagnosis on adverse outcome frequency will provide valuable information to support the justification of early screening.

Sam Cooper

Prevalence and determinants of mental health in recently resettled refugee populations.

Dr Joanne Enticott & Prof Graham Meadows.

I undertook my BMedSc following fourth year. I have an interest in psychiatry, public health and the socio-political context of refugees in Australia and chose my topic accordingly.

This year I've enjoyed learning about the nature of scientific knowledge, psychiatry and epidemiology under the supervision of Dr Jo Enticott and Prof Graham Meadows, who have been tremendous sources of support and expertise. I saw the year as an opportunity to develop the critical appraisal skills touched on in MBBS and apply these to actual research, including my own. The BMedSc year necessitates the invaluable 'critical gaze'.

I would highly recommend the BMedSc to any prospective student looking to learn new skills which will put you in good stead for your future career as a doctor. I have had opportunities to present at conferences, to community based organisations, health network stakeholders and other academics; all great experiences.

Some advice; try to understand the concepts and inherent assumptions of your research before diving into experiments/modelling. I found having a good conceptual grounding (topic specific and also scientific epistemology generally) really beneficial to my work in the latter stages of the year.

More than happy to be contacted for any queries: srcoo3@student.monash.edu.

Abstract

Background: As the numbers of refugees and asylum seekers grow worldwide, understanding the prevalence and determinants of mental illness in resettlement becomes increasingly important. To date, no longitudinal studies have examined the first three years of resettlement in refugee populations settled in Australia.

Aims & Hypotheses: This study aimed to explore changes in mental illness on a population level over the first three years of resettlement for humanitarian migrants (refugees) in Australia. It was exploratory, yet also had some clear a priori aims and hypotheses.

Aim 1: To examine the prevalence and course of mental health over the first three years of resettlement in humanitarian migrants.

Hypothesis 1: Overall, prevalence of mental illness would decrease over time

Aim 2: To examine the role of social support over time in relation to mental health and the difference between like-ethnic and non-ethnic support

Hypothesis 2a: Both like-ethnic and other forms of social support would be negatively associated with mental illness

Hypothesis 2b: Compared with other sources of support, like-ethnic support would show a greater negative association with mental illness

Methods: We examined the first three annual waves from the 'Building a New Life in Australia' survey; a longitudinal, nationally representative cohort study involving 2399 recently resettled humanitarian migrants. Outcomes for our study were mental health variables measured by the Kessler Psychological Distress Scale (K6) and Posttraumatic Stress Disorder-8 items (PTSD-8), which asked participants to rate symptoms from the month before the survey. An abnormal K6 score of 19 or greater was considered consistent with 'serious mental illness'. A positive PTSD-8 screen was considered consistent with 'PTSD'. We used generalised linear mixed models to examine associations between outcomes and predictors.

Results: Our results showed a high prevalence of mental illness among our national representative cohort that persisted over the first three years of resettlement. At baseline, 30.3% (95%CI 28.5-32.2) had PTSD and 15.4% (95%CI 14.0-16.9) had severe mental illness. There was a trough in the prevalence of all outcomes at wave 2 and then an increase to baseline prevalence at wave 3. The three year prevalence of all mental illness was 52.2%.

We failed to detect any significant associations between mental illness and the presence or absence of social support. However, contrary to Hypothesis 2b, like-ethnic support appeared to be significantly positively associated with PTSD.

Severe mental illness appeared to be significantly positively associated with female gender, Middle Eastern region of birth, unstable housing, increasing financial hardship, poor self-rated health, having a chronic health condition and discrimination.

PTSD also appeared to be significant positively associated with older age, female gender, Middle Eastern region of birth, increasing number of traumatic events, increasing financial hardship, having a chronic health condition and poor self-rated health.

Conclusion: Our findings show there is a high risk for mental illness throughout the first three years of resettlement for refugees in Australia. Our novel finding regarding like-ethnic social support raises future avenues for research. Significant predictors of mental illness in the post-migration context represent tangible opportunities for intervention and are likely relevant to similar resettlement settings globally.

Annie G. Cox

Sulforaphane; a novel therapy for preeclampsia?

Bryan Leaw [a,b], Sarah Marshall [a], Euan Wallace [a,b]

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When I started in the lab I had absolutely no experience in basic science, was unsure how to hold a pipette and just wanted to play with the centrifuge. Learning the lab skills I needed for my project was a steep and often challenging learning curve. However it was this challenge that made the successes so rewarding and meant I cultivated a curiosity and love for science.

Though my lab skills have progressed (I now get to play with the megafuge), what I consider my most important skill from this year is not my pipetting, nor is it my ability to plot data, but rather it is the shift in mentality I have adopted. It took me a long time to lose the medical student mindset of wanting to be "right" and instead embrace the scientific attitude of seeking to answer a question, irrespective of what that answer may be. Though undeniably depressing given the huge emotional energy invested into any experiment, I am starting to appreciate the importance of failure and negative results in science. Resilience in the face of unexpected results and the capacity to accept, acknowledge and move forward from my own mistakes are undoubtedly the most important accomplishments of my year.

"There is no success and failure, there is only science… and those too weak to seek it."

–Anon.

Abstract

Background: Clinical management of preeclampsia has plateaued over the past fifty years and is in desperate want of novel therapies. Though much remains unclear regarding the pathophysiology of preeclampsia, the last decade has seen new evidence for the role of placental derived anti-angiogenic factors, such as sFlt-1, sEng, and activin A, in causing the endothelial dysfunction of the disease state. Consequently, the spotlight has fallen on antioxidants as a potential therapy, to reduce placental oxidative stress and improve endothelial resilience. Here, I investigate the antioxidant and Nrf2 activator sulforaphane, as a potential therapy for preeclampsia. I further present a model for the assessment of vasculature after incubation in media containing placental derived anti-angiogenic factors.

Aim: To investigate the efficacy of sulforaphane in reducing placental stress and improving vascular resilience, as a novel therapy for preeclampsia.

Methods: I assessed the effects of sulforaphane (20μM) in mediating hypoxic and hyperoxic (X/XO) injury on placental explants and isolated villous cytotrophoblasts through quantifying secretion of the anti-angiogenic compounds sFlt-1, sEng, activin A and 8-isoprostane. I then used Nrf2 silencing in trophoblasts, to assess the role of Nrf2 in sulforaphane mediated antioxidant effects. Finally, I quantified levels of the downstream protein HO-1, after cell lysis. Moving forward, I used totrophoblast conditioned media (TCM) from isolated cells grown in 1% O2 to develop and optimise a model for incubation of ovine myometrial vessels in media containing preeclamptic anti-angiogenic factors, such as sFlt-1. In optimising this model for the assessment of vascular reactivity using wire myography, I trialled several pharmacological agents, incubation times and incubation temperatures on myometrial arteries from term ewes. I further tested TCM at concentrations of 0% (control) 30%, 50% and 100%, diluted in control media (M199) where appropriate.

Results: In explants, sulforaphane administration ameliorated hypoxic and hyperoxic injury, as evinced through reductions in sFlt-1 (p=0.047), sEng (p=0.005) and activin A (p=0.004). In treated trophoblasts, I measured reduced sFlt-1 (0.0003) and activin A (0.02) secretion, but not sEng (p=0.99) or 8-isoprostane (0.14). These findings were persevered even where Nrf2 was silenced, suggesting that the antioxidant effects in trophoblasts were not all Nrf2 mediated. In developing a model for vascular assessment and co-incubation I found replicable dysfunction in vessels incubated for 1 hour 37°c, normoxia using 50% TCM (p=0.0439) though not 30% (p=0.1) or 100% (p=0.17), compared to control.

Conclusion: In reducing placental oxidative stress, sulforaphane presents an exciting novel therapeutic for the treatment of preeclampsia. In particular, the observed reduction in sFlt-1 and activin A from both explants and trophoblasts warrants future translational investigation into the clinical application of sulforaphane. Indeed the successful development of a model to co-incubate vessels with TCM is an avenue for such experimentation.

Eleanor Danek

Risk-adjustment of diabetes health outcomes for benchmarking of clinical performance

Professor Sophia Zoungas (MBBS, FRACP, PhD, Head of Diabetes and Vascular Medicine Research Program)
Professor Arul Earnest (PhD, MSc, DLSHTM, B.Soc.Sc (Hons))
School of Public Health and Preventative Medicine, Monash University

This year has given me invaluable insight into the exciting world of medical research. My decision to undertake a Bachelor of Medical Science after 4th year was motivated by a desire to try something new. In doing so, I have discovered a love of research and a passion for Diabetes Quality Improvement.

I was privileged to benefit from the guidance and mentorship of two highly dedicated supervisors; Professor Sophia Zoungas and Professor Arul Earnest. Under their kind and patient tutelage, I have developed a range of highly transferrable skills that will no doubt benefit me in my future career.

My research into risk-adjustment of diabetes health outcomes has resulted in a change to current practice. Risk-adjustment will now be integrated into nationwide benchmarking of clinical performance in diabetes care (the Australian National Diabetes Audit). Furthermore, my research into quality measures for diabetes care has informed the development of revised accreditation standards for the National Association of Diabetes Centres. It was been truly rewarding to observe my research translate into practice.

Finally, this year has enabled me to consolidate my passion for diabetes care. I hope to remain actively engaged in diabetes research throughout my career.

Abstract

Background: The growing burden of diabetes in Australia underlines the need for targeted, evidence-based strategies to improve the quality of diabetes care. Benchmarking clinical performance by comparing diabetes health outcomes is a proven strategy for quality improvement. Risk-adjustment may facilitate fairer, more accurate comparisons of diabetes health outcomes. However, there is limited evidence to inform risk-adjustment of diabetes health outcomes for benchmarking of clinical performance. Furthermore, no studies have tested the impact of risk-adjustment on diabetes benchmarking in an Australian context.

Method: The study objectives were:

1) To develop risk models using non-care related patient factors, for adjustment of common diabetes outcome measures

2) To characterise the impact of risk-adjustment on benchmarking of clinical performance in diabetes care

A retrospective, cross-sectional study was performed using data obtained during the 2015 Australian National Diabetes Audit (ANDA). 4670 patients with type 1 (n=3496) and type 2 (n=1174) diabetes across 49 ANDA-participating diabetes centres were analysed. There were two main analytical components to this study.

Study component 1: Developing risk models for adjustment of diabetes outcome measures

Patients were stratified by diabetes type (type 1, T1DM, and type 2, T2DM). Multivariate linear regression and multiple logistic regression were used to analyse associations between non-care related patient characteristics and four diabetes health outcomes: HbA1c (%), LDL-Ch (mmol/L), systolic blood pressure (mmHg) and severe hypoglycaemia. Risk models were constructed for health outcomes.

Study component 2: Evaluating the impact of risk-adjustment on funnel plots of outcome measures for benchmarking of clinical performance

Unadjusted and risk-adjusted diabetes health outcomes were converted into performance measures of average levels or rates. Funnel plots were constructed for unadjusted and risk-adjusted performance measures. The control limit for identifying outliers was set at 99.8%. Unadjusted and adjusted funnel plots were compared to evaluate the impact of risk-adjustment on performance status. The primary outcome of interest was to identify changes to the number of centres identified as high-performing or low-performing outliers.

Results: Study component 1: Significant associations with T1DM and T2DM health outcomes were observed for non-care related patient factors (age, sex, body mass index, disease duration, disease severity and smoking history), but not country of birth. The impact of patient covariates varied across different T1DM and T2DM patient outcomes.

Study component 2: Overall, risk-adjustment resulted in 32 changes to performance status across the four performance indicators. 63% of changes resulted from low-performing outliers ('false positives') being reclassified as inliers after risk-adjustment. 34% of changes resulted from high-performing outliers ('false high performers') being reclassified as inliers. One inlier centre ('false negative') was reclassified as a low-performing outlier after risk-adjustment.

Conclusions: Risk-adjustment of diabetes health outcomes for non-care related patient factors has a significant impact on benchmarking of clinical performance. There were reductions in false positives and false negatives for low performance, as well as a reduction in false high performers. This suggests that risk-adjustment of diabetes health outcomes for benchmarking results in fairer comparisons of clinical performance, and provides more accurate information to inform subsequent quality improvement activity.

Michayla Doherty

Trauma Among the Elderly

Fitzgerald M[1,2], Mathew J[1,2,3], Mitra B[1,3,4]

[1]National Trauma Research Institute, The Alfred Hospital; [2]Trauma Service, The Alfred Hospital; [3]Emergency & Trauma Centre, The Alfred Hospital, [4]Department of Epidemiology & Preventive Medicine, Monash University

I decided to intermit from fifth year to undertake my BMedSc with the National Trauma Research Institute (NTRI). I have a passion for Emergency Medicine, so teaming with the NTRI was a no-brainer.

My project involved firstly conducting a systematic review, then a retrospective study at the Alfred Hospital. My project was investigating the differences in elderly physical trauma, particularly around mortality, compared to younger trauma patients. I then compared current management standards to a proposed standard, to identify areas of improvement for elderly trauma patients, to suggest future practice changes.

This year was so much more than I expected. It's definitely not a year off, and it's certainly not easy! I learnt a great deal not only about research methods and presenting your literature, but also on what to look for when critiquing research, how to succinctly explain yourself, and a great deal about trauma management through a major referral centre. It's been an interesting opportunity, and has allowed me not only to gain an appreciation for trauma medicine, but also network and meet some other amazing people at the NTRI!

Always happy to answer any questions at mdoh3@student.monash.edu

Abstract

Background: In an increasingly ageing society, older patients (≥70 years) comprise one of the largest groups seen with traumatic, physical injuries. Older patients more frequently present following a fall and can sustain substantial injuries due to comorbidities and frailty. The systematic review conducted confirmed that older trauma patients have a higher mortality rate, with an odds ratio of 2.55 (CI 1.55-4.18). However, there are limited elderly-specific assessment and management strategies in trauma management. The London Major Trauma Service (LMTS) released a specific guideline standard to assist clinicians in managing major trauma in older patients. One of these strategies detailed four interventions to be completed within the first 24 hours, including a multidisciplinary team meeting (MDT), tertiary survey, medication reconciliation and the recording of a resuscitation plan.

Aim: To assess the compliance of a Victorian adult major trauma centre with the LMTS standards of elderly trauma management, prior to intervention or specific education on this guideline. The purpose was to determine whether this checklist was already being met, and thus, whether any benefit could be contrived by adopting them.

Method: Data from the Alfred Trauma Registry were extracted retrospectively on patients aged 70 years and over who presented between July 1st 2012 to June 30th 2013, and July 1st 2015 and June 30th 2016. Exclusion criteria included death within 24 hours after admission, missing inpatient notes, and an Injury Severity Score (ISS) of 12 or below. Completeness of this checklist, demographics, clinical data and outcomes were analysed.

Results: Of 639 eligible patients, 584 met criteria for inclusion, with a mean age of 81 years (SD 8) and median injury severity score (ISS) of 18 (IQR 14-25). Falls from ≤1 metre constituted the most common injury cause (53.8%). The overall mortality rate was 16.6%. All 4 items on the checklist criteria were completed within 24 hours for 3/271 patients in 2012/13 and 15/313 in 2015/16 (p=0.007). The frequency of MDT and Medication Reconciliation within 24 hours (p<0.001) demonstrated significant improvement, while documentation of tertiary survey and resuscitation plans were identified as areas requiring improvement.

Conclusions: Components of the LMTS guidelines for assessment of older trauma patients were uncommonly followed in this period when no focused training towards this checklist was provided. This suggests that there is potential for improvement by adopting these strategies. Further education is required on specific assessment and management strategies for older injured patients and the potential to improve patient experience and outcomes.

Chloe Duygu Durukan

Epidemiology of genital herpes infections in Melbourne, Australia

Prof. Christopher Fairley, Dr. Eric Chow, A/Prof Catriona Bradshaw, Dr Tim Read
Melbourne Sexual Health Centre, Alfred Health, Monash University

I decided to undertake a BMedSc (Honours) after finishing Year 4 in 2016. I have always been interested in reproductive and sexual health and decided to further pursue this interest by undertaking research at Melbourne Sexual Health Centre. After discussing possible projects with my team of supervisors I chose to do an epidemiological study as I wanted to learn to analyse large datasets and also improve my knowledge of statistics.

This year has given me a taste of medical research and allowed me to develop skills in scientific writing and presentation, as well as a much better ability to understand and critically appraise evidence. I had a fantastic year working with the team at MSHC and I am extremely grateful to my supportive and passionate team of supervisors. I would like to thank Prof. Christopher Fairley and Dr Eric Chow in particular, for providing me with guidance throughout this challenging and rewarding year. If you are interested in discussing projects as MSHC or have questions about the year in general, feel free to contact me at chloeduygu@gmail.com

Abstract

Background: Genital herpes is a sexually transmitted infection caused by herpes simplex type 1 and type 2. It is characterised by recurrent episodes of painful genital ulcers, as well as increased risk of HIV acquisition and transmission. Genital herpes is the leading cause of genital ulcer disease worldwide. HSV-2 has been universally known as the leading cause of genital herpes; however studies from developed countries showed that the proportion of genital herpes caused by HSV-1 was rising between 1979 and 2006. This is attributed to declining childhood seroprevalence of HSV-1 in these nations, which creates a pool of adolescents who experience their first exposure to HSV-1 with sexual debut. Since 2006, there have been no studies on trends of genital herpes in Australia.

Aims and Hypotheses: This study aimed to describe the trends of first episode genital herpes by serological type amongst women, heterosexual men and men who have sex with men (MSM) between 2004 and 2016. In women and heterosexual men, we hypothesised that the proportion of first episode herpes due to HSV-2 will be declining due to increasing condom use and HSV-1 will be increasing due to declining HSV-1 childhood seroprevalence. In MSM, we hypothesised that HSV-2 will be rising due to significant declines in condom use according to Gay Community Periodic Survey data and HSV-1 will be declining in proportion.

Method: The study was an observational retrospective case series of attendances at MSHC between 2004 and 2016. A case was defined as an individual diagnosed with first episode genital HSV-1 or HSV-2, as confirmed by PCR. 4056 individuals were identified from the electronic patient database. Participants were stratified as women (n=1780), heterosexual men (n=1382), and men who have sex with men (n=924). Temporal trends were analysed in each group using Chi square test for trend. Participants were further stratified by age and HSV type to investigate if younger people had a higher proportion of HSV-1. Further trend analysis on condom use and partner number was conducted on all clinic attendees over the study period to understand demographic changes that can influence genital herpes in a population.

Results: In women (n=1780) and heterosexual men (n=1382) there was a statistically significant increase in the proportion of first episode HSV-1 and a reciprocal decline in HSV-2 (ptrend<.001). Three monthly condom use and partner numbers have increased in both groups (ptrend <.001). In MSM (n=924) there was no statistically significant change in the trends of HSV-1 and HSV-2 (ptrend =.081) MSM's three monthly condom use declined (ptrend <.001) and casual partner number increased (ptrend <.001) Women, heterosexual men and MSM under 25 years of age had the highest proportions of genital herpes due to HSV-1. The proportion of HSV-1 declined with increasing age.

Conclusions: Genital HSV-1 has been increasing in Australia since 1980s. This study found that it is now more common than HSV-2 as a cause of first episode genital herpes in women and MSM. Although HSV-1 has historically been acquired during childhood; this is becoming less common in developed countries. Falling childhood infections is most likely the drive behind rising genital HSV-1, as adolescents to enter sexual activity and become exposed to HSV-1 for the first time.

James Fahey

Identifying Genetic Causes of Spontaneous Coronary Artery Dissection by Whole Genome Sequencing in Related Individuals

Dr Anthony White, Monash Cardiovascular Research Centre
Dr Mirana Ramialison, Australian Regenerative Medicine Institute

My name is James Fahey, and I completed my BMedSc(Hons) degree after my 4th year of medicine. I have a keen interest in being a physician, and I'm particularly interested in the field of cardiology. The BMedSc(Hons) degree enticed me as being an opportunity to focus my attention towards learning research skills that are invaluable as a doctor. Despite having never heard of spontaneous coronary artery dissection before this year, the knowledge and skills I've gained will stay with me throughout my career.

Dedicating a year to research presents many opportunities, and I'd encourage future students to spread your wings and take advantage. You can submit your abstract/s to conferences, become involved in side projects, take some time off for a tactical 'travel break', and maybe even have enough free time to enjoy those hobbies you've neglected for the last four years.

I'd be more than happy to discuss share my experience further. You can contact me at jkfah1@student.monash.edu.

Abstract

Background: Spontaneous coronary artery dissection (SCAD) is a sudden tear within the coronary arterial wall leading to acute coronary syndrome. It typically occurs in younger patients with an overwhelming female preponderance, in comparison with atherosclerotic acute coronary syndrome. Patients with SCAD often have concomitant fibromuscular dysplasia. The aetiology of SCAD is unknown. Most SCAD cases are considered sporadic, however recent reports of familial SCAD suggest a possible genetic component in these cases.

Method: Whole genome sequencing of a mother and daughter with a history of SCAD was performed using an Illumina MiSeq system as single-end 150 base pair reads. Reads were aligned against a reference genome and variants were called. Variants were first filtered to select for non-synonymous coding variants, deleterious variants, rare variants (<1% population) and variants present in both mother and daughter. The remaining variants and their corresponding genes were filtered against the list of genes obtained from a keyword search of the Ensembl database for human gene annotations associated with "cardiac" OR "coronary" OR "arter*" OR "dissection" OR "heart" OR "vascular" OR "vessel" OR "endothel*". The remaining shortlist of candidate genes was then ranked according to a gene prioritisation system that considered gene expression in cells/tissues of interest, gene ontology, phenotypic annotations, and the number of gene transcripts damaged by the corresponding variant.

Results: The total number of variants present in either the mother or the daughter was 4,437,687. After the initial filtering, 278 variants, corresponding to 118 unique genes, were non-synonymous coding variants, deleterious/damaging to respective proteins, rare, and present in both mother and daughter. Nine genes, corresponding to 12 variants, remained when the 118 genes from the initial filtering were then filtered against the 1,380 human genes obtained from a keyword search of Ensembl. In order of priority using the gene prioritisation scoring system, these genes were F11R, OLFM1, TSC1, MAP2K3, MYO18B, MYH9, PCSK5, CACNA1G and PSG4.

Conclusions: The F11R gene emerged as the highest priority genetic candidate for predisposition to SCAD in the mother and daughter. It encodes the F11 receptor, also known as junctional adhesion molecule A, and has a role in the regulation of tight junction assembly in endothelial cells. Considering the SCAD phenotype of endothelial fragility, the F11R gene is a biologically plausible genetic candidate. Future research of this gene and the other high-scoring candidate genes in the pathogenesis of SCAD will involve performing targeted gene sequencing panels in a larger sample of sporadic SCAD cases.

Dilan Giguruwa Gamage

A cluster-randomised group approach to controlling hypertension in rural India

Professor Amanda Thrift – Epidemiology and Prevention Division, Stroke and Ageing Research, Department of Medicine, School of Clinical Sciences at Monash Health, Monash University

Associate Professor Roger Evans – Cardiovascular Disease Program, Biomedicine Discovery Institute and Department of Physiology, Monash University

I decided to complete a BMedSci after fourth year of medicine. I thought about doing one since first year and after fourth year seemed to be the best time for me. Although I am unsure about what field I want to specialise in, I am very interested in public health. I also wanted to gain a better understanding of how research projects are conducted and how to use biostatistics, as well as to take some time away from clinical placements. This all led me towards undertaking a project in epidemiology.

I was very lucky to find a fantastic research project at the Department of Medicine in Monash Medical Centre, and a very supportive team at the Stroke and Ageing Research Group. In particular, my supervisors – Prof. Amanda Thrift and Assoc. Prof. Roger Evans – taught me a great deal throughout the year, for which I am very grateful.

Please contact me if you have any questions about my project or have any questions about doing a research project in epidemiology (email: dgig1@student.monash.edu).

Abstract

Background: Hypertension causes the largest burden of disease of any medical condition worldwide. It is possible to control hypertension with antihypertensive medications and lifestyle changes, aiming for a blood pressure less than 140/90 mmHg. The control of hypertension is poor worldwide and worst in rural regions of low-to middle-income countries. There are numerous barriers to controlling hypertension such as limited access to healthcare and cost of treatment. These barriers are more prevalent in poorer regions; some can be overcome using an education program delivered by a community health worker. In five prior community-based programs, none were group-based and none were conducted to explore the impact of socioeconomic conditions on the success of a program. We aimed to test the effectiveness of a community-based group approach for controlling hypertension. We further aimed to explore the impact of socioeconomic characteristics on the effectiveness of a program to control hypertension.

Method: The study was conducted in three diverse rural regions of India, listed from poorest to wealthiest: Rishi Valley, West Godavari and Trivandrum. Initially, a cross-sectional survey was conducted at the three sites to identify people with hypertension. We then randomised regions to intervention or control groups.

The education program consisted of six fortnightly meetings, focusing on education about hypertension and the importance of lifestyle changes. The program was delivered by health workers who were trained over a 5-day period. Outcomes were assessed 6-8 weeks after the last session of the program and compared to the same assessment conducted during the cross-sectional survey.

Our primary findings were changes in blood pressure and proportions with blood pressure controlled. Our secondary findings were changes in factors associated with the control of hypertension, such as use of medications, physical activity and diet.

Results: At baseline, the intervention (n=457) and control groups (n=1,021) were similar, overall and at each site, for average blood pressure, proportion with control of hypertension and for most factors associated with hypertension. Over the course of the trial, blood pressure in the intervention group was lowered more than in the control group. Additionally, a greater proportion of people in the intervention group gained control of hypertension (<140/90 mmHg) than in the control group. Although larger improvements were observed in the poorer regions than in the richer regions, this was not statistically significant.

Despite the significant improvements in controlling hypertension in the intervention group, we did not detect major differences in factors associated with the control of hypertension between the treatment groups.

Conclusions: Our community-based program appeared to be effective in lowering blood pressure and increasing the proportion with control of hypertension. Our findings suggest a group-based approach can be effective in controlling hypertension. Socioeconomic conditions may influence the success of a community-based program, but this relationship is unclear. Further research with a larger sample size may add to the understanding of this relationship.

Dinesh Giritharan

Use of Decision Support Tools for Discharge Planning in a General Medical Unit

A/Prof Christopher Wright – Monash University
Prof Donald Campbell – Monash Health

I chose to undertake a BMedSc(Hons) after completing my 4th year of medicine. Research, in particular the intersection of medicine and technology, has long been a passion of mine. As such, the decision to do a BMedSc and the process of choosing a project was made easier for me, and I was very glad that I'd be able to formally put my interests into practice under the supervision of A/Prof Chris Wright.

This year has allowed me to take my first steps into a larger world, one that encompasses medicine and health holistically as opposed to just on an individual patient-doctor level. I have learnt skills that I'll be able to use and build upon for the rest of my life, and for that I am very grateful.

All in all, this has been one of my most enjoyable and rewarding years yet. I'd highly recommend anyone with an interest in research to consider a BMedSc(Hons) – please feel free to contact me if you have any questions!

Abstract

Background: Hospital discharge performance is a significant factor in influencing patient safety and flow in an inpatient hospital environment. Discharging a patient too early or too late increases the risk of unplanned readmission, reduces hospital efficiency and results in a greater financial burden. The decision-making processes around discharge in Victorian hospitals are based on discharge planning. There have been a variety of strategies implemented with the aim of improving discharge planning, but these have had limited success at a statewide level thus far. This project aimed to address the gap in the literature regarding decisions in the discharge planning process and the potential for the use of decision support tools in aiding clinicians with deciding when to discharge a patient.

Method: We collected data on discharge decision making for 147 patients admitted to General Medicine at Monash Medical Centre, Clayton. We used the data we collected to develop and test decision support tools for discharge. Importantly, however, during this process we also learned that using clinician decision-making as the gold standard for determining when to discharge patients may not be appropriate, indicating that there are variables that are currently not being properly considered in the discharge process. In order to determine what these variables might be, we analysed our data as well as aggregated data from Monash Health to determine if there were specific cohorts of patients who were more likely to be readmitted within 30 days.

Results: Our explorative, prospective study was able to delineate the main variables used by clinicians to discharge patients and in turn, lead to the development of tools that were able to match clinician decision-making with a high accuracy. As indicated above, we also determined that the unplanned readmission rate for patients admitted to General Medicine was much higher than the statewide average. Our analysis of these readmitted patients indicated that there may be certain patient groups who are overrepresented amongst those who are readmitted to hospital within 30 days.

Conclusions: This study has laid down the foundations for further research into this important public health issue, specifically for determining the variables needed for discharge that haven't been currently accounted for and also for focusing on specific patient groups. It has also shown the potential for decision support tools to be used alongside clinician decision making for discharge.

Deepika Gunda

Factors predictive of response to treatment in adults with chronic rhinosinusitis

Dr Debra Phyland and Ms Joanne Rimmer
Department of Otolaryngology, Head and Neck Surgery, Monash Health Monash University

I was fortunate enough to complete a BMedSc after my fourth year of medicine, with the Monash Health ENT department. I chose to do this year as I wanted to gain exposure to research and to a field that I was interested in.

The year offered me a steep and welcome learning experience into the process of research. I have gained valuable skills that I believe will help me in the future as a doctor and as a researcher. I feel better prepared for final year and internship after having completed this year. As I did a clinical project, alongside research, my year included a lot of patient interaction and the opportunity to observe consultations and surgeries within the department. I am grateful to my supervisors and the department and appreciate all the teaching experiences I had.

For students who are considering doing a BMedSc, I would recommend choosing a project and a field that you are interested in. I am happy to be contacted with questions or for further information (dgun15).

Abstract

Background: Medical and surgical treatment options are available for chronic rhinosinusitis. While endoscopic sinus surgery is a treatment option for chronic rhinosinusitis, success rates are not optimal. There are no clear surgical candidature criteria used to choose surgical treatment over medical therapy for individual patients. It is unknown whether certain patient factors could be used to predict the outcomes of surgery.

Aims: To a) conduct a pilot study to characterise the demographics and disease-specific status of chronic rhinosinusitis patients found in an Australian setting and b) determine which patient factors can be used to better predict treatment outcomes of endoscopic sinus surgery in adults with chronic rhinosinusitis by evaluating previously published appropriateness criteria and a clinical clustering algorithm.

Method: The first part of the project was a "retrospective component gathering cases" which tested the validity of the appropriateness criteria for determining surgical suitability. Retrospective review was undertaken for all adult patients who underwent surgery for CRS from 01/01/2016 to 31/03/2017. Cases were found that met the appropriate criteria and other cases that did not meet the appropriateness criteria. The primary outcome measures used were the preoperative and postoperative 22-item sino-nasal outcome test (SNOT-22) scores.

The second part of the project involved testing a clinical clustering algorithm in a prospective observational study. Patients who were undergoing sinus surgery were recruited and separated into clusters according to the clinical algorithm. A comparison group consisted of patients having medical therapy. All participants completed the SNOT-22 symptom score, a patient questionnaire, a Sniffin' Sticks test, a sinus computed tomography (CT) scan which was graded using the Lund-Mackay scoring system and a blood test that measured serum levels of eosinophils, vitamin D and Immunoglobulin E (IgE).

At 3-months post treatment follow-ups, participants repeated the SNOT-22 score, the Sniffin' Sticks test, had a blood test to check serum levels of eosinophils and underwent nasal endoscopy.

Results: There were 26 suitable cases found in the retrospective search, consisting of 14 patients who met the criteria and 12 patients who did not meet the appropriateness criteria. All patients who met the criteria achieved the minimum clinically important difference in SNOT22 scores of 8.9. However, only 7 patients who did not meet the appropriateness criteria achieved the minimum clinically important difference in SNOT-22 scores. The average preoperative SNOT-22 score was 52.3 while the average postoperative SNOT-22 score was 28.0.

Of the 24 participants recruited prospectively, 22 patients underwent surgery while the remaining 2 received medical therapy. The average pre-treatment SNOT-22 score was 61.6 (range 29-98). There were also large ranges for the number of days of productivity lost and the pre-treatment CT scan grading scores.

Conclusions: Chronic rhinosinusitis is a complex disease and many factors need to be considered when management decisions are made. There is no standard approach in the management of the disease. The appropriateness criteria and the clinical clustering algorithm are the best tools that have been created so far and need to be tested further so they may be incorporated into clinical practice.

Jason Ha

Is the spectral effect of cataract in hyperspectral imaging random or well-defined?

Xavier Hadoux[1,2], Flora Hui[1,2], James Bourne[3], Jonathan Crowston[1,2]

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[3]Australian Regenerative Medicine Institute, Monash University, Clayton, VIC, Australia.

One of the most amazing things about research is that you might dive into a project with certain expectations, but have those expectations completely reinvented by a 180° change in topic direction, failed experiments, or even a fortuitous finding! Research is never as linear as one expects, and perhaps more fundamentally, a very simple idea can get very complicated very quickly. These were some of the biggest learnings for me having undertaken my project with the Glaucoma Research Unit at the Centre for Eye Research Australia with the support of my stellar supervisors, and I am incredibly grateful for their wonderful support and mentorship.

The BMedSc year is a brilliant opportunity to experience the scientific end of medicine, where you can answer the questions, or perhaps more often than not, question your answers! If you are interested in discussing the project further, my inbox is always open at jha11@student.monash.edu.

Abstract

Can the effect of cataract surgery on hyperspectral images be characterised?

Background: Hyperspectral imaging is an emerging imaging modality in ophthalmology, and its ability to capture both spectral and spatial information can be harnessed to detect changes in retinal reflectance. It is increasingly used in clinical research for its potential in early disease diagnosis and monitoring, such as glaucoma and Alzheimer's disease. However, with an ageing population, the increased risk of retinal pathologies is also confounded by cataract, which affects the measured light spectrum. While the lens' bulk transmittance properties are known, the effect of cataract on hyperspectral images is yet to be established.

Aims/Hypotheses: This study aims to characterise the effect of cataract surgery on hyperspectral imaging. It is hypothesised that (1) the change in retinal reflectance between hyperspectral images taken from the patients pre- and post-cataract surgery can be used to obtain the spectral influence of cataract, (2) this change is non-trivial and well-defined, and can be consequently modelled.

Methods: Forty-five participants (20 male and 25 female, mean age ± SD, 68.9 ± 8.8) booked for cataract surgery at the Royal Victorian Eye and Ear Hospital were recruited. Exclusion criteria were diabetic retinopathy, glaucoma, age-related macular degeneration, eye surgery in prior 6 months, prior eye trauma. The eye undergoing surgery was imaged using a Metabolic Hyperspectral Retinal Camera (450 – 900 nm, 5 nm steps, 30° field-of-view, Optina Diagnostics, Montreal, Canada), prior to and 4 weeks post-surgery. Cataracts were graded using the Lens Opacities Classification System III. The resultant set of hyperspectral images for each patient were co-registered, and the change in retinal reflectance between the pre- and post-surgery images was measured.

Results: Across all wavelengths, there was a statistically significant increase in retinal reflectance after cataract surgery by a factor of 1.4 (95% CI = 1.34 to 1.50, $p<0.0001$). The maximum change was obtained at 450 nm, where retinal reflectance increased after cataract surgery by a factor of 2.9 (95% CI = 2.54 to 3.24, $p<0.0001$).

Conclusion: The change in retinal reflectance between hyperspectral images taken from the same set of patients pre- and post-cataract surgery could be used to obtain the spectral influence of cataract, and this spectral effect could be modelled. Understanding the spectral influence of cataract is a necessary step in developing techniques to correct for the effect of cataract in hyperspectral images, and facilitate the future detection of spectral changes occurring in retinal pathologies.

Floranne Hansa

Hepatic Encephalopathy assessment in Liver clinics using iPad technology (HELIPAD)

Associate Professor Amanda Nicoll: Department of Gastroenterology, Eastern Health.
Dr Siddharth Sood: Department of Gastroenterology & Hepatology, Royal Melbourne Hospital.
Eastern Health Clinical School, Monash University.

I chose to undertake a Bachelor of Medical Science (Honours) following my fourth year of MBBS. I was very unfamiliar with research prior to this year, and for me this project was a wonderful introduction into the world of clinical research.

Having developed an interest for liver disease during my clinical years as a medical student, I chose to undertake a project in the gastroenterology departments at Eastern Health and at the Royal Melbourne Hospital. Conducting research in these departments allowed me the opportunity to develop my clinical, analytical and presentation skills, with the help of two wonderful supervisors and a supportive environment. I also have a new found appreciation for all the time, consideration and team effort that is required to effectively carry out a research study. This year for me, although challenging, has been an extremely rewarding experience, and I would definitely recommend it to anyone looking to explore research during their medical school years.

Abstract

Background: Hepatic encephalopathy is a common complication of liver cirrhosis. Overt hepatic encephalopathy is a straightforward diagnosis based on common clinical characteristics, however minimal hepatic encephalopathy (MHE) is substantially more difficult to diagnose. MHE is associated with impairment to quality of life, driving performance and employment, but is likely underdiagnosed due to the lack of availability of specialised psychometric and neuropsychological tests in outpatient liver clinics.

Without practical screening methods or diagnostic tools, the true prevalence of MHE amongst cirrhotic patients remains unknown. This is particularly true in Australia, as there have been no MHE prevalence studies conducted in an Australian cirrhotic population.

A new screening tool in the form of a smart device application, EncephalApp: Stroop Test, aims to make it more practical to diagnose MHE in an outpatient setting. It has been validated in several centres in the United States as a useful screening method for MHE.

This study aims to determine the prevalence of MHE in a cirrhotic outpatient population, and assess the feasibility of EncephalApp: Stroop Test as a screening tool in outpatient real-world clinic settings. It also aims to identify factors independently associated with MHE.

Methods: Participants diagnosed with cirrhosis were recruited for a cross-sectional study from liver clinics at two Victorian public health services – Eastern Health and the Royal Melbourne Hospital – between March 2017 and July 2017.

Participants were approached and recruited in the outpatient waiting room, prior to their liver clinic appointment. EncephalApp was performed by the participants on an iPad under supervision. The time taken to perform the application was documented to determine its feasibility as a diagnostic tool. EncephalApp scores were blinded to clinicians until after the initial clinical assessment had been undertaken.

After the patient's appointment, further information regarding the clinician's MHE assessment, patient demographics and features of cirrhosis were collected from the patient's case file. This was to identify factors associated with EncephalApp results.

Results: A total of 125 patients (median age 56 years, 65.6% male) were recruited for this study. From the recruited participants, 46 (36.8%) had MHE according to EncephalApp. Of these 46 participants, 13 (28.3%) were also diagnosed with MHE by the clinician. There were 5 patients diagnosed with MHE by the clinician but not by EncephalApp.

The median time taken to explain EncephalApp was 1 minute and a median of 7 minutes was taken to complete the application, giving a median total time of 8 minutes to administer EncephalApp. On multivariate logistic regression, increasing age (odds ratio 1.08) and lactulose therapy (odds ratio 22.5) were independently associated with MHE according to EncephalApp.

Conclusions: This is the first Australian study examining the prevalence of MHE in a cirrhotic cohort, and as expected, MHE was significantly underdiagnosed by the clinician. EncephalApp: Stroop Test was a feasible tool for the outpatient clinic setting, and these findings support further research into the monitoring and management of MHE in the liver outpatient community.

Timothy Harkin

Characterising prostatic ductal adenocarcinoma: morphometry, clinical outcomes, and the Pi-RADS scoring system.

Prof. Mark Frydenberg (Department of Surgery, School of Clinical Sciences at Monash Health, Monash University); Prof. Prokar Dasgupta (The Urology Centre, Guy's and St Thomas' NHS Foundation Trust, London; MRC Centre for Transplantation, NIHR Biomedical Research Centre, King's Health Partners, Guy's Hospital, London); Dr. Oussama Elhage (The Urology Centre, Guy's and St Thomas' NHS Foundation Trust, London; MRC Centre for Transplantation, NIHR Biomedical Research Centre, King's Health Partners, Guy's Hospital, London)[3]Australian Regenerative Medicine Institute, Monash University, Clayton, VIC, Australia.

I commenced my BMedSc year after completing Year 4C of the MBBS, and decided to undertake the year working in one of the top urology departments in the United Kingdom. I chose the team based on previous work of theirs that I was familiar with, the recommendations of urologists that I've worked with in clinical placements, and their reputations within the specialty. Ductal adenocarcinoma, among other rare diseases, is a focus of the department at Guy's Hospital, and so it followed naturally to plan a related project.

The year quickly became the greatest year of my medical career so far, in a number of ways. The networking that was available – and both facilitated and encouraged by the incredible supervisors that I worked under – was phenomenal, and something that I would not have been able to access without the BMedSc year. I learned a broad array of skills, and developed the ability and confidence to design studies independently in future. Living abroad and experiencing another culture and medical system was invaluable, and something that I am beyond grateful for.

I am more than happy to be contacted regarding undertaking research overseas, particularly within London, and could not recommend it more strongly.

Abstract

Background: Ductal adenocarcinoma is a rare variant of prostate cancer, demonstrating a more aggressive phenotype than conventional acinar adenocarcinoma. Morphometric variables, including distance from the urethra and tumour volume, remain unclear in present literature. Similarly, the relationship between the proportion of ductal components and the clinical outcomes of this aggressive tumour is unknown.

The Pi-RADS scoring system, while studied comprehensively for acinar adenocarcinoma, has not been examined in the context of this rare variant of prostate cancer, and underestimation of ductal lesions on MRI constitutes a significant, but unknown, concern.

We aimed to provide a more comprehensive understanding of the morphometry and clinical outcomes of prostatic ductal adenocarcinoma, while examining the accuracy of reporting and point of diagnosis of ductal tumours in a high-volume, specialised uropathology unit. This study further aimed to identify clinically-significant cut-off points in proportion of ductal components, and to assess the Pi-RADS scoring system in a small sample of ductal tumours.

Method: We conducted a retrospective, observational study of ductal and Gleason 8+ acinar adenocarcinoma patients who had undergone radical prostatectomy between February 2007 and February 2017. Ductal and acinar foci were outlined under direct microscopic examination for all available prostatectomy specimens. Slides were scanned at high resolution and morphometry measurements taken. Clinical and imaging data were obtained from electronic patient records. Characteristics of each cohort were studied using Chi-square and Mann-Whitney U tests, and logistic regression models used for binomial outcomes. Cox multivariate survival analyses were conducted to examine biochemical recurrence and overall adverse event rates.

Results: A total of 95 ductal and 209 acinar adenocarcinoma cases were included, with 68 ductal and 72 acinar prostatectomy specimens available. Pi-RADS scores were reported for 13 ductal and 28 acinar patients. Ductal tumours were located further from the periphery by only 0.3 mm ($p = 0.023$), and involved 5.1% more prostate area on average ($p = 0.021$). Ductal proportions were reported in 52.7% of cases, with proportions underestimated by 5.4 (IQR -3.8–14.1). Ductal tumours were identified in 15% of specimens initially labelled as acinar-only. Only 21% of cases were diagnosed prior to radical prostatectomy. Risk of biochemical recurrence increased per 10% ductal components (HR 1.129, 95%CI 1.023–1.246, $p = 0.016$), and was substantially higher in tumours with ductal components greater than 50% (HR 2.226, 95%CI 1.110–4.464, $p = 0.024$) and 80% (HR 4.080, 95%CI 1.821–9.140, $p = 0.001$). No difference between cohorts in number of MRIs reported as Pi-RADS 4+ was observed ($p = 0.104$).

Conclusions: This is the first study to demonstrate a significant relationship between the proportion of ductal components and clinical outcomes, and our findings suggest that more aggressive management strategies are required for patients with higher ductal proportions. The Pi-RADS scoring system shows promise in assessing ductal tumours.

Stevi Harman

Investigating the Relationship Between tPA-Induced Plasmin Activity in Plasma to Predict Effectiveness of Thrombolysis in Ischaemic Stroke

Prof. Robert Medcalf , Dr Dominik Draxler (Australian Centre of Blood Disease)

I am a fourth-year medical student from Universitas Indonesia. This BMedSci(Hons) is a compulsory program to take one year of research year with affiliating universities of Universitas Indonesia. This year abroad has been a very happy year for me. First, I get to live independently of my parents in a foreign environment. Second, I feel very lucky to be a part of Medcalf Group in ACBD and a part of Monash University. I meet very kind and respectful people, and I realize the importance of a learning environment for one's growing and developing process. They created a very comfortable environment for me to learn, they are like my lab family. Third, I get to experience lab work and have my own thesis. And finally, I get to experience Australia with friends from Universitas Indonesia, they bring a piece of home with me to this foreign environment. I hope we can all be successful doctors in the future. Thankyou for Universitas Indonesia and Monash University for making this happen!

Abstract

Background and Objective : Intravenous tPA thrombolysis is the only pharmacological treatment approved for ischaemic stroke. However less than 50% patients successfully recanalise and 3-5% patients develop symptomatic intracranial haemorrhage (sICH), a major complication of tPA treatment. We sought to investigate whether the activities and levels of key fibrinolytic system; inducible plasmin activity rate, inducible plasmin-antiplasmin complex (PAP) levels, plasminogen, and antiplasmin levels correlates with patient's thrombolysis outcome.

Methods : We evaluated plasma samples of 71 patients with ischaemic stroke recruited to the Targeting Optimal Thrombolysis Outcome (TOTO) trial and Tenecteplase VS Alteplase for Stroke Thrombolysis Evaluation (TASTE) trials. These samples were obtained prior to thrombolysis. Samples were tested for the rate of plasmin generation and plasmin-antiplasmin (PAP) complexes before and after ex vivo addition of plasminogen activators. Baseline antigen levels of Plasminogen and Antiplasmin levels were also determined. Patients outcome was evaluated from National Institute of Health Stroke Scale (NIHSS), recanalisation status at 24 hours, incidence of haemorrhagic transformation, and modified rankin scale at 3 months (mRS).

Results: The variability of individual's plasma ability to generate plasmin as found to vary 40-fold after addition of uPA and 7.7-fold after addition of tPA. Despite this variation, plasminogen and antiplasmin levels positively correlated with each other ($p<0.0001$). When these findings were correlating to patient outcome, significantly higher antiplasmin levels were found in patients > 75 years who did not recanalise (n =6) compared to those who did recanalise (n=18) (123.6 ± 13.8 ug/ml VS 76.6 ± 8.3 ug/ml, p =0.02). Baseline levels of PAP complexes were also significantly higher in patients who had excellent outcome in 3 months (n=28) compared to those who died (n=9) (543.8± 145.2 ng/ml VS 809 ± 395.9 ng/ml, p = 0.01). Fold increase in levels of PAP complexes after tPA addition were also found to be significantly higher in patients who had excellent outcome.

Conclusion: alpha2- antiplasmin levels in elderly patients (> 75 years old) with acute ischaemic stroke predict recanalisation. Higher baseline levels PAP complex is also predictive of mortality at 3 months. However, the sample size of the patients who developed haemorrhagic transformation was too small for evaluation in this study and will need a larger patient cohort. Overall, this study supports the hypothesis that markers of fibrinolysis could be used to predict outcome of patients with ischaemic stroke subjected to thrombolysis.

Dean Hayden

Resuscitation of Preterm Infants in Low and Middle-Income Countries: An Ethical Analysis

Prof Dominic Wilkinson – Oxford Uehiro Centre for Practical Ethics, University of Oxford
A/Prof Justin Oakley – Centre for Human Bioethics, Monash University

I undertook the BMedSc after finishing my fourth year of the MBBS. I was fortunate to be accepted into the Oxford Bioethics program, which combined two of my interests – medical sciences and philosophy. I have been passionate about philosophy for many years, particularly the ethics surrounding animal welfare and effective altruism– and chose my topic with the intention of learning more about health issues in low and middle-income countries. Oxford has a very intellectually stimulating environment – I really enjoyed attending random lectures, debates and events as well as the great student culture. Happy to be contacted if anyone is interested in a similar project: dbhay3@student.monash.edu

Abstract

Preterm birth is a leading cause of mortality and morbidity for newborn infants. Medical treatment is possible, but sometimes costly and associated with complications. Professional organisations and societies around the world have developed management guidelines about when resuscitation of extremely preterm infants (EPIs) should be provided, however these focus on High-Income Countries (HICs) and set aside considerations of limited resources. The vast majority of preterm births occur in low and middle-income countries (LMICs) where resource limits may profoundly impact the provision of medical care.

I conducted a systematic review of the published literature, seeking to identify either clinical practice guidelines or evidence of resuscitation practices for preterm infants in LMICs.

The search failed to locate any practice guidelines specifically tailored to an individual LMIC or LMIC settings more broadly. Studies from 7 different LMICs were located describing resuscitation practices of preterm infants. These showed marked variation between and within countries as to the gestational thresholds used for resuscitation.

In light of this, the second part of this paper seeks to answer the key research question: 'How should clinicians make decisions about resuscitation of EPIs in LMICs?' The methodology employed consists of an ethical analysis, combining ethical theory with pragmatic considerations. Throughout, reasoning has been applied in the context of the Philippines as a case study.

I first explore the possibility of guiding clinicians through a cost-effectiveness analysis. This method was ultimately excluded based on two types of epistemic uncertainties. The first relates to the paucity of local data on costs and outcomes, and the marked variation in estimates dependent upon assumptions applied to imported data. The second relates to the moral status of the neonate – a necessary input in determining an acceptable cost-effectiveness threshold when assessing newborn interventions.

Drawing on the ethical principle of consistency, the thesis then moves to adapt existing prognosis-based guidelines (applied in HIC) to LMICs, proposing a new framework (the Weight And Gestation Equivalent (WAGE) mortality framework) capable of integrating the limited data available from neonatal intensive care units in the Philippines. Under this framework, clinicians may use inputs of both gestational age (GA) and birthweight to determine an infant's chance of survival, and apply mortality-based thresholds to guide treatment decisions.

Finally, this thesis examines a range of practical considerations in the implementation of this framework. It postulates that the WAGE framework would be most appropriately employed through a national workshop of relevant professionals. It also examines heterogeneity between the private and public systems, arguing for a uniform upper-threshold (point of mandatory resuscitation) between these sectors, whilst allowing for regional differences across the urban and rural sectors.

The thesis concludes with a suggested pragmatic step-by-step approach for clinicians in LMICs wishing to develop local guidelines for resuscitation of EPIs.

Chloe Higgins

The role of NLRC5 in Helicobacter-induced inflammation

Associate Professor Richard Ferrero and Dr Le Son Tran (Centre for Innate Immunity and Infectious Diseases, Hudson Institute)

I took a BMedSc year after finishing fourth year. I chose to do a lab-based project because I wanted to try something different. I have learnt a lot about research and lab techniques. It has made me realise how hard scientific research is and I definitely wouldn't recommend a lab project to someone wanting a relaxing year!

Abstract

Background: Helicobacter pylori (H. pylori) infects more than 50% of humans and leads to asymptomatic colonisation accompanied by gastritis. In some individuals, however, H. pylori infection results in peptic ulcers or malignancy. Host factors appear to play a more significant role than bacterial factors in determining pathogenesis. To enable its successful colonisation, H. pylori manipulates the host immune system, such as via regulation of the nuclear factor-αB (NF-αB) signalling pathway. The innate immune receptor NLRC5 (NLR family CARD domain containing 5) has been identified to both up- and down-regulate NF-αB signalling in different models. Unpublished data from our laboratory suggested that NLRC5 is activated by H. pylori infection and dampens gastric inflammatory responses.

Aims: The aims of this study were:

1) To characterise NLRC5 and its cytokine responses in human monocyte cell lines

2) To examine NLRC5 production in gastric tissues during Helicobacter infection.

Method: To investigate the functions of NLRC5, human wild type and NLRC5-/- macrophages were infected with H. pylori or the zoonotic species, Helicobacter felis. NLRC5 gene expression, localisation and effect on pro-inflammatory cytokines were determined by quantitative polymerase chain reaction (qPCR), immunofluorescence and enzyme linked immunosorbent assay (ELISA), respectively.

Mouse models were used to study Nlrc5 in splenic and gastric tissues. Macrophages from wild type mice or animals with a selective knockout of Nlrc5 in myeloid cells (Nlrc5mØ-KO) were infected with H. pylori or H. felis, then analysed by immunofluorescence.

Human gastric biopsy samples that were categorised according to H. pylori and gastritis status were analysed by immunofluorescence.

Finally, immunofluorescence was used to determine the subcellular localisation of NLRC5 in human gastric epithelial (AGS) cells.

Results: NLRC5 gene expression was significantly up-regulated at 48 hours in wild type macrophages in the presence of Helicobacter infection. Immunofluorescence showed a cytoplasmic aggregation of NLRC5 in these cells. Additionally, the absence of NLRC5 in knockout cells was associated with an increase in pro-inflammatory cytokines involved in the NF-αB pathway such as C-X-C motif chemokine 8 (CXCL8, also known as IL8). The inflammasome dependent cytokine interleukin-1α (IL-1α) was also increased in the absence of NLRC5, suggesting that in Helicobacter infection, NLRC5 may act as a negative regulator of NF-αB signalling and inflammasome formation.

Immunofluorescence studies on murine and human tissues showed that the predominant cells responsible for NLRC5 production were not macrophages, but were more likely epithelial cells. The levels of NLRC5 expression did not appear to be altered by Helicobacter infection or gastritis.

Conclusions: Our study has explored NLRC5 as a possible immune modulator by which H. pylori manipulates the host immune system. We have demonstrated a relationship between NLRC5 and H. pylori infection, while also demonstrating a context in which NLRC5 acts as a negative regulator of pro-inflammatory cytokine responses in macrophages. We also found that gastric epithelial cells appeared to be primarily responsible for the production of NLRC5 in the gastric mucosa. This study adds to the growing knowledge on NLRC5 and provides evidence to support further research into the relationship between NLRC5 and Helicobacter related pathology.

Helen Huang

Current management practices for suspected cervical spine injury in emergency departments: a prospective cohort study

Helen Huang [1], Dr. Gabriel Blecher [2], A/Prof Diana Egerton-Warburton [2]
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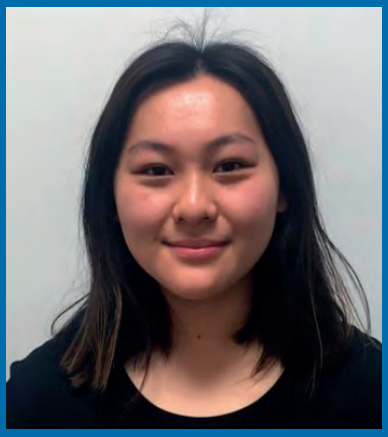

This year, I decided to complete a BMedSc(Hons) year to explore another aspect of medicine – research. For me, previous years of medical school were plagued by amorphous concepts of research, epidemiology and statistics, without knowing what they meant. I decided to explore for myself what clinical research truly entails.

Looking back on the BMedSc(Hons), I would say it was a year of discovery. I learnt a great deal about medical practice – I was surprised by how much "standard practice" is not supported by evidence, and the ability of medicine's good intentions to cause suffering. I truly appreciate now, the number of moving parts and effort involved in creating any project.

I also learnt a great deal about myself. There were times that were challenging, but I found the strength to overcome these obstacles. I now have much more self-belief in what I can achieve. Of course, I must credit my supervisors, family and friends – I was lucky to have their support, and without them, nothing would have been possible.

Overall, I would say the BMedSc(Hons) is challenging, but if you are willing to invest the effort, it is very rewarding. I have absolutely no regrets, and have thoroughly enjoyed the experience!

Abstract

Background: Suspected cervical spine injury (CSI) is a common presentation in Emergency Departments (EDs). Despite frequent use of cervical spine immobilisation, there is limited evidence for this practice in a low-risk, non-major trauma setting. There is evidence that cervical spine immobilisation is associated with harms, such as pain, pressure ulceration, increased agitation and respiratory compromise. In non-major trauma settings, the rate of cervical spine imaging and immobilisation is anecdotally high, while the rate of clinically significant CSI is low – therefore, there is a possibility that this practice may cause some patients more harm than benefit. There is a lack of published literature on the management of suspected CSI that is of appropriate methodology, setting, sample size or conducted on appropriate participants. Thus, there is a lack of evidence applicable to non-major trauma settings.

Aims: The primary aims of our study were to investigate, in patients with suspected CSI: 1) the rate of diagnostic imaging; 2) the rate of cervical spine immobilisation; and overall, to describe current emergency physician practices. The secondary aim was to address the rate of collar-related complications.

Methods: A prospective observational cohort study was performed across Monash Medical Centre (MMC) and Dandenong Hospital EDs for four months. Adults, able to give informed consent, with a suspected CSI were recruited. Exclusion criteria was applied to patients who had definitively excluded or confirmed CSIs prior to arrival, or patients unable to give informed consent. Quantitative statistical analysis was performed using descriptive and comparative statistics as appropriate, using Stata/IC 15 (StataCorp, College Station, Texas, USA).

Results: A total of 270 patients, from 271 episodes of care were recruited – 94 from MMC and 177 from Dandenong Hospital. In our cohort, 1) 72.3% underwent cervical spine imaging, and 2) 96.3% underwent cervical spine immobilisation, 95.2% with collars. 64.6% underwent imaging with a collar in-situ. Of these, 65.1% of treating physicians had a low suspicion for clinically significant CSI and collar requirement. In these scenarios, the most common reason given for collar maintenance, was due to "policy/procedure" (94.7%), specifically due to surgical (24.6%) or radiology (9.6%) input.

49.4% of all patients who had a collar in-situ at any point in their care experienced a collar-related complication. There were 6 (2.2%) cases of clinically significant CSI; but no cases of cervical cord injury. There were no cases of missed CSI in patients who did not undergo diagnostic imaging.

Conclusions: The rate of cervical spine imaging and immobilisation in a low-risk, non-major trauma setting is high. Despite this, there is a low incidence of clinically significant CSI. The rate of collar-related complications is also significant. Therefore, there is scope to reduce the rate of cervical spine imaging and immobilisation in some patients without causing additional harms. This may be assisted by the formation of guidelines that clarify areas of diagnostic uncertainty and address external party input.

Nalian Ibrahim

Novel therapeutic strategies in thyroid cancer

Professor Peter Fuller (Centre for Endocrinology and Metabolism, Hudson Institute of Medical Research)
Dr. Simon Chu (Centre for Endocrinology and Metabolism, Hudson Institute of Medical Research)

Following my fourth year of Medicine, I decided to take a year to try something different and found myself doing a lab-based BMedSci. My project in thyroid cancer allowed me to combine two of my areas of interest, endocrinology and oncology.

I had a fantastic experience over the course of this year – learning plenty of lab techniques, how to interpret and appraise scientific literature and honing my public speaking and written communication skills. With the support of my supervisors, I was also incredibly fortunate to have the opportunity to present my project at the Endocrine Society of Australia's Annual Conference in Perth and this was a great highlight of the year.

I'd be more than happy to answer any questions via email at nhibr4@student.monash.edu.

Abstract

Background: Thyroid cancer is the most common endocrine malignancy. It is often indolent and responds well to routine management, with a 5-year-survival of 96%. However, a small subset of thyroid cancer can become refractory to radioiodine (a key component of therapy), which is associated with a significantly worse prognosis. Currently, treatment options for radioiodine-refractory epithelial thyroid cancer (ETC) are limited to tyrosine kinase inhibitors (TKIs), which are associated with significant adverse effects and are not curative.

An emerging approach is to redifferentiate refractory disease to restore radioiodine response. Several targets have been investigated, with one of the most promising being the nuclear receptor peroxisome proliferator-activated receptor-gamma (PPARγ) and another being tyrosine kinase inhibitors (TKIs). Although targeting PPARγ has shown promise in vitro, this success has only been partially reflected clinically, suggesting an enhanced response may be achieved with a second target.

The inhibitors of apoptosis (IAP) protein family may be one such target, as they are known to have oncogenic properties and overexpression of one of their members, X-linked IAP (XIAP), in papillary thyroid carcinoma (PTC) is associated with a poor prognosis. Our group has previously reported a synergistic interaction between SMAC mimetics (SM) (IAP antagonists with XIAP and cIAP1 specificity), and PPARγ agonists in granulosa cell tumours (GCT). Such an approach has not been explored in ETC.

Method: Four ETC-derived cell lines (Nthy-ori 3-1, SW-1736, TPC1 and K1) were examined for cIAP1, cIAP2 and XIAP expression by RT-PCR. The TPC1 and K1 lines (PTC origin, BRAFV600E and PI3KCA mutation positive) were chosen to investigate the effects of an SM in combination with either a PPARγ agonist (rosiglitazone) or a broad-spectrum TKI (sorafenib). Cell proliferation was examined using xCELLigence Real-Time Cell Analysis. Viability was assessed using total cell counts at 24 and 48 hours. Apoptosis was investigated using TUNEL staining and Annexin PI staining with flow cytometry analysis.

Results: When an SM was used in combination with either rosiglitazone or sorafenib, we observed significant impairment of cell proliferation and viability with a clear morphological response. These effects appear largely SM-dependent in combination with the PPARγ agonist, however, these effects were markedly enhanced when combined with sorafenib, which was ineffective alone.

An unexpected finding was that SM treatment alone also showed significant effects on proliferation, apoptosis and viability that were superior to the effects of the PPARγ agonist alone.

Conclusions: Our findings suggest a novel role for SM alone or in combination with other agents in the treatment of or in the augmenting of, redifferentiation of radioiodine-refractory ETC. Clinically, this may involve lower doses of individual agents than when used alone, thereby reducing adverse effects.

James Ingram

Investigating a 5-day Intensive Mindfulness Retreat for Adolescents: A Mixed Methods Approach

A/Prof Craig Hassed, Dr Debbi Long

Having completed fourth year, I decided to undertake a BMedSc in order to explore a field outside the clinical hospital environment, and I hoped to gain some knowledge and skills of the research process along the way. I wanted to do something around mental health and was lucky to find such an interesting project. Performing mixed methods research was a challenging but rewarding process, which allowed me to learn about quantitative and qualitative research methods, the important roles they each play, and the benefits offered by combining them. The qualitative component, which involved attending the retreat and interviewing participants, was a particularly rewarding experience. To anyone considering a BMedsc, the Department of General Practice is a great place to do it – really inclusive and supportive environment, and allowed me to be flexible with where I worked. I would also recommend a qualitative or mixed methods project to anyone who wants to go beyond statistics and explore the complexity of health and healthcare. I am very happy to be contacted (james.ingram1992@gmail.com) to answer any questions.

Abstract

Background: Stress and mental illness are significant public health issues in adolescents, both of which impact negatively on social and academic functioning and have ongoing implications for an individual's health. There is growing evidence to support the efficacy of mindfulness training (MT) in fostering positive coping strategies and enhancing emotional well-being in adolescents. To date, most research into MT for adolescents has occurred in school and clinical settings, which are often limited by lack of time and experienced teachers. Intensive retreats offer an alternative approach to providing MT to adolescents, however there has been little research undertaken in this area to date. This study aims to explore the impact of an intensive mindfulness-based retreat on the mental and emotional well-being in a self-selected group of Australian adolescents. It aims to measure the impact of the retreat on the emotional well-being of participating adolescents as well as provide a comprehensive picture of the changes experienced by adolescents following attendance at a retreat.

Methods: A mixed methods, convergent triangulation design was adopted in which quantitative and qualitative data were collected and analysed separately before converging the findings in the discussion. Quantitative data (n = 23, Mage = 17.7 years, 83% female) included questionnaires administered at pre-retreat, immediately post-retreat, and 3-months follow-up to measure self-report levels of mindfulness, self-compassion, mental well-being, perceived stress and rumination. Qualitative data included participant observation at two retreats and semi-structured interviews with seven participants. A thematic analysis was applied to the analysis of interview data.

Results: Quantitative findings indicated pre-post improvements in mindfulness, self-compassion, mental well-being, stress and rumination. Repeated measures ANOVA found statistically significant improvements in all measures at three-months follow-up ($p < 0.05$). Data suggested that within-person changes in mindfulness and self-compassion predicted improvements in perceived stress ($p < 0.05$), and approached significance for predicting reductions in rumination and improvements in mental well-being ($p < 0.1$). Qualitative data suggested that the intensive mindfulness retreat was both acceptable and beneficial to the majority of adolescents attending. The unique environment of the retreat allowed adolescents to feel supported and being there as a group was an important normalising and validating experience. Many of the participants reported challenges in returning to everyday life. Despite this, participants attributed various positive changes experienced after the retreat to their attendance, including increased emotional regulation, greater self-compassion, improved interpersonal relationships, and greater self-confidence. Data indicated that participants internalised the retreat space, and used various methods, such as mindfulness practices learned at retreat, to tap back into this space.

Conclusion: The results of this convergent mixed methods study suggest that intensive mindfulness retreats are an acceptable and effective method of delivering MT to adolescents, although larger trials are needed to confirm these findings. Implications for mindfulness-based approaches to supporting adolescent well-being in other contexts are discussed, as well as future directions for research into MT in adolescents.

Danica Joseph

Inducing antigen-specific tolerance as a novel treatment for experimental autoimmune uveitis

Professor Paul McMenamin - Department of Anatomy and Developmental Biology, Monash University, Australia
Professor John Forrester - Department of Ocular Immunology, Institute of Medical Sciences, University of Aberdeen, UK

I was lucky enough to be given the opportunity to travel to Scotland to conduct my project with the Forrester laboratory at the University of Aberdeen. Whilst there I was able to explore a new skillset and expound upon laboratory skills introduced to me by the McMenamin laboratory over the summer.

Though a lab-based project is often a steep-learning curve, one that can be especially challenging to a student familiar only with clinical medicine, this is dwarfed by the immense professional and personal growth it engenders. The skills and knowledge I have obtained through the course of this project are unlike anything I could have expected, and I look forward to returning to applying these skills to clinical medicine with an enriched, more comprehensive understanding of underlying cellular mechanisms.

I am very grateful for the support provided to me throughout the year by both laboratories, and the valuable friendships forged whilst living abroad. Doing my BMedSc in Scotland was one of the best decisions I have ever made, and I would like to thank my supervisors, Professors Paul McMenamin and John Forrester, without whom this incredible opportunity would not have been possible.

Abstract

Background: Autoimmune uveitis (AIU) is a CD4+ T-cell mediated, sight-threatening disease characterised by intraocular inflammation and responsible for 10-15% of vision loss worldwide. The majority of patients present with idiopathic disease and are subject to a range of systemically-acting immunosuppressive agents as means of treatment. Using mouse models of experimental autoimmune uveitis (EAU), it has been proposed that the disease is due to a breakdown of tolerance to self-antigens, specifically naturally occurring retinal antigens. Other models of autoimmune disease have explored the use of biologic therapies to re-establish tolerance to auto-antigens and thereby ameliorate disease. Dendritic cells have been found to have the property to induce CD4+ and CD8+ antigen-specific tolerance to antigenic peptides endocytosed by the DEC-205 receptor. The use of anti-DEC205/antigen fusion proteins have successfully been applied in mouse models of experimental autoimmune encephalitis (EAE) and autoimmune diabetes to induce tolerance to specific disease-causing antigens. Using a spontaneous model of EAU where mice develop uveitis in response to Hen Egg Lysozyme (HEL, HELxTCR mice), it was purported that delivery of a HEL/anti-DEC205 fusion protein will reduce severity of EAU. The aim of this project was to determine the effects of anti-DEC205/HEL on the severity of EAU by examining retinal wholemounts of HELxTCR mice.

Method: HELxTCR mice were given injections of either PBS (vehicle) or anti-DEC205/HEL fusion protein at postnatal day (P) 18 and P25. Clinical fundus imaging was performed on P26 after which the animals were euthanised and the eyes were enucleated. Eyes were fixed in 2% paraformaldehyde (PFA) and retinal wholemounts were immunostained for endothelial cells, macrophages, microglia and CD4+ T-cells. Wholemounts obtained from non-diseased adult wildtype mice were also used for comparison

Confocal microscopy images were obtained using a Leica SP5 confocal microscope and a x40 oil objective. Z stack images were processed into maximum projections using FIJI.

Results: Clinical fundus imaging and confocal microscopy confirmed that HEL/anti-DEC205 administration resulted in reduced severity of disease (namely reduced vasculitis and the presence of retinal lesions), and a decreased inflammatory response evidenced by fewer infiltrating CD4+ T-cells and Iba-1+ myeloid cells.

Despite preventing the development of severe disease, the administration of anti-DEC205/HEL did not prevent migration/accumulation of amoeboid Iba-1+ microglia into the outer retina (outer nuclear layer and subretinal space).

Conclusions: This is the first study that has examined the effects of anti-DEC205/HEL treatment on modulating the immune response in spontaneous EAU and suggests that DEC205-mediated antigen-specific tolerance may reduce the severity of disease. The presence of mild disease in anti-DEC205/HEL population would indicate EAU is not prevented by anti-DEC205/HEL administration, but rather is suppressed. Outer retinal accumulation of Iba-1+ microglia supports the presence of underlying disease in these mice however suppressive disease mechanisms have not been definitively identified.

It is hoped that these novel findings will prompt further investigation into how HEL/anti-DEC205 works to abate disease in the spontaneous EAU model, and that this along with the identification of human uveitis-causing retinal antigens, may form a novel therapeutic which re-establishes tolerance to causative autoantigens.

Natasha Juchkov

Placental pathology and abnormal birth weight

Dr Hayley Dickinson, Dr Padma Murthi, Dr Miranda Davies-Tuck, The Ritchie Centre, Hudson Institute of Medical Research

I embarked on my BMedSc journey after my fourth year of medicine. Having a long time passion for research and paediatrics, I chose my research in the field of neonatal health as it combined my two passions. I found the premise of the study engaging and I wanted to do something clinically oriented. Overall this year has given me real insight into the initial planning to fruition and completion of a research project. Having dealt with delays in ethics approval, learning new placenta specific medical jargon and somewhat understanding statistics, my research year was definitely filled with uncertainty, challenges and growth. All of which would not have been possible without the guidance and support of my colleagues and supervisors. If you are considering a BMedSc, be prepared for times of confusion but also times of triumph. Most of all, embrace the experience and take everything in your stride, as like me, you will come out having gained a whole new set of skills and memories.

Abstract

Background: Abnormal birth weight has been associated with increased risk of neonatal mortality, and complications both in the short-term and later in life. Although advancements have been made in reduction of neonatal morbidity and mortality over the last century, in Australia, the incidence of abnormal birth weight has remained steady for the past decade. Many maternal risk factors have been associated with abnormal birth weight, of which some can monitored throughout pregnancy. However, little is known about the role of placental function or rather malfunction and birth weight, particularly in an Australian population. The aim of this study is to determine what placental pathologies are present in small for gestational age (SGA) and large for gestational age (LGA) placentas, and whether these findings are associated with adverse neonatal outcomes in a Melbourne population.

Method: This retrospective cohort study began with 8525 patient records for women who had birthed at Monash Health throughout 2016. 1378 cases were suitable, comprising of 813 SGA births, 467 LGA births and 98 were preterm appropriate for gestational age (AGA) births, as the control. Demographic, pregnancy and placental pathology data were extracted from two Monash Health electronic databases. Comparison of characteristics between the three cohorts was completed using one-way ANOVA and Kruskal-Wallis test for continuous variables, and chi-square tests for categorical variables. Linear and logistic regression were also completed for relationships between placental pathology and neonatal outcomes.

Results: Of the 1378 participant records extracted, all had demographic and pregnancy data available, but only 672 placental pathology reports were completed candidates (53.1% of all SGA births, 38.5% of LGA births and 61.2% of preterm AGA).

Regarding pregnancy data, more SGA babies were born to South Asian mothers (38%) while more LGA babies were born to Australian/New Zealand mothers (55.0%). Significantly more SGA babies were born to nulliparous mothers (54.4%). The mean birthweight across the groups was 2664.7g for SGA and 4320.1 for LGA, with the babies size (birth length and head circumference) being proportional to their weight. Significantly more LGA babies needed resuscitation.

Regarding placental pathology findings, placental weight, placental size and umbilical cord size were all significantly different across the three groups with SGA placentas and cords being the smallest and vice versa for LGA. Malperfusion features including: features of maternal vascular under-perfusion and uteroplacental insufficiency were most common in the SGA cohort while no findings were significantly more common in the LGA cohort. Relationships between placental pathology findings and neonatal outcomes were statistically significant for chorioamnionitis on SCN or NICU admission in the SGA cohort. In the LGA cohort, intervillous thrombi on resuscitation and SCN or NICU admission, and abnormal cord coiling on SCN or NICU admission showed significant results.

Conclusions: In conclusion, we were able compare demographic and pregnancy features of SGA and LGA births, and for the first time, were able demonstrate differences in placental pathology findings between SGA and LGA cohort. Future research is needed to affirm our results with a need for prospective studies to determine causation.

Debora Roselita Karo Sekali

Understanding the mechanisms of failure to progress during labour

Professor Helena C. Parkington, Department of Physiology, School of Biomedical Science, Monash University;Professor Shaun Brennecke & Dr Penny Sheehan, Department of Maternal-Fetal Medicine, Pregnancy Research Centre, Royal Women's Hospital

I am a fourth-year medical student from University of Indonesia completing my honours of medical science in Monash University. I've got passion for pregnancy and childbirth. Throughout the year, I've seen a collaboration between clinicians and researchers who worked together to solve the problem of failure to progress during labour. This is a challenging year at the first because of so many disconnected ideas in a pile of literatures and it seems impossible to do all the experiments in one honours year. Self-discipline is the key. In the end, I am deeply thankful that this research year finally completed and the rewards bountiful.

I am very grateful that I work with a hardworking and down-to-earth supervisor, Prof Helena Parkington. The year proved rewarding in many more ways than I expected. I was asked to give my first talk in an annual meeting of Australian Physiological Society (AuPS) in Adelaide, 2016, with a title "Sustained expression of KV7 channels during labour is associated with a highly negative uterine muscle resting membrane potential and dysfunctional labour in women". The experience hugely impacts my characters, knowledge, and communication skills. This is an opportunity that I would recommend to all.

Abstract

Background: Poor uterine contraction, leading to failure to progress (FTP), is a major indicator for cesarean section (CS). Older, first time and obese mothers are more likely to have prolonged labour. In addition, oxytocin is ineffective to resolve poor contractions in many cases. Uterine contraction is dependent on calcium influx through voltage-gated calcium channels, and hence membrane potential is critical for strong labour progress. Excessive negative RMP has been discovered to suppress action potential and thus no contraction. Our hypothesis is that older (>35 years old) first-time and obese (>30 kg/m2) women are more likely to have poor uterine contraction due to ion channels dysfunction leading to FTP during labour.

Aims: The aim of this study were to investigate the underlying switch mechanisms from the quiescent state during pregnancy to the active-contractile state at labour and to determine the ion channels or signaling mechanism involved, and how they change in FTP during labour.

Methods: Human myometrium was obtained at term (> 37 weeks) during CS and classified into 3 groups; not-in-labour/NIL, in-labour/IL normal progress (CS due to problems other than slow labour progress), and in-labour/IL failure to progress (poor contractions). Myometrium contraction was recorded simultaneously with calcium imaging in uterine strips loaded with Fura-2-AM and membrane potential using sharp microelectrodes. Pharmacological tools were used to identify the role and nature of receptors, ion channels, and signaling systems. Excess tissue was frozen at -80oC for western immunodetection.

Results: Almost all IL were first parity and most of NIL are repeated CS. Resting membrane potential (RMP) in myometrium from NIL was -60.0 + 0.8 mV (n=26) and in IL was -63.6 + 1.5 mV (n=26), p=0.001. RMP increased linearly with maternal age (r2=0.58, p=0.0002), but there was no correlation with maternal BMI (p=0.28). Western blotting showed that expression of Kir7.1 in IL was reduced by half in both normal and FTP labour compared with NIL, and blockade of Kir7.1 with VU-590 was similar in normal and FTP labours. Western blotting also revealed that Kv7.4 protein expression was significantly lower in normal progress IL (30% p=0.001), but it remained high in FTP (p=0.42). When Kv7.4 channels were blocked using XE-991 it triggered larger depolarization in FTP than in NIL (p=0.0004). Sustained expression of Kv7.4 was associated with excessive negative RMP (p=0.0002). Advanced maternal age was also correlated with decreased number of OTR expression in IL FTP women (p=0.013). The depolarization evoked by OT was reduced from 15.3¤2.4mV NIL to 6.70.9mV in FTP labour.

Conclusions: The results of this study provide novel insights in understanding the underlying mechanisms regulating uterine contraction before and during labour. Failure to progress is mainly caused by excessive negative RMP and decreased of OTR levels in older and first parity women. Kv7.4 has a major input into determining RMP. Increased Kv7.4 expression was associated with excessive negative RMP in FTP IL. This study highlights novel therapeutic targets worthy of further study in the fight to improve contractions and efficient labour, and reduce the incidence of FTP.

James Kemper

In vitro fertilisation outcomes associated with preimplantation genetic screening in blastocyst-stage embryos

Dr. Alon Talmor: Adjunct Senior Lecturer, Monash University; Department of Obstetrics & Gynaecology, Monash Health; Monash IVF.
Professor Beverley Vollenhoven: Monash University; Department of Obstetrics & Gynaecology, Monash Health; Monash IVF.

I completed my BMedSc after my 4th year of medicine to gain an insight and understanding into research, and to trial a different experience than that of clinical medicine. I was interested in obstetrics and gynaecology, and after speaking to my supervisors, saw the benefit of doing a project regarding IVF, an area many people are aware of but are not able to explore in depth. I was able to utilise the resources of both Monash IVF and Monash Health to complete my project, and my supervisors allowed me the independence and freedom to conduct the project myself. This maximised my experience, by granting me the flexibility to pursue other extracurricular activities, and to have some time to myself as well. I am very grateful for the support and encouragement my supervisors provided me with. I would encourage other students to consider conducting a research project alongside their medical training, and would be happy to have students contact me to ask questions.

Abstract

Background: Preimplantation genetic screening (PGS) seeks to identify euploid and aneuploid embryos prior to transfer to the mother. This is achieved by conducting embryo biopsy to obtain the genetic material that is then analysed. It is reasoned that by reducing the incidence of implantation failures and miscarriages arising from aneuploid embryos, by transferring only euploid embryos, the in vitro fertilisation (IVF) journey can be shortened for infertile couples. Both biopsy and genetic analysis techniques have undergone significant development over the history of PGS. There remains uncertainty about the latest procedures, namely blastocyst (day five/six) biopsy and next-generation sequencing, and their impact on pregnancy outcomes.

Aims: We aim to demonstrate a clinical difference in pregnancy outcomes in IVF cycles undergoing blastocyst-stage embryo biopsy and preimplantation genetic screening in comparison to patients undergoing standard (non-preimplantation genetic screening) IVF treatment.

Methods: We conducted a retrospective case-control analysis of a private IVF clinic in Melbourne, Australia. Details of patients undergoing PGS utilising blastocyst biopsy and next-generation sequencing from 2015-2016 were extracted and compared to patients receiving standard IVF treatment and a blastocyst transfer. Patients were matched using propensity score index, based on maternal age, body mass index, cycle number, total FSH dose, number of eggs in stimulation cycle, and gravidity.

Results: Matching eliminated any statistically significant differences between the two groups for all but two of the six matched variables; 491 PGS cases were compared to 522 controls. Three outcomes were analysed: implantation rate, clinical pregnancy rate, and live birth rate. Live birth outcomes were not available for the 2016 cohort, so a decision was made to only examine implantation and clinical pregnancy rates for the whole cohort. Following adjustment for the matched variables, statistically significant superior implantation rates (PGS vs. matched controls: 0.47 vs. 0.41; p=0.031) and clinical pregnancy rates (PGS vs. matched controls: OR=1.37 (95% CI 1.06-1.76); p=0.016) were determined. Analysis of only the 2015 cohort to include live birth rates found no statistically significant difference for all three rates (implantation rate PGS vs. matched controls: 0.48 vs. 0.44; p=0.07; clinical pregnancy rate PGS vs matched controls: OR=1.34 (95% CI 0.90-2.00; p=0.15); live birth rate PGS vs. matched controls: OR=1.11 (95% CI 0.73-1.69; p=0.62)).

Conclusion: This study provides evidence for the use of PGS, illustrating statistically significant superior implantation and clinical pregnancy rates. These results are in line with both expectations and other previous studies. Whilst the 2015 cohort results illustrate no statistical difference in outcomes, readers should focus on the whole cohort results, given the small sample size, learning curve, and potential for a difference in patients' prognoses amongst the 2015 cohort. This study provides an Australian perspective on the evidence for the use of PGS, and should facilitate confidence amongst clinicians and patients that PGS produces superior pregnancy outcomes.

Susanne Kitching

Rural Ice-olation: a sub-study of VMAX: Understanding Methamphetamine Use in Victoria

Professor Paul Dietze – Burnet Institute, Dr Alisa Pedrana – Burnet Institute, Dr Brendan Quinn – Burnet Institute

With an interest in public health and addiction medicine, I was fortunate to complete my BMedSc at the Burnet Institute after finishing year 4C in 2016. I worked on the VMAX project, interviewing more than 75 participants and analysing data from one of the largest cohorts of methamphetamine users in Australia, spanning both metropolitan and rural Victoria. The Burnet provided a welcoming and supportive environment to engage in public health research, challenge my critical thinking, and development many valuable skills that I am confident I will use in the future. I had a great time working with the team, and was involved in several other projects in addition to the VMAX study. I would highly recommend doing a project at the Burnet Institute to any future students interested in public health, and thank my supervisors and the fieldwork team for their support over the year.

Abstract

Background: Recently, methamphetamine use in Victoria has received extensive media coverage, and been the focus of several government reports and inquiries. These reports suggest that there have been increases in methamphetamine-related harms across the state, including in rural areas. However, much of the available data about methamphetamine use comes from metropolitan Melbourne, whereas little is known about methamphetamine use, especially via non-injecting methods, in rural locations. Further research is warranted to better understand the differences in patterns of methamphetamine use and methamphetamine-related harms across these regions.

This study aimed to describe the population of predominantly non-injecting methamphetamine users in Victoria, including patterns of methamphetamine use and experiences of harms, and compare these between metropolitan and rural sites.

Compared with methamphetamine use in metropolitan regions, those in rural areas were expected to have different patterns of methamphetamine use and increased experiences of harm.

Method: This cross-sectional observational study used a subset of the VMAX longitudinal cohort study. It involved 531 participants from four main regions: Melbourne, Loddon-Mallee, Gippsland, and Hume. Recruitment took place via respondent-driven sampling, social media advertising, and flyers located in places where methamphetamine users were suspected to frequent including supermarkets, educational facilities and healthcare services. Eligibility criteria included being aged 18 years and over, having self-reported methamphetamine use at least monthly in the last six months through primarily non-injecting methods. A face-to-face structured questionnaire was administered, covering domains including socio-demographics, use patterns, service access and experience of harms. Statistical analysis was conducted using Stata 14, with a significance at $p<0.05$. Descriptive, bivariable and multivariable logistic regression analyses were used to examine participant characteristics and differences in key outcomes between metropolitan and rural populations.

Results: The majority of respondents from both rural and metropolitan locations used crystal methamphetamine by non-injecting methods at least four times per week. There were variations in patterns of use and experiences of harm across all rural regions when compared with Melbourne after adjustment. Participants from the Loddon-Mallee reported a significantly lower frequency of use (adjusted odds ratio (AOR) 0.582, 95% confidence interval 0.376-0.902), along with higher likelihood of dependence (AOR 1.813, 1.063-3.093), while no significant differences were found for these outcomes in the other two sites compared with Melbourne. Participants from Hume were less likely to report methamphetamine-related ambulance attendances (AOR 0.115, 0.076-0.814), with a similar finding in Loddon-Mallee (AOR 0.301, 0.129-0.702). Participants from Hume were also less likely to report psychological harms such as anxiety (AOR 0.286, 0.155-0.526) and depression (AOR 0.162, 0.088-0.299). The only consistent patterns of harm across all three rural regions compared with Melbourne were significantly increased experiences of legal problems or arrest in the past year (AOR 2.410-3.783, 1.166-7.332), and decreased likelihood of experiencing methamphetamine-related work or study problems (AOR 0.305-0.506, 0.141-0.986).

Conclusions: This preliminary investigation identified significant variations across patterns of use and experiences of harms among people using methamphetamine in rural locations compared with Melbourne. Understanding these findings can help inform public health policy and programs required to reduce methamphetamine-related harms throughout Victoria.

Joshua Kontrobarsky

Exploring antisaccades in schizophrenia: a dopaminergic candidate gene study

Dr. Caroline Gurvich, Prof. Susan Rossell, Ms. Elizabeth Thomas (PhD), Dr. Kiymet Bozaoglu
Monash Alfred Psychiatry Research Centre (MAPrc), The Alfred Hospital

I completed my Bachelor of Medical Science (Honours) after 4th year. I have always had a keen interest in psychiatry and was excited to work on a project looking at schizophrenia at the Monash Alfred Psychiatry Research Centre (MAPrc). My project involved recording and analysing eye movements in schizophrenia patients and healthy controls, something I had never done before! I really enjoyed my year and would highly encourage future students to consider doing their project at the MAPrc.

Abstract

Background: Cognitive impairment is a cardinal feature of schizophrenia, with significant functional outcomes for patients. Improved pathophysiological models of these impairments are necessary, as current antipsychotic treatments do not alleviate cognitive symptoms. The dopaminergic system is highly implicated in the schizophrenia disease process. Two dopaminergic genes of interest are COMT and DRD2, which encode for a dopamine-degrading enzyme in the prefrontal cortex (PFC) and D2 receptors, respectively. Single nucleotide polymorphisms (SNPs) of the COMT gene (rs4680, rs737865 and rs165599) and the DRD2 gene (rs6277 and rs6275) have been identified as potential mediators of cognition. Antisaccades are a well-established trait marker of illness in schizophrenia and are a robust cognitive endophenotype. Based on the existing literature there existed scope to explore the influence of dopaminergic allele variation on antisaccade performance in schizophrenia patients and healthy controls. The primary aim of this project was to explore the influence of allelic variation of COMT and DRD2 SNPs on antisaccade error rate. A secondary aim was to compare the performance of patients and controls in order to evaluate the utility of antisaccade error rate as a reliable cognitive endophenotype.

Method: Thirty-three patients (22 with schizophrenia and 11 with schizoaffective disorder) and 115 healthy controls underwent antisaccade eye movement assessment. Genotyping was performed for COMT (rs4680, rs737865 and rs165599) and DRD2 (rs6277 and rs6275) SNPs. One-way ANOVAs were performed using age as a covariate to evaluate the impact of genotype on antisaccade error rate.

Results: Patients demonstrated a significantly higher error rate compared with controls ($P < 0.001$). The GG allele of the rs4680 SNP was significantly associated with a lower error rate in patients only ($P = 0.002$). There was no observed effect of genotype in healthy controls. Despite a relatively small sample size, the rs4680 had a significant impact on antisaccade performance in schizophrenia and schizoaffective disorder patients.

Conclusions: This project reiterated previous understandings about the significant influence that COMT has on cognition due to modulatory effects of dopamine in the PFC. Furthermore, the reliability of antisaccades as a trait marker for schizophrenia was reinforced lending support to its use in future studies.

Katherine Kuek

Non-alcoholic fatty liver disease in a centrally obese psoriasis cohort.

Main supervisor: Dr Alexander Hodge, Centre for Inflammatory Diseases, School of Clinical Sciences, Monash University, Department of Gastroenterology, Monash Health

Co-supervisor: Dr Adrian Mar, Department of Dermatology, Monash Health

I completed my fourth year in 2016, and it was half-way through that year that I had an epiphany! I had never even remotely planned to take a year off to do research, but listening to previous BMedSc(Hons) students inspired me to take the plunge!

I have had an absolutely amazing year, and have gained valuable insight into what it takes to conduct both a clinical and laboratory project. These skills will be useful moving forward into future research opportunities. I would highly recommend the BMedSc(Hons) year to anyone interested, and am happy to be contacted via email, kkkue1@student.monash.edu.

Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) is the accumulation of fat (steatosis) in liver cells (hepatocytes). Psoriasis is a chronic, autoimmune inflammatory dermatitis which results in scaly plaques on the skin, Current literature supports a strong association between psoriasis and non-alcoholic fatty liver disease (NAFLD), with the prevalence of NAFLD in psoriasis cohorts being significantly higher than that of their control counterparts. Though the exact aetiology is still unclear, the literature suggests that the relationship involves the metabolic syndrome and its separate components, most notably obesity. It is suggested that increased visceral adiposity (central obesity) potentiates insulin resistance and causes a dysregulation in pro-inflammatory cytokines. Despite the significance of central obesity, no studies have investigated the burden of NAFLD in a centrally obese psoriasis cohort. Thus, this observational study aims to determine the prevalence of NAFLD in a centrally obese psoriasis cohort, and assess the association between pro-inflammatory cytokines and severity of psoriasis and liver disease.

Method: Adults with psoriasis and central obesity (increased waist circumference) were recruited from an outpatient dermatology clinic in a tertiary hospital. Those with excessive alcohol consumption or other liver pathology were excluded. Participants were arranged to have a FibroScanα of the liver and blood tests. Serum was then used to quantify cytokine levels using enzyme-linked immunosorbent assays (ELISA). Statistical analysis was performed using Mann-Whitney U tests for continuous variables and Fisher's exact tests for categorical variables.

Results: A total of 48 participants were seen for FibroScanα and blood tests. 87.5% of participants had NAFLD and 56.3% had the metabolic syndrome. Liver stiffness due to hepatic steatosis (measured by FibroScanα) was higher in the obese (BMI≥30) than the non-obese (6.55 kPa vs 4.85 kPa, p= 0.0018), as was steatosis (319 dB/m vs 255 dB/m, p= 0.0009). Those with high grade liver stiffness tended to be more insulin resistant (p= 0.0248), as did those with high grade steatosis (p= 0.0019). Additionally, high grade steatosis was found to be associated with higher alanine aminotransferase (ALT) (p= 0.0083), and having the metabolic syndrome was associated with high grade steatosis (p= 0.0215). No association was found between pro-inflammatory cytokine levels and disease severity of the skin nor liver.

Conclusions: The results of this pilot study support the strong association between psoriasis and NAFLD documented in the literature. The results also suggest that central obesity has a large influence, as our centrally obese cohort's NAFLD prevalence of 87.5% is much higher than in other studies which have only investigated the general psoriasis population. This study also suggests a link with the metabolic syndrome and its components, notably insulin resistance and obesity. These findings have potentially significant clinical implications, and so further studies of NAFLD in centrally obese psoriasis patients are warranted.

Shimona Lai

The Effect Of Embryo Quality In Single- And Double-Embryo Transfer On Clinical Outcomes In IVF

Dr Tiki Osianlis[1], Professor Beverley Vollenhoven[1,2,3] and Associate Professor Martin Healey[3,4,5]

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After completing my fourth year of MBBS, I undertook a BMedSc(Hons) to experience the opportunities within medical research. I sought to explore my interest in reproductive medicine with a translational research project that would have clinical implications. With the guidance and support of my wonderful supervisors, I found an ideal project that allowed me to gain valuable insight into the in-vitro fertilisation process as well as a greater appreciation of evidence-based medicine. This year has been incredibly rewarding, and I'm grateful for all the opportunities it has afforded me – from presenting my research at an international conference, to having a regular sleep cycle. My experience from this year has made me a more confident and resilient individual, and has inspired me to continue seeking opportunities in research. I would highly recommend a BMedSc(Hons) to any prospective students looking for a change of pace or with an interest in research.

Abstract

Background: The transfer of multiple embryos during in vitro fertilisation (IVF) was originally utilised to maximise rates of implantation and pregnancy; however, its use has subsequently led to an unacceptably high risk of multiple pregnancy and its associated complications. This has resulted in current recommendations that suggest only a single embryo be transferred per cycle.2, 3 Despite the industry shift towards single-embryo transfer (SET)4, double-embryo transfer (DET) still remains a popular option for those who maintain it has clinical benefits – with a variety of factors influencing the decision to concurrently transfer a second embryo.5 One factor that has yet to be appropriately considered is the quality of embryos implanted together, and the impact that these interacting embryos have on one another in terms of influencing clinical outcomes.

Aim: Our primary aim was to compare clinical outcomes following SET and DET, and to understand the effect that embryo quality and embryonic interactions have on this comparison.

Method: Our study was a retrospective cohort analysis, using data extracted from a standardised database of a private multi-site IVF clinic, based in Australia. All blastocysts at day 5 involved in SETs and DETs between 2005 and 2015 were eligible for inclusion. Quality assessment was performed using an in-house clinic morphological grading system, with embryos assigned a grade from A: very good quality to D: very poor quality. The main comparisons in our study were between SETs of an A-grade embryo, and DET combinations with at least one A-grade embryo. The outcomes investigated in our study were: implantation rate, clinical pregnancy, clinical pregnancy loss, live birth, and multiple pregnancy.

Results: Over the study period there were 4,275 SETs involving Grade A blastocysts, and 881 DETs involving at least one Grade A blastocyst. Following our multivariate analysis, the transfer of a single Grade A embryo was found to significantly reduce multiple pregnancy rates whilst significantly increasing the implantation rate against all DET pairings. Additionally, there were no significant deviations on multivariate analysis in the clinical pregnancy, clinical pregnancy loss, or live birth rates when comparing DETs to SET.

Conclusions: Our study found that a cycle has better outcomes when a high-quality embryo is transferred alone, rather than with another embryo of any other quality. The results demonstrated that there is no clinical advantage in DET as there is no improvement in the clinical pregnancy or live birth rates over a single transfer, and instead DET lowers the implantation rate whilst increasing the multiple pregnancy rate. This contradicts the historical precedence that transferring multiple embryos may compensate for low clinical success rates, and instead suggest this has a negative interaction. As SETs have shown superior clinical outcomes over DETs, these should be viewed as the gold standard.

Callie Lambert

The effect of sustained inflation on the hypoplastic lung at birth

Professor Stuart Hooper PhD, Head of the Ritchie Centre, Hudson Institute for Medical Research, Department of Obstetrics and Gynaecology, Monash University

Dr Erin McGillick PhD, Postdoctoral Fellow at The Ritchie Centre, Hudson Institute of Medical Research Department of Obstetrics and Gynaecology, Monash University

I chose to complete a BMedSc after 4th year as I wanted to dip my toes into the world of research before embarking on a career in medicine. I had a great time learning about the world of science and understanding how scientific research may be translated into clinical medicine.

Delving into an animal research project has allowed me to see the full process of experimental research from conception to thesis submission. I don't think the important lessons I learnt this year, ranging from highly technical skills to developing a higher level of independence and resilience, would have occurred if I hadn't chosen such a challenging project.

A BMedSc is a unique opportunity to try out research whilst still a medical student. Nothing develops your critical thinking skills like starting a project with no answers and following the experimental process to figure it out. I'm more than happy to answer any questions or generally discuss the BMedSc year at calista.j.lambert@gmail.com.

Abstract

Background: Fetuses with lung hypoplasia (LH) have difficulty transitioning to neonatal life due to their underlying abnormal physiology, often requiring resuscitation, intubation and mechanical ventilation at birth. While these interventions improve survival, they are independently associated with increased morbidity and mortality making it essential to optimise these strategies to ensure the smoothest transition possible (1-3). Current guidelines for LH do not exist with the closest being guidelines for congenital diaphragmatic hernia (CDH), a severe form of LH (4). However, the gentle ventilation strategy recommended by these guidelines is based on expert opinion rather than evidence, leading to a need for research regarding the optimum ventilation strategy at birth for neonates with LH. One ventilation strategy, sustained inflation (SI), has been proposed as an alternative to the conventional ventilation (CV) strategy in premature neonates and those with birth asphyxia. However, the use of SI in LH has not been investigated and there is little agreement in the literature about the ideal method, benefits and risks of using SI.

Aims: The aims of this thesis were:

(1) investigate the use of sustained inflation (SI) in the literature and identify parameters for its use and

(2) determine whether use of sustained inflation (SI) in a pre-clinical lamb model of LH improves the transition to newborn life compared to conventional ventilation (CV).

Methods, Results and Conclusions (1): A systematic search of the literature was conducted, with relevant study characteristics tabulated for all eligible human and animal studies. Based on current evidence, it appears that SI is most effective when a pressure-based strategy based on gestational age, is used for at least 20 seconds. Human and animal studies both showed benefits, with human studies suggesting that SI is safe and beneficial in reducing intubation and mechanical ventilation and animal studies suggesting that SI supports the cardiorespiratory transition without increasing lung injury.

Methods, Results and Conclusions (2): A tracheal catheter was surgically inserted in fetal lambs at 110 days' gestation to facilitate airway liquid (AL) drainage and induce LH. AL was continuously drained until lambs were delivered at approximately 135 days' gestation. Lambs were instrumented prior to delivery to allow continuous recordings of physiological parameters. 6 lambs received SI at 35cmH2O for 30 seconds followed by CV in data collected last year, and 4 lambs received only CV this year. Both groups were ventilated for a total of 3 hours. After the experiment, lambs were euthanised and their lungs collected for lung weight analysis. CV lambs had significantly more compliant lungs and required less inspired oxygen to maintain oxygen levels in the blood than SI lambs. However, it appeared that these changes are attributable to differences in the severity of LH between groups, rather than the different ventilation strategies used. This study was not able to determine whether there was a difference between SI and CV on the physiology of LH, as the results were confounded by differences in the severity of LH between groups.

Ned Latham

Understanding the acceptability of community-based, rapid point-of-care hepatitis C testing in people who inject drugs

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I decided to undertake a BMedSc (Hons) at the end of my fourth year of medicine. Completing a project at the Burnet Institute was an immersive experience that provided invaluable mentorship opportunities and allowed me to develop public health research skills. I was particularly drawn to the Burnet Institute for its focus on improving the health of vulnerable populations that often experience significant stigma when accessing healthcare. I was specifically attracted to this project as I found the idea of exploring a novel approach to addressing a public health problem to be especially exciting.

This year provided an inspiring insight into the possibilities of a medical degree beyond full-time clinical practice. In addition, the year also provided the flexibility and time to explore interests outside of medicine. I am more than happy to be contacted by prospective students, including those interested in public health research, qualitative research, or studying at the Burnet Institute – ned.latham@gmail.com

Abstract

Background: Recent advances in treatment mean that it is possible to eliminate hepatitis C as a public health threat in Australia by 2030. Hepatitis C is primarily transmitted amongst people who inject drugs (PWID). As such, elimination will only be achieved if the number of PWID engaged in testing and treatment is significantly increased. Known barriers to accessing healthcare for PWID include the burden of returning for appointments, and experiencing stigma in the healthcare setting. Rapid point-of-care (RPOC) hepatitis C tests can diagnose current infection in 20 to 108 minutes and can be performed in non-clinical settings by non-clinical staff. Our study aimed to understand the acceptability of offering RPOC hepatitis C testing to PWID attending needle syringe programs (NSPs).

Methods: Participants were recruited from an existing study – the Rapid-EC study. The Rapid-EC study offered clients attending two NSPs in inner-Melbourne RPOC testing. Clients were first offered a mouth swab test for hepatitis C antibodies, with the result available in 20 minutes. Those that returned a positive antibody result then had blood taken from a vein for an RPOC RNA test to identify current infection. The results of the RPOC RNA test were available after two hours. A convenience sample of 19 participants that had completed all required testing as part of the Rapid-EC study were recruited for a semi-structured interview A thematic analysis of the interview transcripts was performed using NVivo11. Inductive and deductive codes were first applied to the transcripts. Selective coding was then performed to identify core themes.

Results: Three core themes emerged from the thematic analysis: people and place, method of specimen collection, and rapidity of result return. Participants reported that it was convenient and highly acceptable to be offered testing by non-clinical staff when attending an NSP. For most participants, venepuncture was preferable to mouth swab or finger-stick specimen collection, as it allowed other blood-borne virus tests to be performed on the same specimen. In terms of rapidity, the two hours required for the RPOC RNA test result to be returned was universally unacceptable. None of the interview participants waited onsite to receive the result of this test, and most did not receive the result on the same day.

Conclusions: The acceptability of RPOC testing was shaped to varying degrees by: the place where testing is offered, the people that offer that testing, the way in which the specimen for testing is collected, and finally both how, and how quickly, the results are returned. These factors were not of equal importance to PWID. As such, a test that is simultaneously rapid, non-invasive and point-of-care may not necessarily be most acceptable to people who inject drugs.

Felix Lee

Characterization of The Immune Response Following t-PA Administration in Stroke

Supervisors: Prof Robert Medcalf, Dr Be'eri Niego, Dr Dominik Draxler
Institute: Australian Centre for Blood Diseases (ACBD), Central Clinical School, Monash University

Hi, allow me to introduce myself. My name is Felix from Indonesia and I was taking my honours degree at ACBD (Australian Centre for Blood Diseases) under the supervision of Prof Robert Medcalf. I underwent this program at Monash University when I was at my fourth year of my medical school at University of Indonesia. I chose a project related to stroke and neurotrauma since I have a huge interest in the field of neurovascular and haemostasis. During my awesome honours year, I was fortunate and lucky to have wonderful supervisors (Rob, Be'eri and Dom) who had guided and taught me well. Moreover, all my laboratory colleagues (Heidi, Maria, Saffanah, Anushka, Sonia, Maithili, Fiona, Li Chow and Stevi) were also very amazing and they all really helped and constantly supported me a lot throughout the year. Honestly speaking, I couldn't ask for a better supervisor and lab teammates! Honours year was the best year I had so far in my entire life and I would love to repeat it again.

Abstract

Background: Stroke is an acute clinical condition in which there is a lack of blood supply to the brain. Ischemic stroke, being the most common form (80%), is caused by blood clot formed in the brain's blood vessel. To date, the approved management for ischemic stroke is only through thrombolysis by a drug called tissue-type plasminogen activator (t-PA) with a dose of 0.9 mg/kg. Ischemic stroke is known to lead in immunosuppression through the mechanism of bidirectional communication between the immune and nervous system. Consequently, it could lead to infection, which is further confirmed by Stanley et al. who reported that stroke promotes infection in mice within 24 hours. A recent study also discovered that plasmin can promote immunosuppression by preventing dendritic cells transmigration to draining lymph node and hence stopping T cells activation. Since plasmin is generated by t-PA in blood, it was suggested that t-PA could also lead to immunosuppression especially if the drug is not successful in recanalizing the blood vessel.

Method: In this project, middle cerebral artery occlusion model for 1 hour was used to assess the immune system effects of t-PA administration to stroke-affected mice at 24 hours. Several behavioral tests were conducted to assess the basic mechanistic and neuromuscular function after stroke. Blood, spleen and cervical lymph node sample were obtained. Blood underwent Hemavet Blood profiling, whereas spleen and cervical lymph node were stained and analyzed in flow cytometry to evaluate specific immune cells in these samples at 24 hours after stroke.

Results: It was found that there was a worsening of deficits on all mice at 24 hours after stroke and t-PA administration further significantly reduced the mobility and neuromuscular function. In the blood sample at 24 hours after stroke, there was a decrease of total and differential while blood cell counts as expected. Interestingly, differential leucocyte counts were further lowered by t-PA. Moreover, both pro-inflammatory and immunosuppressive cytokines in blood plasma also were further increased with t-PA administration to stroke-affected mice. In spleen and cervical lymph node, there was a dramatic reduction of overall cellularity of both organs after stroke. Looking at specific key immune markers, there were major modifications of myeloid populations at 24 hours after stroke and t-PA further suppressed some of these specific populations. However, lymphoid population mostly had not responded yet at 24 hours in both spleen and cervical lymph node due to a very early time point for adaptive immune system to react.

Conclusions: In conclusion, given that t-PA is still widely used and it is the main treatment for ischemic stroke to date, it was found that t-PA could lead to worsening of clinical outcomes and immunosuppression if the drug does not play its role well in removing the clot in ischemic stroke.

Tim Lee

Noninvasive prenatal testing in in vitro fertilisation conception

Dr Melody Menezes – Head Genetic Counsellor and Scientific Director, Monash Ultrasound for Women
Dr Daniel Rolnik – Maternal Fetal Medicine Fellow, Monash Health
Associate Professor Fabricio Costa – Medical Director, Monash Ultrasound for Women

Well, I really didn't think I'd ever be writing this. Research never interested me, but two weeks before the BMedSc application deadline I took a leap and found a project! The decision was based on a mix of changing it up from clinical placement, doing something different while I had the opportunity, and putting a foot down in terms of speciality decision. Looking back now, I've learnt the ins and outs of clinical research, made valuable relationships, spent time with family, and have opened up a world that I would have never likely been exposed to if I didn't give it a shot. If you're interested in similar research or want to find out more about my experiences please send me an email!

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Abstract

Background: In-vitro fertilisation (IVF) is responsible for 4.4% of births in Australia. IVF conceptions have higher stakes than spontaneous conceptions, are associated with maternal anxiety and have higher rates of aneuploidy due to increased maternal age. Noninvasive prenatal testing (NIPT) analysing fetal cell-free DNA in maternal blood, has been shown to have very high accuracy and reliability for detection of Down syndrome in the general obstetric population. There remains to be focused and high-powered evidence for the reliability and test characteristics for NIPT in an IVF population. The aim of this study is to compare IVF and spontaneous conception, in regards to fetal fraction, test failure rate and high-risk results of NIPT, and to specifically investigate the effect of IVF modalities on these test characteristics.

Method: This was a single-centre, retrospective observational study of singleton pregnancies who underwent NIPT from 10 weeks gestation. Chi-square test was used to compare the failure rates between the groups of spontaneous and IVF pregnancies, and differences in fetal fraction between the groups were investigated with Student T test after logarithmic transformation. Multivariate linear regression was used to determine significant predictors of log10 fetal fraction amongst maternal and obstetric history, and multiple logistic regression was used to determine significant predictors of failed result. False positive rate was compared for significance using Fisher.

Results: In total, 5,625 singleton pregnancies were included in the analysis. Of these, 992 (17.6%) were IVF conceptions and 4,633 (82.4%) spontaneous conceptions. In IVF conception, median fetal fraction was lower (10.4%, interquartile range (IQR) 4.8-15.0%) compared to spontaneous conception (11.9%, IQR 6.1-17.7%; $p<0.001$). Fetal fraction decreased with IVF conception, earlier gestational age, increased BMI, South and East Asian ethnicity; and for IVF pregnancies, use of donor eggs. In IVF conception, test failure rate after first sampling was higher (5.2%) compared to spontaneous conception (2.2%; $p<0.001$) and failed result following redraw(s) was higher (2.4%) compared to spontaneous conception (0.7%; $p<0.001$). Only increased BMI and IVF conception were predictive of test failure. Positive predictive value (PPV) for T21 was 100% in both groups, but was lower overall, and individually for T18 (50.0% vs. 76.9%), T13 (00.0% vs. 25.0%) and sex chromosome aneuploidy (00.0% vs. 31.8%); but these were non-significant.

Conclusions: IVF pregnancies have significantly lower fetal fraction, higher test failure rate and higher false positive rate using NIPT as compared to spontaneously conceived pregnancies. While there is similar performance for prediction of T21, high-risk results for T18 and T13 are less reliable and should be followed up with detailed ultrasound examination. Cycles using donor eggs were associated with lower fetal fraction. This provides further insight into the effect that IVF modalities has on the placenta and fetal fraction.

Albert Prabowo Limawan

Pre- and Postnatal Inflammation and the Development of Atherosclerosis

Associate Professor Tim Moss (Perinatal Inflammation Research Group, The Ritchie Centre, Hudson Institute of Medical Research)
Professor David Burgner (Murdoch Children's Research Institute)

This year has been one of the best year in my life. It is a privilege for me to do research in The Ritchie Centre, Hudson Institute. I am a 3rd year medical student and I am planning to become a paediatrician for my specialist degree. Thus, I applied for this project which is the closest to paediatrics among other projects offered. Furthermore, cardiovascular disease is the leading cause of death in the world and interestingly, the etiology may develop as soon as conception. I came to Melbourne with no experience in animal studies nor wet lab and by the end of my honours year, I have learned so many skills. Starting from animal work, which includes mice handling, injecting, and organ collection, to lab work, such as macrophage isolation and ELISA. I also learned about performing surgery on mice, which much resembles surgery in human, but small. My writing and presentation skills improved as well. This is all thanks to the people in The Ritchie Centre and Monash University that has been supportive and patient with me. All those hard work and weekend shifts paid off and I am really glad that I did my honours in Monash University.

Abstract

Background: Cardiovascular disease is the leading cause of death, and 80% of these are related to atherosclerosis. Postnatal inflammation increase atherosclerosis development and prenatal inflammation may have a similar effect. However, there are no studies about the combination of both postnatal and prenatal inflammation on atherosclerosis development.

Method: ApoE-/- mice were used in this study. Dams underwent abdominal surgery at E15.5 to administer intra amniotic injections of lipopolysaccharide (LPS) (1 ng/amniotic sac) or saline. Dams were allowed to give birth and pups were weaned at 4 weeks of age. At 8 weeks of age, pups started to receive weekly LPS (50 µg) or saline by intra peritoneal injection for 5 weeks. Pups were culled for tissue collection at 13 weeks of age. Hematoxylin and Eosin staining was performed to observe atherosclerosis lesion stage. Masson's Trichrome staining was performed to observe collagen deposition in the aortic sinus. CD45 immunohistochemistry was performed to identify white blood cells in the aortic sinus. Plasma lipid profile was measured using microplate reader. Slides were scanned and analysed in Fiji. Statistical analyses were performed using analysis of covariance (ANCOVA) in IBM® SPSS®.

Results: Animal work produce four different treatment groups: saline – saline (n = 14), saline – LPS (n = 12), LPS – saline (n = 14), and LPS – LPS (n = 11). Higher stage of atherosclerosis lesion was observed in pups that received LPS with the highest stage (stage V) observed in LPS – LPS group. There was no significant difference in lesion size between saline – saline and saline – LPS group ($p = 0.154$). Lesion size difference was significant between LPS – saline and LPS – LPS group ($p = 0.003$). Collagen deposition difference was significant between saline – saline and saline – LPS group ($p = 0.038$). Data between LPS – saline and LPS – LPS group did not have equal variance (Levene's Test = 0.018) and transformation was not successful (Levene's Test = 0.046). CD45 immunohistochemistry has been performed, but sections have not been analyzed for macrophage count. There was no significant difference in plasma lipid level between treatment groups. There was significant difference in HDL level between male and female ($p < 0.0005$ and $p = 0.001$). There was significant difference in triglyceride level between male and female ($p < 0.0005$ and $p = 0.003$).

Conclusions: Postnatal inflammation in pups without prenatal inflammation accelerates atherosclerosis lesion development and increase collagen deposition, but did not significantly increase lesion size. Postnatal Inflammation in pups that were exposed to prenatal inflammation cause accelerated atherosclerosis lesion development, increased lesion size, but did not increase collagen deposition in the aortic sinus. Plasma lipid profile was not affected by inflammation challenges.

Emily Lin

Interleukin-1 Family Cytokines and Macrophage migration inhibitory factor in Systemic Sclerosis

Dr Tali Lang, Department of Medicine, School of Clinical Sciences
Dr James Harris, Department of Medicine, School of Clinical Sciences
Professor Eric Morand, School of Clinical Sciences, Monash University

I chose to complete my BMedSc(Hons) year after my fourth year of MBBS, and had the incredible privilege of undertaking a research project with the Rheumatology Research Group at Monash Medical Centre. I wanted to experience research, was keen to learn laboratory techniques and had an interest in scleroderma due to my increased exposure through clinical years. Under the able guidance of Dr Tali Lang, Dr James Harris and Professor Eric Morand, and with significant assistance from other members of the research group, I have learnt more than I could have imagined and thoroughly enjoyed this year. I am incredibly grateful for all the opportunities I have received, and highly recommend taking a BMedSc(Hons). If you would like to ask me any questions at all, feel free to email me at: eylin3@student.monash.edu

Abstract

Background: Systemic sclerosis (SSc) is an autoimmune connective tissue disorder characterised by fibrosis of the skin and/or internal organs and vascular abnormalities. Although the pathogenesis of SSc remains unknown, excessive extracellular matrix production, vasculopathy and aberrant immune function have been implicated in the process. Recent findings suggest that innate immune system activation and resultant cytokine dysregulation are important in the induction and maintenance of SSc. The interleukin (IL)-1 family cytokines are key mediators of innate immunity and regulators of the inflammatory response. IL-1α and IL-1β have both been described as pro-inflammatory cytokines with roles in the pathway of fibrosis. Despite their similar actions, IL-1α and IL-1β have little sequence homology and are released via different pathways. However, it has been demonstrated that IL-1β and IL-18 are processed via the same pathway requiring NLRP3 inflammasome activated caspase-1, though current literature regarding the role of IL-18 is conflicting. Macrophage migration inhibitory factor (MIF) is a pro-inflammatory cytokine with emerging evidence on its role in mediating IL-1β secretion via the NLRP3 inflammasome. Thus, the role of MIF, IL-1α, IL-1β and IL-18 in SSc is of significant interest.

Aims: This study investigates the relationship between serum levels of MIF, IL-1α, IL-1β and IL-18, and whether associations with clinical features of SSc exist, thereby reviewing the possible role of these cytokines in the pathogenesis of SSc and their potential for clinical application.

Method: Serum samples were obtained from 115 SSc patients and 52 healthy controls. Levels of serum MIF, IL-1α, IL-1β and IL-18 were quantified using specific enzyme-linked immunoassay kits. Clinical and laboratory data corresponding to the time of serum sampling were extracted from the ASIG database. Statistical analysis was carried out with chi squared test and Mann-Whitney U test in Graphpad Prism v7.0b.

Results: Median serum levels of MIF and IL-18 were significantly higher in SSc patients than in healthy controls, but no difference was observed in any of the serum cytokine levels between diffuse (dcSSc) and limited (lcSSc) subgroups. A weak positive correlation was present between IL- 18 and EUSTAR Activity score which increased in magnitude when analysis was restricted to the lcSSc subgroup. Some significant associations with clinical phenotypes were also observed. Lower serum MIF was seen in lcSSc patients with pulmonary arterial hypertension, and dcSSc patients with a history of synovitis. Higher serum IL-1α levels were seen with anti- topoisomerase I positivity, joint contractures and dcSSc patients with digital pulp atrophy. Serum IL-1β was elevated in dcSSc patients with interstitial lung disease, and serum IL-18 was lower in patients with pulp atrophy and sclerodactyly. Positive correlations were found between MIF and both IL-1α and IL-1β whilst no significant correlation was seen between MIF and IL-18. Negative correlations were observed between IL-18 and both IL-1α and IL-1β.

Conclusions: These results suggest that MIF, IL-1α, IL-1β and IL-18 may each play a distinct role in the pathogenesis of SSc, with evidence of phenotypic-specific relationships. In particular, the roles of MIF and IL-18 in SSc justify extensive further research.

Yizhen Liu

The Pharmacokinetics of Sulforaphane: towards a novel therapy for pre-eclampsia

Euan Wallace and Kirsten Palmer
Department of Obstetrics and Gynaecology Monash Health

I started BMedSci after finishing fourth year. I've done some summer research projects previously so I knew I wanted to be involved in research in some way, and having found Women's health the most enjoyable rotation, the decision to do a project in this area was an easy one. Whilst a large portion of this year has been spent on troubleshooting, it gave me great appreciation for the importance of scientific methodology and the logistical difficulties faced by research. I've gained a multitude of knowledge in laboratory techniques, ethics application process and how to co-ordinate a clinical trial. My advice for future students is to organise the administrative aspect of the project such as ethics early so you can hit the ground running and use the literature review to get a good grasp of your project. Also important is to enjoy the year, even though it's a demanding year, there is more capacity to be involved in extracurricular activities. I was lucky enough to be a part of Monash debating and do a bit of traveling in the holidays, which has been great additions to the year.

Abstract

Background: Pre-eclampsia is a pregnancy complication characterised by new onset hypertension after 20 weeks with evidence of end organ damage. It complicates around 1 in 20 births in Australia and poses significant burden of disease. Currently, management focuses on blood pressure control but does not prevent disease progression. Continued effort in understanding disease pathophysiology has enabled identification of therapeutic opportunities and emergence of novel therapies. Sulforaphane, a naturally occurring isothiocyanate, is one such therapy. Its ability to induce Nrf2 activation and subsequent endogenous antioxidant upregulation may be beneficial in mitigating oxidative stress, inflammation and anti-angiogenic factors released in pre-eclampsia.

Sulforaphane are found in cruciferous vegetables with broccoli sprout being a rich source. Broccoli sprout extracts may be a safe and efficacious method of supplementation. We aim to investigate the pharmacokinetic profile of a commercially available broccoli sprout extracts to evaluate if it is a valid method of sulforaphane delivery for the treatment and/or prevention of pre-eclampsia.

Method: Pertaining to this aim, I conducted an open label, exploratory studies involving 6 healthy participants who were administered a single dose of broccoli sprout extract (100 µmol sulforaphane) followed by blood sampling at 8 time-points. Post sampling, serum was extracted from whole blood and protein was removed through incubation with polyethylene glycol. Protein depleted samples were then reacted with 1,2-benzenedithiol to merge all metabolic products of sulforaphane into a single compound 1,3 benzodithiole-2-thione. This is followed by analysis with High pressure liquid chromatography (HPLC) to quantify serum concentrations.

Results: All 6 participants completed the study. Serum samples were processed and analysed with HPLC. However, results appeared physiologically implausible and repeat analysis of the same samples yielded differing results which suggested methodological problems. Therefore, I was unable to complete a pharmacokinetic profile for the sulforaphane extract, as planned. However, I undertook detailed troubleshooting experiments to identify the source(s) of the methodological error with a view to improving methodology for future experiments. The results from the troubleshooting experiments were: (1) different protein extraction methods gave similar pharmacokinetic profiles, excluding this step as source of inconsistency. (2) Repeats of chemical reaction on the same sample aliquot found vastly different results both in profiles and concentrations, implicating the chemical reaction and HPLC. (3) Repeat of HPLC on the same reacted samples gave identical results excluding column error. (4) Some reproducibility of results was found when consistency between reaction conditions was maintained. However, interpretation of results was limited as chemical reactions performed were found to be inefficient in validation experiments. To date, the cyclocondensation reaction remains the greatest source of variation, however ways of optimising this step has also been identified.

Conclusions: Differences in sample reaction step were identified as the source of the apparent PK differences. While PK data were unable to be derived I did identify opportunities for optimisation of quantification process, to achieve consistent and validated pharmacokinetic data in the future.

Sarah Luu

Improving Splenectomy Care

A/Prof. Ian Woolley, A/Prof. Robert Andrews, Dr Zane Kaplan, Dr Claire Dendle Monash Infectious Diseases, Clayton
Australian Centre for Blood Diseases, Prahran • Monash University, Clayton

I chose to do my BMedSc(Hons) after completing fourth year of MBBS. I wanted to explore my interests in Infectious Diseases, and was drawn by my own curiosity towards this project in splenectomy. Throughout this year, I have had the privilege to explore the both clinical and laboratory research at Monash Medical Centre and the Australian Centre of Blood Diseases at the Alfred, and have expanded my skills and knowledge in both ID and haematology. I have enjoyed working with my supervisory team, my project, and overall my whole year. I would recommend it for anyone with an inkling of interest in research!

Feel free to reach out to me on Facebook or via email sarahluu01@gmail.com if you have any questions about undertaking a BMedSc(Hons) – more than happy to help you make a decision and choose the right project and team!

Abstract

Background: Splenectomy or surgical removal of the spleen is indicated for trauma, haematological conditions, malignancy or iatrogenic damage. In splenectomised individuals, there is a well-established increased risk of overwhelming infection and an increased risk of thromboembolism. Infection risk is reduced through education, immunisations and chemoprophylaxis. Adherence to recommendations is supported through the use of a registry. Residual splenic tissue can be seen in patients splenectomised for trauma and is suggested to protect against infections in the setting of splenectomy. The risk of thromboembolism in this cohort is poorly understood, and there are no current recommendations for prophylaxis. One of many suggested mechanisms is that platelets from splenectomised individuals are more adherent. We assessed a potential role for platelets by analysing surface expression of key platelet-specific receptors.

Materials and Methods: Splenectomised patients (n=50) over 18 years of age, registered to the Australian Spleen Registry, who had their splenectomy at least 1 year prior, were recruited. Adherence (n=49) was assessed using current Australian guidelines,(1) and education using the Hegarty et al. questionnaire.(2) Patients (n=47) were screened for residual splenic function by visualising Howell-Jolly bodies and performing an IgM memory B cell panel, and 99m-Tc-labelled heat-denatured erythrocyte scan was performed to confirm functional splenic tissue (FST). Patients were categorised into degrees of FST. Platelets were assessed using whole blood from healthy controls (n=15) or splenectomy (n=30) centrifuged to obtain platelet-rich-plasma, and stained with phycoerythrin(PE)-labelled antibodies against GPIbα (PE-AK2), GPVI (PE-1G5), αIIb (PE-CD41a), CD9 (PE-CD9), and P-selectin (PE-CD62P) using standardized protocols, and analysed using a FACSCalibur.

Results: We observed high adherence rates to use older vaccines, but lower rates in vaccines introduced after 2010. One-third of patients did not have a valid supply of emergency antibiotics. Patients had good quality of knowledge. 7 trauma patients had FST. Only 5 patients were categorised as having probable FST. 1 patient had no FST despite normal initial screening tests. Platelet analysis suggested that compared to controls, platelets from splenectomy cases showed significantly decreased surface expression of GPIbα ($p<0.0001$) and GPVI ($p=0.0035$), but no significant difference in relative surface expression of αIIbβ3 ($p=0.2088$) as well as CD9 ($p=0.1117$). Further, consistent with increased platelet activation/secretion, expression of surface P-selectin was more variable and significantly elevated in splenectomy ($p<0.0001$).

Discussion: Our adherence rates suggest the need for better access and availability of vaccines, and education to health professionals. Despite seeing high rates of residual FST, the degree of protection offered remains unknown. It became apparent that splenic function was continuous and domains of functions (erythrocyte, immune and platelet function) work independently. Platelet results support a role for hyper-activated platelets post-splenectomy and identify platelet-specific markers related to these changes.

Conclusion: We described potential avenues to improve adherence rates and showed an abnormal platelet phenotype post-splenectomy. We established that we lack a thorough understanding of the basic nature of the spleen and pathophysiology post-splenectomy, and suggest an alternative perspective of splenic function. Results here enable further investigation of the spleen, the platelet role and potential therapeutic targets to improve management and outcomes.

Patrick Maclean

Rapid identification of bloodstream infection in sepsis: the potential of infrared spectroscopy

Professor Anton Peleg, Department of Infectious Diseases and Microbiology, Alfred Health
Dr Christina Chang, Department of Infectious Diseases and Microbiology, Alfred Health
Dr Philip Heraud, Centre for Biospectroscopy, School of Chemistry, Monash University

I completed my project evaluating infrared spectroscopy in infectious diseases diagnostics after my 3rd year of medicine. This area interested me scientifically because it is challenging, multidisciplinary and has the potential to improve the lives of many people around the world. My project was based in the Department of Infectious Diseases and Microbiology at the Alfred, and also collaborated with world experts at the Centre for Biospectroscopy at Monash University. During my time I encountered some challenges around the introduction of a novel technique, but found the skills I picked up in research, analysis and collaboration across disciplines to be invaluable. I am very grateful to my supervisors and would recommend the Alfred to anyone interested in a project in infectious diseases and microbiology - please feel free to get in contact if that describes you!

Abstract

Background: Sepsis arising from bloodstream infection is a major cause of morbidity and mortality, and there is an unmet need for new tools for rapid diagnosis. Infrared spectroscopy is an emerging tool for the rapid detection of bloodstream infection, potentially direct from infected blood. We aimed to test the ability of infrared spectroscopy to detect and identify organisms, analysing samples from pure colonies and from liquid suspensions.

Method: We acquired spectra from 21 bacterial strains drawn from 13 species. Multivariate chemometric techniques were used to determine the degree of spectral difference across species and Gram stain categories. We then used a linear model to predict the lower limit of detection in 6 species suspended in water at various concentrations. Finally, multivariate chemometric techniques were used to determine the degree of spectral difference between 6 species at each concentration level.

Results: We found that infrared spectroscopy could classify organisms grown in pure colony by Gram stain category, but classification by species was not consistently observed. The presence of bacteria and fungi was detected in water at a mean organism density of 2.7 x 107 and 2.0 x 106 colony forming units per milliliter respectively. Differentiation of organisms by Gram stain category was possible at higher concentrations (greater than 108 colony forming units per milliliter) for bacteria but was unreliable below this level.

Conclusions: This work demonstrates that infrared spectroscopy is a promising candidate for the direct detection of infectious organisms at high concentration. However, the exceedingly low organism concentration encountered in clinical bloodstream infection presents a major challenge. Further instrumental and analytical optimisation is needed for detection standards to reach the clinical range.

Andrew Martin

Prediction of cardiac surgery associated acute kidney injury: urinary oxygen tension versus plasma and urinary biomarkers

Professor Julian A. Smith[1,2], Associate Professor Andrew D. Cochrane[1,2], Associate Professor Roger G. Evans[3]

[1]Department of Cardiothoracic Surgery, Monash Medical Centre
[2]Department of Surgery, School of Clinical Sciences at Monash Health, Monash University
[3]Cardiovascular Disease Program, Biomedicine Discovery Institute and Department of Physiology, Monash University

I completed my BMedSc(Hons) project in the Department of Cardiothoracic Surgery at Monash Medical Centre, as well as in the Department of Physiology at Monash University. My project was a prospective clinical study, so I have been fortunate to still undertake clinical work in my year away from being a medical student. I have also spent time in a laboratory and have gained skills that I may otherwise have missed out on in the MBBS course. This has been a challenging, but ultimately rewarding year, and I have been very lucky to have both great supervisors and a very interesting project.

I would encourage any student with an interest in research to consider a BMedSc(Hons) year. I am happy to be contacted at amar110@student.monash.edu.

Abstract

Purpose: Acute kidney injury (AKI) occurs in approximately 30% of patients after cardiac surgery. The development of AKI leads to worse outcomes in both the short term and long term. Serum creatinine (SCr) is a marker of kidney function and is used to diagnose AKI. The major limitation of the use of SCr is that increases in the concentration of SCr seen in AKI occur 48-72 hours after cardiac surgery. Emerging biomarkers of AKI, such as cystatin C (CysC) and neutrophil gelatinase associated lipocalin (NGAL), are markers of kidney injury. These emerging biomarkers can only predict AKI, at best, 1-2 hours after surgery. Monitoring of intraoperative urinary oxygen tension (urinary PO2) may predict AKI earlier than available biomarkers. This may facilitate intervention to prevent post-operative AKI. Thus, we compared the predictive efficacy of urinary PO2 to several emerging biomarkers of AKI in adult patients undergoing on-pump coronary bypass grafting (CABG) or valvular procedures.

Methods: Blood and urine samples were obtained from 54 patients at three intra-operative (induction of anaesthesia, during and after cardiopulmonary bypass (CPB)) and five post-operative (0, 3, 6, 24, and 48 hours following intensive care unit (ICU) admission) timepoints. The urinary and plasma concentrations of NGAL, and serum concentrations of CysC and creatinine were determined. Urinary PO2 was measured intra-operatively and up to 48 hours post-operatively using a fibre optic probe positioned in the tip of the urinary catheter.

Results: Twenty two of the 54 patients (41%) developed AKI as defined by an absolute increase in SCr of ≥26.5 µmol/L within 48 hours, or ≥50% increase in 5 days of surgery. In most patients, AKI was diagnosed at 24 hours following ICU admission. For urinary PO2 threshold values of ≤15 mmHg, ≤10 mmHg, or ≤5 mmHg, neither the area under the curve nor the time at or below threshold values differed significantly between patients who did or did not develop AKI. Similarly, intraoperative mean and nadir levels of urinary PO2 did not differ significantly between patients who did or did not develop AKI. No significant association between urinary PO2 and later development of AKI was found. Intra-operatively, serum CysC concentration greater than the normal range was associated with 7-fold increase in the odds of development of AKI (95% CI 1.3-37.9, p = 0.02) when measured following the termination of CPB. No other biomarker was associated with AKI when sampled intra-operatively. Post-operatively, urine NGAL concentration greater than the normal range was associated with a 4.3-fold increase in the odds of AKI when measured at ICU admission (95% CI 1.3-14.7, p = 0.02). Plasma NGAL concentration greater than the normal range was associated with a 5.2-fold increase in the odds of AKI when measured 3 hours following ICU admission (95% CI 1.0-26.6, p = 0.05).

Conclusion: Urinary PO2 was not significantly associated with AKI in this study. Novel biomarkers of kidney injury in the blood and urine were associated with AKI, but not until the termination of CPB, at the earliest. Therefore, on the basis of the current preliminary findings, we cannot propose the use of any of these methods to assess risk of post-operative AKI while patients are still on CPB.

Salsabil Bilqis Maulida

The Impact of Smoking on Population Health and Productivity

Professor Danny Liew, Doctor Alice Owen, Doctor Ella Zomer
School of Public Health and Preventive Medicine, Monash University

I undertook BMedSci (Hons) in 2017 as part of my research year, after completing my third year in Faculty of Medicine at University of Indonesia. I chose the project on the impact of smoking on productivity since I have interest in public health and this project output give a new perspective on the burden of smoking. I am very grateful to have the opportunity to learn and gained research skills under the supervision of Professor Danny Liew, Doctor Alice Owen and Doctor Ella Zomer at School of Public Health and Preventive Medicine, Monash University. It has been a wonderful opportunity and hopefully, all the experiences and lessons during my honours year here will enrich my knowledge and will be useful for my future as a doctor.

Abstract

Background: Despite that the prevalence of smoking in Australia has decreased in the past 20 years, the number of smokers of working age (aged 15 to 64 years) is still high compared to other age groups. While the burden of diseases related to smoking in terms of mortality and morbidity has been well studied, the impact of smoking on productivity at population levels has not.

Methods: Life-table modelling using contemporary Australian data simulated follow-up of current smokers aged 20-69 years until age 70 years. Excess mortality associated with smoking was based on data published by the World Health Organisation. The relative reduction in productivity attributable to smoking (due to both absenteeism and presenteeism) was conservatively assumed to be 1.5% across all ages, as per published data. The gross domestic product (GDP) per equivalent full-time (EFT) workers were used to estimate the cost of productivity loss attributable to smoking at a population level.

Results: At present, approximately 2.5 million Australians (17.4%) aged between 20 to 69 years are smokers. Assuming follow-up of this population until the age of 70 years, 382,787 years of life would be lost to smoking, as well as 5.9 million QALYs and 2.4 million PALYs. This equates to 4.0% of years of life, 9.1% QALYs and 5.7% PALYs less than if the cohort had been non-smokers. At an individual level, this is equivalent to 1.2 years of life, 2.3 QALYs and 1 PALY lost per person. Assuming (also conservatively) that each PALY in Australia is equivalent to AUD156,684 (which is the current GDP per EFT worker), the economic impact (excluding healthcare expenditure) of lost productivity would amount to AUD376 billion.

Conclusion: Smoking imposes a significant burden on health and productivity in Australia, highlighting the importance of prevention. PALYs is a novel measure of the impact of smoking (and indeed, any condition) on productivity.

Rachel Mende

Relationship between MIF and IL-1 family Cytokines in Systemic Lupus Erythematosus

Dr James Harris (main) and Dr Tali Lang (co)
Centre for Inflammatory Diseases
Southern Clinical School Monash University, Department of Medicine
Monash Medical Centre

I wanted to partake in a B Med Sc (Hons.) the year after fourth year because I was seeking a change of pace and wanted to throw myself in the deep-end. My skills in terms of searching and interpreting the literature were not as good as they could have been and I thought the best way to improve would be to actually partake in research that I cared about.

This year not only enabled me to conduct research in an area that I'm interested in but it also allowed me to become part of a lab group where we had informed scientific discussion amongst people who've done some amazing work in the immune field. I have learnt an exponential amount from these people and I have my supervisors to thank for this and the entire Morand Lab group for being so welcoming.

Someone said to me early this year, that science could be defined by long periods of procrastination followed by short, sharp spells of frantic and panicked activity. On reflection, I thought this was eerily accurate and whilst this year has been a steep learning curve it has been undeniably, very enjoyable.

Abstract

Background: Systemic Lupus Erythematosus (SLE) is a chronic, inflammatory, autoimmune disease, which primarily affects women. It presents heterogeneously, the pathogenesis is largely unknown and there is a paucity of objective disease markers. As a result, current treatment is inadequate in controlling symptoms and limiting end-organ damage accrual in many patients. Thus, investigation into mechanisms of inflammation is required in order to better understand pathogenesis and develop more targeted therapeutic approaches. The pro-inflammatory protein Macrophage Migration Inhibitory Factor (MIF) plays a key role in induction of systemic inflammation and has been implicated in clinical SLE as a potential therapeutic target. Further, unpublished data from my supervisors' lab indicates that MIF could potentially regulate NLRP3 inflammasome mediated production of biologically active IL-1α and IL-18. These IL-1 family cytokines have also been significantly implicated in SLE pathogenesis and tissue injury. There are no human studies with large patient cohorts and comprehensive clinical data that observe this relationship in SLE.

Methods: I designed an observational study to quantify and examine the relationship between MIF, IL-1β and IL-18 in the serum of 186 SLE patients and 52 healthy controls, in addition to their correlations with clinical phenotype. Healthy control serum samples were obtained from volunteers. SLE patient samples were donated by the Australian Lupus Registry and Biobank, from patients who satisfied the diagnostic SLE criteria and whom regularly attend the Lupus Clinic. Patient serum samples had paired clinical data sets, including but not limited to data from the clinical visit that corresponded with the serum for analysis. Cytokines were quantified via Enzyme Linked Immunosorbent Assay (ELISA). Statistical analysis was performed using Prism 7.0 Software.

Results: Levels of MIF, IL-1β and IL-18 were all detectable in the serum of SLE patients and healthy controls. Levels of MIF were upregulated in SLE patients of Asian ethnicity ($p = 0.02$). In line with this, increased MIF correlated with increased IL-1β in this cohort ($p = 0.03$). Levels of IL-18 did not correlate with MIF or IL-1β. However, IL-18 levels were significantly upregulated across all SLE patients ($p < 0.0001$). Additionally, IL-18 levels correlated with increased ESR ($p = 0.0007$) and increased CRP ($p = 0.007$), important markers of inflammation. Further, IL-18 was upregulated in patients with active LN ($p = 0.02$).

Conclusions: The hypothesised relationship between MIF and IL-1β was observed within the systemic circulation of SLE patients of Asian ethnicity. Given, the potential novel mechanistic pathway via NLRP3, this opens avenues for further studies of NLRP3 inflammasome activity in this patient cohort. This also potentially identifies Asian SLE patients as a sub-group in whom MIF inhibition may be effective for future targeted therapies. The up-regulation of IL-18 but not IL-1β in patients with increased disease activity was an intriguing finding and indicated that these two structurally similar cytokines may play very different pathological roles in SLE. Further studies are required to identify the exact mechanism through which IL-18 production is increased in SLE, in addition to the mechanism of tissue injury in LN..

Anna Mitchell

Effect of Tissue Plasminogen Activator (tPA) on Auditory Cortex Plasticity

Professor Robert Medcalf: Australian Centre Blood Disease
Professor Alexander Thiele: Institute of Neuroscience, Newcastle University, UK

I decided to study my BMedSci after 4th year of the MBBS. I wanted to do a hands-on lab based project, as I enjoy learning the intricacies of how things work. I was fortunate that the opportunity arose for me to undertake the year in Newcastle, in Northern England, and I spent 7 months living in 'Geordie Shore'.

Academically it was a really challenging year, as I had to quickly learn many new skills, such as electrophysiology and computer programming to undertake my experiments. I learnt an abundance about animal- based research and was taught to conduct mice surgeries and anaesthesia independently.

Living overseas was a highlight for me. I got very used to the British lifestyle of whinging about the bad weather, whilst eating copious amounts of cake and drinking tea. Being able to meet other students from around the world and explore the UK and Europe with my spare time an unforgettable experience!

Abstract

Background: Traditionally, Tissue Plasminogen Activator (tPA) is appreciated as an important enzyme in the fibrinolytic system, which leads to clot breakdown. More recently, its role as a mediator of plasticity has been explored. It is now well established that tPA can modulate glutamate N-Methyl-D-aspartate (NMDA) receptors, which are important for a molecular process underlying synaptic plasticity, Long Term Potentiation (LTP). This has become a growing field of interest, yet relatively little is known as to how tPA modulates receptor function and its primary biological purpose behind this neuromodulator role. Moreover, the effects of tPA in vivo are inadequately understood. The auditory cortex, which is plastic into adulthood, has never been used to explore the role of tPA in plasticity. Auditory neurons are tuned such that they have a best frequency, a frequency in the auditory range of the animal which elicits a maximal response from the neuron. In the adult brain, the tuning curves of auditory neurons are plastic, and change can be induced by conditioning stimuli with a neuromodulator or behavioural influence. This process is thought to replicate normal experience dependent plasticity of the auditory cortex.

Aim: We aimed to assess the effects of tPA on frequency tuning curves in auditory cortex neurons of mice.

Methods: Exogenous tPA was injected into the auditory cortex of adult mice. Extracellular electrophysiology was used to establish baseline tuning curves of neurons in the auditory cortex. The best frequency was identified as the frequency which elicited the maximal response the recorded cells. A pairing protocol was used to pair a sound of non-best frequency with tPA, to assess whether there could be underlying changes to the tuning curve, such as a change to the best frequency, or spike rates of neurons.

Results: Compared to the controls, the cases where tPA was injected show both a greater increase in tone evoked spike counts (25% vs 8%), and a greater increase in spontaneous firing rate (73% vs 30%) in post-conditioning tuning curves.

Conclusion: This is the first study to examine the effect of exogenous tPA on tuning curves of neurons, and in-vivo effects of tPA in the auditory cortex. The results show preliminary evidence that tPA has a role in modulating processes involved in synaptic plasticity. This study supports the notion that tPA is a significant modulator of NMDA function, which highlights a role for tPA in neurobiology outside of its role as a fibrinolytic enzyme.

Rachel Morley

Utility of circulating tumour DNA and cell-free RNA for non-invasive monitoring in multiple myeloma

Professor Andrew Spencer – Australian Centre for Blood Diseases, Alfred Hospital-Monash University, Melbourne, Victoria, Australia; Malignant Haematology and Stem Cell Transplantation, Alfred Hospital, Melbourne, Victoria, Australia.
Dr Sridurga Mithraprabhu - Australian Centre for Blood Diseases, Alfred Hospital-Monash University, Melbourne, Victoria, Australia

I completed my BMedSc project at the Australian Centre for Blood Diseases following my fourth year of medicine to get a taste of medical research. I chose a project in the field of malignant haematology as it lent itself well to a laboratory work as well as being a particular interest of mine. It was a fantastic opportunity for self-direction while still having the support of my supervisors and research team.

This year has challenged me to develop new skills in and out of the lab; including problem solving, scientific writing, presenting and working as part of a team. While not without hiccups along the way, the year as a whole has been very rewarding.

I would thoroughly recommend a lab project for anyone wishing to step outside of their comfort zone and develop some hands-on skills. I am more than happy to answer any questions at rmmor1@student.monash.edu.

Abstract

Background: Multiple myeloma (MM) is an incurable haematological malignancy characterised by the clonal proliferation of plasma cells within the bone marrow (BM). Current monitoring of disease burden includes paraprotein (PP) and serum free light chain (SFLC) measurements, however, these provide limited information and can be inconclusive. BM biopsy does not represent the disease's spatial heterogeneity and is inappropriate for repeat sampling due to its invasive nature. A liquid biopsy utilising plasma (PL) derived cell-free nucleic acids (cfNAs) for non-invasive monitoring has been a recent focus of research in malignancy. Previous studies in MM have identified mutations in cell-free DNA (cfDNA) and tracked their abundance to monitor disease burden, however, these aims have not been explored in a homogeneously treated cohort.

Aim: We aimed to evaluate the utility of cfDNA and cell-free RNA (cfRNA) for non-invasive monitoring in a cohort of homogeneously treated and monitored MM patients. The role of a liquid biopsy for mutational characterisation, monitoring disease burden, and assessing treatment response was investigated.

Method: BM and PL samples from 26 relapsed and/or refractory patients enrolled on the ROAR trial were analysed. Genomic DNA extracted from BM MM cells and PL (2 ml) were assessed by Boreal Genomic's OnTargetTM Mutation Detection (OMDTM) for the presence of KRAS, NRAS, BRAF and TP53 mutations. Detected mutations were tracked in sequential PL extracted cfDNA using Droplet DigitalTM PCR (ddPCRTM), at time points cycle one day five (C1D5), C1D15, end of cycle three (EOC3), and EOC6. cfRNA was assessed to observe changes in the expression of treatment related genes (CRBN, IKZF1, IKZF3, IRF4, BCL2L10, GPX3, RBP1, SPARC, TGFB1, NCAM1, RASD1, CD38, and PDK4) between screening and C1D5.

Results: 53 mutations were detected in the 21 patients assessed by OMDTM (mean 2.5 mutations per patient.) 14 (26.4%) of these were BM specific, 19 (35.9%) were PL specific, and 20 (37.7%) were detected in both compartments. There was a significant correlation between the number of PL specific mutations detected and the patient's overall survival (OS) (p-value 0.04). PL fractional abundance (FA) of detected mutations correlated with clinical parameters (SFLC, PP, BM MM cell infiltration) in 8/15 patients tracked, and increased with disease progression in 6/11 patients who reached this end point. Overall, sequential tracking was informative in 10/15 patients (66.7%). The expression of CRBN in cfRNA increased in responders (R) (median fold change 0.437), and decreased in non-responders (NR) (median fold change -0.491), however, this difference was not statistically significant (p-value = 0.13). There was, however, a significant correlation between the fold change in cfRNA CRBN expression and OS (p-value 0.04).

Conclusions: Through the detection of PL specific mutations, this project demonstrated the benefit liquid biopsy may have as an adjunct to BM biopsy for mutational characterisation. Furthermore, tracking of mutations in sequential PL derived cfDNA was informative in 66.7% of patients assessed, highlighting a potential role in monitoring disease burden. We observed a relationship between the change in cfRNA CRBN expression with respect to response and survival, encouraging further investigation to assess its utility as a biomarker of response.

Stephanie Naidu

APRI as triage to FibroScan: can a simple serum biomarker reduce barriers to care in a HIV/HCV co-infected cohort?

Primary Supervisor: Dr Joseph Doyle, Co-supervisor: Professor Margaret Hellard

Department of Infectious Diseases, The Alfred and Monash University
Disease Elimination Program, The Burnet Institute

I decided to undertake my BMedSc (Hons) research project with the Alfred Hospital Department of Infectious Diseases and the Burnet Institute following my fourth year of medicine, as I thought that it was a great opportunity to take a break from the traditional learning environment and gain a broader understanding of medical science and research. I've had a great year and thoroughly enjoyed working alongside leaders in Hepatitis C research. The knowledge you pick up throughout the year is really invaluable; I've gained practical skills in data analysis, statistics and problem solving and gained insight into public health policy. I'd recommend the BMedSc to all students, as it really is a fantastic opportunity to get involved in your field of interest and a great introduction to the world of research.

Abstract

BACKGROUND AND AIMS: Hepatitis C (HCV) is a disease of global significance, with 71 million people chronically infected worldwide. Complications of the infection include liver cirrhosis, hepatocellular cancer and death, with the risk of hepatitis C complications exacerbated in a subpopulation of individuals co-infected with Human Immunodeficiency Virus (HIV). In Australia, Transient Elastography (FibroScan) is the recommended technique for detecting the presence of cirrhosis in HCV. However, this assessment technique is largely limited to specialist and hospital settings. This is causing a delay to HCV treatment and cure in Australia. The Aspartate aminotransferase to platelet ratio index (APRI) is a simple, widely available serum biomarker that has been validated for excluding cirrhosis individuals with chronic HCV mono-infection; however, its utility in the HIV/HCV co-infected cohort has not been adequately explored. We investigated the utility of and APRI as a method for excluding cirrhosis in a population of HIV/HCV co-infected individuals in a real-world community setting, aiming to correlate the APRI scores of below 1 with FibroScan liver stiffness measurements of below 12.5 kPa.

METHODS: This APRI-FibroScan analysis was a sub-study of the trial 'Eliminating Hepatitis C transmission by enhancing care and treatment among HIV co-infected individuals (the co-EC study)'; an open-label trial of DAA treatments among HIV/HCV co-infected individuals in real-world primary care and specialist settings. A cross-sectional study design was selected for the APRI-FibroScan study. Eligibility criteria for the APRI-FibroScan study required participants to have pre-treatment AST and platelet count results taken within 30 days for an APRI score to be calculated and pre-treatment FibroScan assessments performed within 90 days of each of the components of the APRI. The APRI cut-off of 1 was compared with FibroScan classifications of cirrhosis using liver stiffness measurements of above 12.5 kPa. The correlation between an APRI score of 1 and a FibroScan LSM of 12.5 kPa was reported with diagnostic test summary statistics including sensitivity, specificity, positive and negative predictive values, likelihood ratios, alongside corresponding 95% confidence intervals. The area under the receiver operating characteristic curve (AUROC) was also calculated. Sensitivity analysis was performed to examine the impact of prevalence of cirrhosis on the reported summary statistics.

RESULTS: Sixty-eight participants were included in the analysis. The diagnostic summary statistics were as follows; sensitivity 66.7% (95% CI 9.40 – 99.20%), specificity 70.8% (95% CI 58.20- 81.40%), positive predictive value 9.5% (95% CI 4.20 – 20.20) and negative predictive value 97.9% (95% CI 90.20 – 99.60%). The AUROC was calculated at 0.81 (95% CI 0.61- 1.00).

The negative predictive values calculated in the sensitivity analysis demonstrated the utility of the APRI in settings with low cirrhosis prevalence.

CONCLUSION: In individuals with HIV/HCV co-infection, an APRI score below 1 was able to correctly identify a significant proportion of individuals with FibroScan LSM of below 12.5 kPa. This suggests that an APRI cut-off of 1 is an appropriate threshold for excluding cirrhosis in individuals with HIV/HCV co-infection. These findings support the application of the APRI as a triage test for cirrhosis to reduce the total number of FibroScans assessments required in the community, in this subpopulation.

Tuzana Nawar

Establishing the technique, ex vivo dual placental perfusion, for assessment of creatine transport in the human placenta.

Dr. Stacey Ellery and Dr. Hayley Dickinson, The Ritchie Centre, Hudson Institute Monash University

I decided to do the Bachelor of Medical Science after Year 4C of Medicine, because I was interested in the field of obstetrics research and wanted to experience it first-hand. I had the opportunity to work with the Dickinson laboratory and learnt a great deal about how research is carried out and the hurdles that are faced in the laboratory and the translation into the clinical setting. Overall, despite many challenged faced in the year, I still found the experience greatly rewarding due to the enthusiasm and support of everyone in the lab and especially my supervisors.

Abstract

Background: Creatine supplementation has shown great promise for protecting the fetus against hypoxia in numerous animal models, due to its role in oxygen-independent role in ATP turnover. Tissue creatine loading prior to hypoxic insult is essential for creatine to protect the fetus. To replicate the beneficial protection creatine provides to the fetus in human pregnancy, the placenta must be shown to transport creatine. Ex vivo dual placental perfusion is the best technique to examine this transport, however, it can be a difficult technique to establish due to its non-standardisation and other variables that need to be controlled.

The objectives of this study were to establish and optimise the technique of ex vivo dual perfusion at Monash Medical Centre (MMC), by recruiting and characterising study participants from a population of women with low risk pregnancies undergoing elective caesarean section, and then optimising the perfusion technique. This could then be used to examine creatine transfer in healthy term human placentas.

Method: Low-risk healthy women with normal pregnancies who were electing for caesarean section delivery were identified from the MMC antenatal clinics, and were then screened along certain inclusion and exclusion criteria, with eligible women approached for consent. Data was collected to characterise the available pool of women, through noting the reasons for ineligibility, and extracting the demographics, pregnancy outcomes, and birth outcomes data of those who consented. These were compared to another data-base of low risk pregnancy parameters development at MMC.

The perfusion technique was optimised through first setting up the perfusion circuit to regulate variables, and validation of 4-amino antipyrine as an internal control. Placentas from consented patients were then collected from theatre and perfusion was attempted. A viable cotyledon was selected, cannulated and flushed. If the preparation was considered viable, it was then perfused through the maternal and fetal circuits.

Results: There was a total of 60 women identified who were undergoing elective caesarean section delivery at MMC. Of these, 41 women were excluded; the majority due to gestational diabetes. 12 of the 19 women eligible consented to participate in the study. Compared to the control population, these women were more likely to be of South Asian descent, multigravida, increased parity and the babies born were likely to be have a younger gestational age at birth and have smaller birth lengths. In total, four attempts at perfusion were undertaken, with one placenta meeting all checkpoints for successful perfusion, and used to validate the internal control.

Conclusions: A population of low risk women electing for caesarean selection, with similar demographic profiles to the general low risk population, is available for perfusion experiments at MMC. One of four placentas were successfully perfused within the time-frame of this study. This success rate of 25% is similar to other centres around the world. This indicates that the ex vivo perfusion technique was successfully adapted and established for use at MMC. Continuing these perfusion studies with creatine will be the next step in determining creatine transfer in the human placenta.

Toby O'Brien

Utility of Head Computed Tomography (CT) in geriatric patients following minor head trauma

Professor Biswadev Mitra (School of Public Health and Preventive Medicine, Monash University, Australia. National Trauma Research Institute, Alfred Hospital, Melbourne, Australia) & Dr Eric Mercier (Unité de recherche en Traumatologie - Urgence - Soins Intensifs, Centre de recherche du CHU de Québec, Université Laval, Québec, Canada)

I decided to undertake a BMedSci after completing my third year of MBBS. I completed my research project in my primary area of interest, emergency and trauma medicine. I enjoyed joint supervision from two supervisors, Professor Mitra at the Alfred Hospital and Dr Mercier from L'Hôpital de l'Enfant-Jesus in Québec City, Canada. I was fortunate enough to spend most the year working in Québec with Dr Mercier. I was thus able to gain insight into the world of emergency research whilst experiencing a new lifestyle in a new country and of course a new language. This has been an unforgettable year, characterised not only by academic pursuits but a fresh perspective on life as a medical student - it can be fun!

I invite any student considering a Bachelor of Medical Science in this area to contact me if they have any questions. My email is tfobr3@student.monash.edu.

Abstract

Background: Head trauma is an increasingly common presentation to emergency department (ED) for the elderly population, many of whom are taking oral anticoagulant or anti-platelet (ACAP) therapies. Although current evidence suggests the use of computed tomography of the brain (CTB) following a mild traumatic brain injury (TBI) in elders, there is currently a lack of evidence to guide the management for minor head trauma patients who do not display signs or symptoms TBI.

Aims: This study main objective is to determine the incidence of clinically significant traumatic intracranial haemorrhage (ICH) following a minor head trauma in geriatric patients. Secondary objectives are to explore the role of ACAP therapies in the development of traumatic ICH and to determine the factors associated with the use of CTB for patients who have sustained head trauma but do not present with any signs or symptoms of TBI as defined by the ACRM criteria (12).

Methods: This is a single-centre retrospective cohort study of electronic patient records. The patient cohort consisted of patients presenting after a fall or with suspected head trauma between 1 March 2010 and 31 July 2017 in a tertiary trauma centre. Patients were included in the analysis if they were head trauma patients of 65 years and over, had an unchanged Glasgow Coma Scale (GCS) and did not fulfil criteria to diagnose TBI. Data was collected using a standardised excel sheet documenting each patients' demographic data, medication history, clinical presentation, injury mechanism, CTB referral and results. details of the presentation, CT referral and imaging results

Results: 1000 electronic files were investigated, of which 311 met inclusion criteria. The mean age was 80.1 years with 36 patients (11%) aged over 90 years old. Twenty-three (7.4%) patients showed acute traumatic ICH, with 20 (6.4%) of these deemed to be clinically relevant. Of these patients, 16 were taking an ACAP. Only two patients (0.64%) required a surgical procedure but one patient decided to do not have the neurosurgery and passed away as a result of a complication from the minor head trauma. Across the cohort, 189 patients were taking ACAP medications compared to 122 with no ACAP history. There were no statistically significant differences between patients taking an ACAP and those who did not in terms of age or injury mechanism. 205 patients (65.9%) of patients received a CTB in the ED. The use of CTB was higher in ACAP patients (76.7%) compared to those without ACAP exposure (49.2%). The adjusted relative risk for CTB referral after ACAP exposure was 1.70 (CI 1.51-1.92).

Conclusions: Whilst a relatively low proportion of patients were found to have ICH (6.4%), there is a potential for clinically significant and even fatal outcomes. A higher rate of ICH was observed in ACAP-exposed patients, suggesting that ACAP exposure merits consideration as an independent risk factor, including anti-platelet monotherapies. Our findings suggest that CTB remains a useful tool in the initial assessment of minor head trauma, even in the absence of TBI criteria. Future research should be targeted to specify risk factors for the development of traumatic ICH and to better determine the need for emergency CTB referral and clinical observation.

Charlotte O'Leary

Lay attitudes towards risk and moral responsibility in gain-of-function research

Prof Michael Selgelid (Monash Bioethics Centre, Monash University), Dr Hannah Maslen (Uehiro Centre for Practical Ethics, University of Oxford), Dr Jonny Pugh (Uehiro Centre for Practical Ethics, University of Oxford)

I completed my BMedSci after fourth year of the MBBS. For me, it was an opportunity to see the world, try out research and have a break from clinical medicine. I was keen to do my research in bioethics to expand my interests and knowledge outside of medicine and discover a totally different way of thinking and researching. The year has not disappointed! Aside from my project, I have been exposed to so many new ideas in philosophy and ethics. Living in Oxford has been a huge adventure and I feel so lucky to have had the opportunity to study here.

I'd definitely encourage other students to take a BMedSci, especially if you have diverse interests and are keen for a bit more time to challenge yourself intellectually. Always happy to answer any questions via Facebook or email (charlotte.a.oleary@gmail.com).

Abstract

Background: Advances in technology and science have lead to an increase in capacity for gain-of-function research (GOFR). This is defined as scientific experimentation that increases the virulence and/or transmissibility of infectious agents. Whilst potentially contributing knowledge of infectious diseases, this research also poses significant biosafety and biosecurity risks to public health. A series of GOFR studies in the early 2000s sparked debate and contention, and eventually led to the US government implementing a pause on new funding for GOFR involving influenza, MERS and SARS (effective October 2014). To date, the GOFR discourse has been largely concentrated in the scientific community and national governments/ regulatory bodies. Despite wide recognition that there is a need for greater consultation with civil society in the GOFR debate, there has been minimal engagement of the general public to date.

Aim: The empirical component of this research aimed to gauge the general public's attitudes towards the topic of GOFR. The overarching aim of the empirical and ethical analyses is to inform the ethical literature around dual-use research and contribute to the policy debate in the US (and globally) around the regulation of GOFR.

Method: The empirical component of this research project took the form of a cross-sectional study performed through an online survey platform. In order to maintain a high degree of relevance to the current GOFR political climate, survey participants were taken only from the US. The study assessed respondent attribution of prospective responsibility for decision-making in GOFR scenarios amongst three stakeholders, as well as their beliefs on the role of the general public in the GOFR problematic. The bulk of the survey was comprised of risk benefit decision-making questions involving GOFR scenarios.

Results: When asked to indicate how they attribute prospective moral responsibility in a GOFR scenario, respondents agreed that: a) scientists (mean agreement score 5.98/7 (seven-point Likert Scale); b) universities and other institutions that fund scientific research (5.85); and c) governments and other regulating organisations (5.29) all had a role to play. The general public were less inclined to agree that they themselves should have a say in permissions and restrictions applying to potentially dangerous scientific research. Respondents demonstrated a high degree of risk tolerance and willingness to perform experiments. Favouring expected utility was a compelling decision-making value. However, respondents were pluralistic in their preferred decision-making values.

Conclusions: To our knowledge, this research project was the first to assess lay attitudes on GOFR. It contributes new insights into the GOFR problem that will inform bioethical debate, and contribute to policy-making that is representative of the people. This study offers a strong foundation for further research into the broader issue of the inexorable advance of technology and science and its intersection with the moral foundations of modern society.

Mohammad Reka Ananda Putra

Potential Synergistic Effects of Cardiovascular Disease Risk Factors on Vascular Inflammation

Prof Jaye Chin-Dusting, Dept. of Pharmacology, Monash University

am an Honours student batch 2016-2017 in Monash University. Cardiovascular diseases have been studied extensively, yet there are still new discoveries made which makes it interesting for me. During this research, I learned various lab skills and I also understand how important research is. It was a year full of sweat and blood (literally because my research requires blood), but it was worth it in the end.

Abstract

Background: In Australia, cardiovascular disease (CVD) accounts for ~50,000 deaths/year. Notably, 64% of the adult population have >3 modifiable risk factors for CVD. Accordingly, assessment of absolute CV risk, based on the patient's gender, age, systolic blood pressure (BP), total and high density lipoprotein (HDL)-cholesterol, diabetes and the presence of left ventricular hypertrophy, is currently widely adopted. Although the goal is to reduce absolute CVD risk, this is usually by managing individual risk factors such as high BP and lipid levels. Since both have a continuous association with CVD events, moderate alterations in several factors may however be more effective than a major change in any one factor.

We aimed to investigate if HDL has sufficient anti-inflammatory properties to restore leukocyte adhesion and inflammatory gene expression in pressure-induced and OxLDL exposed arteries.

Method: Carotid arteries were excised from 8-week old Sprague Dawley rats. In the first instance, we performed a pre-incubation study, where arteries were incubated in either nothing (control), HDL (50µg/ml), OxLDL (50µg/ml) or a combination of both for 1 hour, then pressurized at 120 mmHg on the vessel chamber for a further 1 hour. We then performed a post-incubation study, reversing the order of incubation and pressure. Fluorescently labelled human blood was then perfused to visualize leukocyte adhesion per field of view (FOV). The vessel was then processed to assess gene expression of VCAM1, ICAM1, MCP1, IL6, and Cav1.

Results: High intraluminal pressure increased leukocyte adhesion significantly compared to the control group (n=9-10, 31 ± 2.9 vs. 10 ± 1.6 leukocytes/FOV/vessel at 10 min, respectively, $p<0.001$). OxLDL also induced significant increase of leukocyte adhesion in comparison to the control group (n=6-9, 29 ± 2.7 vs. 10 ± 1.6 leukocytes/FOV/vessel at 10 min, respectively, $p<0.001$). The combination of risk factors resulted in significantly higher leukocyte adhesion compared to OxLDL or 120 mmHg alone (n=6-10, 46 ± 12.1 vs. 29 ± 2.7 or 31 ± 2.9 leukocytes/FOV/vessel at 10 min, respectively, $p<0.001$). HDL alone had no effect on leukocyte adhesion (n=9-11, 12 ± 1.5 vs. 10 ± 1.6, $p=0.99$). It was, however, effective in reducing leukocyte adhesion in the 120 mmHg group (n=9-10, 11 ± 2.1 vs. 31 ± 2.9 leukocytes/FOV/vessel at 10 min, respectively, $p<0.001$). When OxLDL exposed vessels were incubated with HDL, we found a decrease of leukocyte adhesion compared with OxLDL exposure alone (n=6-7, 15 ± 1.0 vs. 29 ± 2.7, $p<0.01$). Lastly, the combination of OxLDL and HDL, followed by pressure at 120 mmHg, saw a significant drop compared to the combination of OxLDL and 120 mmHg (n=6-8, 13 ± 1.8 vs. 46 ± 12.1, $p<0.001$). There were significant increases in gene expression of VCAM1, ICAM1, MCP1, IL6 and Cav1 in 120 mmHg exposed group compared to control. We observed similar trends in the OxLDL incubated group, although not all increases were significant. We also found that HDL restored the inflammatory gene expression back to basal levels when given in combination with OxLDL or 120 mmHg or combination of both. In the combination of 120 mmHg and HDL, we observed a significant decrease of leukocyte adhesion compared to 120 mmHg alone (n=7-11, 12 ± 0.9 vs. 27 ± 2.1 respectively, $p<0.001$). When we combined 120 mmHg and incubation with OxLDL + HDL and we saw a significant reduction of leukocyte adhesion compared to 120mmHg + OxLDL (n=2-6, 12 ± 0.8 vs. 51 ± 6.2 respectively, $p<0.001$).

Conclusions: High intraluminal pressure and OxLDL work synergistically to increase leukocyte adhesion and inflammatory gene expression, and HDL can prevent as well as rescue this effect.

Liang Qu

Hormone Receptor Biomarkers in Advanced Prostate Cancer: Do Oestrogen Receptor Variants Play a Role?

Dr Carmel Pezaro, Eastern Health Clinical School, Monash University; Department of Oncology, Eastern Health
Dr Pavel Sluka, Eastern Health Clinical School, Monash University

I completed an Honours year this year so I could have a break away from the stress of 4th year medicine. This year turned out to be a very productive and enjoyable year where I was able to explore research in prostate cancer with an experienced Uro-Oncology laboratory team, at Eastern Health. I was primarily under the supervision of Dr Carmel Pezaro and Dr Pavel Sluka, both amazing and supportive mentors who helped guide me through a project that was challenging yet rewarding.

If you are interested in discussing my project further, feel free to contact me via email, at lqu8@student.monash.edu.

Abstract

Background: Treatment-related biomarkers are being studied to better guide management of castration-resistant prostate cancer (CRPC), a disease that is incurable despite current therapies. Current blood-based biomarker studies for CRPC have focused on androgen receptor mutations and splice variants. While oestrogen receptor (ER) mutations and splice variants have been investigated in breast cancer blood samples, their blood-based detection has not been studied in CRPC, despite the role that oestrogens may have in prostate cancer.

Our aim was to develop assays to detect and quantify ER mutants and splice variants in blood samples of patients with CRPC, and to associate their detection with disease or treatment parameters.

Method: An exploratory cohort of men with advanced prostate cancer was recruited from the Box Hill Hospital Uro-Oncology clinic between 2015 and 2017. Sequential blood samples were collected from these patients throughout their management. Cell-free DNA (cfDNA) and cell-free RNA (cfRNA) were extracted from these blood samples and tested for ER mutants and splice variants.

The selected ER markers included six ERα point mutations (E380Q, L536Q, Y537C, Y537S, Y537N & D538G), and six ER splice variants (ERα-66, ERα-36, ERβ1, ERβ2, ERβ4 & ERβ5) that have been well described in ER biology. These were quantitated in patient samples using droplet digital polymerase chain reaction (ddPCR) assays that were developed and validated for this study.

The distribution of detection in samples was reported for each assay. Associations of the markers with clinical variables were examined for the cohort using descriptive statistics. Serial analysis was conducted to explore the utility of ER mutants and splice variants as potential progression or response markers. Formal statistics were not performed for this exploratory study.

Results: Altogether, 44 men with advanced prostate cancer were included, with a median of two (range: 1-6) sequential blood samples per patient. There were 92 cfDNA and 94 cfRNA samples in total. Of the six mutations investigated, two (E380Q & D538G) were detected in cfDNA, and four (E380Q, L536Q, Y537S & D538G) were detected in cfRNA.

The splice variants ERα-66, ERβ1, ERβ2, ERβ4 and ERβ5 were detected in all cfRNA samples. ERα-36 was detected in 84/94 samples, at lower concentrations than the other splice variants investigated ($p<0.0001$).

Of the clinical variables analysed for the cohort, splice variant detection may be associated with the use of castration therapy, castration resistance status, as well as number of previous treatments. No convincing associations were observed for the investigated mutations.

Sequential sample analysis generated hypotheses regarding possible associations between the E380Q and L536Q mutations with individual patient disease progression. ERα-36 concentration increased in response to docetaxel or abiraterone. ERα splice variant concentrations decreased with disease progression on each of the studied therapies. These associations were not statistically verified.

Conclusions: Development of ddPCR assays for CRPC blood samples has resulted in the novel quantitation of ER mutants and splice variants in cfDNA and cfRNA. These mutants and splice variants may add insight into disease phenotypes and warrant further investigation into their utility to better predict treatment response or disease progression.

Anjali Raghavan

Health system literacy acquisition in female Afghan humanitarian migrants in South East Melbourne

Professor Grant Russell, Dr I-Hao Cheng and Dr Shiva Vasi
Southern Academic Primary Care Research Unit (SAPCRU), Department of General Practice, Monash University

I have undertaken my BMedSc(Hons) in between my fourth and fifth years of medicine. There were many reasons for why I took this year – I wanted to gain some research experience, I was looking for a change of pace after fourth year, and I hoped to gain a better understanding of issues around global health. I chose to do undertake my research with SAPCRU because I knew that it would be a very supportive environment, and the focus on refugee and asylum seeker health gave me a lot of insight into global health issues on a domestic scale. I've had a wonderful year, and I've learnt so much, particularly around qualitative research, which is an area that is often missed in medical research and medical teaching, and I am very grateful for this experience. If anyone has any further questions, I'm happy to be contacted at arag6@student.monash.edu.

Abstract

Background: With rising numbers of forcibly displaced people worldwide, the health and wellbeing of humanitarian migrants is an increasingly pressing global issue. The welfare of this group is particularly pertinent to Australia, which is one of the few developed countries to offer permanent resettlement opportunities. In South East Melbourne, there is a large community of Afghan humanitarian migrants facing poor health and poor access to health services. Women within this community are particularly at risk of not knowing how to access the health services they need. Health system literacy may facilitate access to the healthcare system for Afghan women.

Method: We undertook a qualitative study with a phenomenological focus. This involved semi-structured interviews using credentialed interpreters with Afghan women attending a community program in South East Melbourne. Interviews were transcribed and thematically analysed using an inductive approach to identify key themes concerning the experiences of these women in learning about and navigating the Australian healthcare system.

Results: Nine Afghan women, between the ages of 21-38, participated in the study. Participants had varying levels of confidence in navigating the Australian healthcare system. Skills and knowledge around health services played an important role in helping women to overcome a range of challenges as they navigated the Australian healthcare system. In acquiring health system literacy, women drew upon contextual factors such as their time in Australia, English fluency, and education levels. They also made use of resources such as their husbands, other family and friends, community programs, schools, and healthcare workers. Although formal education was available from settlement agencies to help humanitarian migrants acquire health system literacy, women supported by family to resettle in Australia were often unaware of or unable to access these resources, and instead relied upon their community to help them build capacity.

Conclusions: Afghan women often sought support from their family and friends in overcoming challenges related to health service access, and perceived this support to be highly valuable. However, there are potential disadvantages to receiving support from the community. It may place an excessive burden on other humanitarian migrants, and women may also become dependent upon those who support them, and unable to access healthcare without them. As women developed greater health system literacy, however, they were better able to access health services independently without being reliant on others. The data highlights the importance of Afghan women being well linked in with the community and with settlement services. It also highlights the importance of community resources being well integrated and knowledgeable of the health system, in order to facilitate health system literacy development and optimal navigation of health services for these women.

Suveena Ranzil

Altered placental serotonin pathway in fetal growth restriction (FGR): potential role of vitamin D supplementation in FGR

Dr Padma Murthi, Professor Euan Wallace. The Ritchie Centre, Hudson Institute of Medical Research.

The BMedSc(Hons) year has been such a great learning experience. Having not stepped into a lab since year 12, the beginning of the year involved a steep learning curve, but I'm glad I was able to step outside my comfort zone. Over the course of the project, I've come to understand what exactly is involved in research, its unique challenges and its rewards. From long hours pipetting at the lab bench to time spent reading and synthesising written material, I have gained a number of useful skills this year that I would not have been able to develop otherwise. I know this experience has shaped my thinking and will influence my work as a doctor in the future, as I can now fully appreciate the hard work behind any new development in the field of medicine.

Abstract

Background: Fetal growth restriction (FGR) often results in fetal neurodevelopmental problems. Whether disrupted placental serotonin (5-HT) synthesis contributes is currently unclear. Therefore, the expression of placental 5-HT pathway components and 5-HT concentrations, and the potential role of vitamin D supplementation in optimising disrupted 5- HT levels, were investigated in FGR pregnancies.

Objectives: The primary objective was to determine whether the placental 5-HT pathway is disrupted in placental tissues collected from 1st and 3rd trimester FGR compared to healthy control pregnancies. The secondary objective was to identify whether hypoxia (contributing to placental insufficiency in FGR) disrupts the placental 5-HT pathway in vitro, and if vitamin D supplementation mitigates these effects.

Methods: The mRNA expression of 5-HT pathway genes (SLC6A4, TPH1, HTR5A, HTR5B, HTR1D, HTR1E) was measured using Fluidigm Dynamic array in placental tissues from 1st trimester small-for-gestational age (SGA) (n=25) and healthy control (n=48) pregnancies, and 3rd trimester FGR (n=16) and healthy control (n= 38) pregnancies. Correlations were performed between gene expression and certain patient characteristics. Placental 5-HT concentrations were measured in 3rd trimester tissues (n=14 FGR, n=12 control) using an ELISA and correlated with placental vitamin D concentrations (n=11 FGR, n=11 control). Vitamin D concentrations were also correlated with TPH1 mRNA expression (n=9 FGR, n=14 control). Additionally, an in vitro model of placental hypoxia was used to mimic FGR in healthy 3rd trimester villous explants and trophoblast cells, with or without vitamin D supplementation. 5-HT concentrations were measured villous explants using an ELISA, and SLC6A4 mRNA expression measured in trophoblast cells using PCR.

Results: Gene expression of 5-HT pathway components was present in both 1st and 3rd trimester placental tissues. Although there were no significant differences in mRNA expression between 1st trimester SGA and control tissues, in 3rd trimester FGR tissue, there was a significant decrease in the mRNA expression of SLC6A4 ($p<0.0001$) and TPH1 ($p=0.037$), and a significant increase in HTR5A ($p=0.002$), HTR1D ($p=0.002$) and HTR1E ($p=0.012$). In 3rd trimester control samples, there were significant correlations between gestational age and SLC6A4 ($r=-0.385$, $p=0.022$) and HTR1D ($r=-0.385$, $p=0.023$) expression, as well as between birth weight and HTR5A ($r=-0.394$, $p=0.019$), HTR1D ($r=-0.435$, $p=0.009$) and HTR1E ($r=-0.376$, $p=0.026$) expression. In 3rd trimester FGR samples, there were significant correlations between maternal age and TPH1 ($r=-0.726$, $p=0.021$) expression, gestational age and SLC6A4 ($r=-0.371$, $p=0.026$) expression, and birth weight and SLC6A4 ($r=0.515$, $p=0.044$) expression. There was no significant difference in 5-HT concentrations between FGR and control 3rd trimester tissues, and no significant correlations with placental vitamin D concentrations. There were also no significant correlations between vitamin D concentrations and TPH1 expression. Preliminary data from the in vitro study showed no significant differences between treatment groups.

Conclusions: These findings demonstrate that gene expression of placental 5-HT pathway components is present in both 1st and 3rd trimester placentae, and disrupted in 3rd trimester FGR pregnancies. However, the implications of this disruption are unclear. Interestingly, this study also found a number of significant correlations between 5-HT pathway gene expression and maternal and newborn characteristics in 3rd trimester pregnancies.

Charlotte Russo

Patient related factors that determine use of total knee arthroplasty for osteoarthritis

A/Prof Anita Wluka, Prof Flavia Cicuttini

School of Preventative Health and Preventative Medicine, Department of Epidemiology and Preventative Medicine, Monash University

In the pre-clinical years of my MBBS I was adamant that I'd never do a Bachelor of Medical Science Honours. However after finishing fourth year I realised I wasn't quite ready to finish, and wanted to do something else before graduating and starting work. So I ended up doing one after all. This year I've learnt a lot about concepts I never fully grasped in my clinical years and now recognise you never truly understand research until you've done it for yourself. I would recommend BMedSc (Hons) to other students, even if you don't have a particular field of interest yet, so that you gain a better understand of the roots of evidence based medicine.

Abstract

Background: Total knee arthroplasty (TKA) for treatment of severe knee osteoarthritis (OA) has been increasing over the past 20-years. Studies assessing patient related characteristics and their influence on odds of receiving TKA are conflicting and out-dated.

Objective: To examine the significance of patient related characteristics in determining who receives TKA. To determine if female gender or interpreter use, signifying poor English proficiency, disadvantages those seeking TKA in the public health sector.

Design: Cohort study with nested case-control.

Participants: All patients (n = 718) referred to Osteoarthritis Hip and Knee Service (OAHKS) between 2013-2015 for knee pain or knee OA.

Methods: Data was obtained from the Alfred Hospital's OAHKS physiotherapy database and medical records. All data was routinely collected prospectively. Parametric and non-parametric descriptive analysis was performed to determine any significant differences in characteristics between those who did and did not receive TKA. Similar analysis was performed to ascertain gender, or interpreter use differences. The cohort was confined to KL3+4 so all cases would be considered "eligible" for TKA. A case control study of those who received TKA within 2 years of initial appointment and those who did not was performed using logistic regression to determine the odds ratio of each variable.

Results: 700 patients were included in the analysis. Incidence of TKA during the study period was 22.6% (n=158). There were no significant demographic or social differences between those who did and did not receive TKA. Pain scores, multi attribute prioritisation tool (MAPT) scores and radiological severity were higher in those who received TKA.

Equal proportions of males (23.4%) and females (22.1%) progressed to TKA, however gender differences were demonstrated in relation to pain and radiographic severity. Pain at rest was higher in women than in men who underwent TKA (p=0.01), and women had a higher proportion of KL 4 in the TKA group than men (p=0.02).

The only significant difference between TKA patients who used an interpreter and those who did not was age, which was on average 6 years higher in those who used an interpreter (p=0.002).

In the case-control analysis, multivariate analysis of revealed that presence of pain at rest, intensity of pain at rest and on movement, MAPT score, and flexion were all found to be influential the odds of TKA. Interaction between NPRS pain at rest and gender was shown to be significant (p=<0.001). Pain at rest was influential on female (p=<0.001) but not male (p=0.78) odds of TKA.

Conclusions: Higher pain at rest and greater disease severity in women suggests there may be a female disadvantage, however the scope of the present study is unable to explain why. Further prospective research is required to establish the cause of the described gender discrepancy. Analysis demonstrated no significant differences between TKA patients who used and interpreter and those who didn't. However, small sample size and disproportionately high amount of missing data within this population significantly limited statistical power. Further research is needed to further assess any disadvantage in accessing TKA caused by limited English proficiency.

Kate Shearer

Placental Pathology in Expedited Births due to Suspected Fetal Compromise

Dr Hayley Dickinson, Dr Padma Murthi, Dr Miranda Davies – The Ritchie Centre, Hudson Institute

I undertook my Bmedsc(Hons) at the Ritchie Centre/Hudson institute after finishing fourth year. I chose my project (in Women's Health) before I had even done my women's health rotation (so I had no idea if I'd even like it!), but it sounding really interesting. I was also fortunate enough to help recruit patients for a prospective study being conducted currently. This has been a really challenging year, but I've learnt a lot about research, the placenta, and myself. My main pieces of advice would be to set out your goals and expectations early with supervisors, get ethics in ASAP, say yes to opportunities that come your way, and find a good support network – there are really long days (and weeks) and I couldn't have gotten through this year without many supportive people, and our coffee breaks.

Abstract

Background: Placental pathology examination is used to investigate adverse obstetric and neonatal outcomes. There is extensive placental pathology research regarding certain adverse obstetric outcomes, such as preterm birth, and known differences in the rates of placental pathology across gestation. However, there is limited research regarding the relationship between expedited birth due to suspected fetal compromise and placental pathology, despite its use as an indication for examination in tertiary level facilities, including Monash Health. This study aimed to: identify the prevalence of expedited birth due to suspected fetal compromise at Monash Health and the proportion of these cases receiving a placental pathology examination; identify placental pathology lesions that related to expedited birth due to suspected fetal compromise; and identify if placental pathology lesions related to neonatal outcomes.

Method: De-identified Birth Outcome Summary (BOS) data from singleton births was used to identify expedited births due to suspected fetal compromise. The expedited birth cases were divided into preterm and term groups (34 – 36+6 and 37+ weeks gestation, respectively). The maternal and neonatal UR numbers were used to identify if a placental pathology examination was conducted. If present, the report details were extracted using two Google Forms, created specifically for this project. Maternal demographics, pregnancy complications and neonatal outcomes were compared between expedited births that did and did not receive a pathology examination using Chi2 and Mann-Whitney U tests. For all expedited births with a placental pathology examination (cases), the above factors, as well as placental lesions, were then compared to uncomplicated, late (34-36+6 weeks) preterm births (controls), using Chi2 and Kruskal-Wallis tests. Logistic regression was then used to determine any relationships between placental lesions and the pregnancy groups, while adjusting for covariates - maternal age, body mass index (BMI), country of birth, smoking status and neonatal sex.

Results: The major findings of this study was that preterm and term expedited births had 2.0 and 2.2 times the odds of having a vascular/malperfusion lesion compared to the control group. Regardless of pregnancy grouping, neonates who had a vascular/malperfusion placental lesion had a 1.5 times the odds of being small for gestational age compared to those without these placental lesions. Neonates who had an infectious/inflammatory placental lesion had 2.0 and 1.5 times the odds of being admitted to special care nursery (SCN) or neonatal intensive care unit (NICU), and having a neonatal morbidity respectively, compared to those who did not have these placental lesions.

Conclusions: In conclusion, there is significant evidence that vascular/malperfusion placental lesions are related to expedited births and small for gestational age, whilst infectious/inflammatory lesions are related to neonatal morbidity and neonatal admission, regardless of pregnancy grouping. This study is the first of its kind to explore the relationship between placental pathology and expedited births due to suspected fetal compromise, and further exploration could help stratify compromised fetuses and identify those at greatest risk of morbidity and mortality.

Thomas Shiels

EEG detection of discrete movement states for brain-computer interfacing

Associate Professor Paul Fitzgerald – Monash Alfred Psychiatry Research Centre
Doctor Thomas Oxley – Melbourne Vascular Bionics Laboratory, Royal Melbourne Hospital
Doctor Sam John - Melbourne Vascular Bionics Laboratory, Royal Melbourne Hospital and University of Melbourne, Department of Biomedical Engineering

After finishing 4th year of MBBS as an ERC student, I wanted a change. I wanted to be able to live in the same place for a whole year and I wanted the opportunity to pursue some of my non-medical interests. This project ticked all my boxes. I worked primarily with engineers in developing technology that will ultimately enhance people's lives. I was given full control over my own time, which meant I had to learn how to motivate myself and structure my time. BMedSc (Hons) helped me grow up a lot, I feel like I am more mature, better capable of managing myself and taking initiative. I also learned a lot about computer science and coding which I hope will be very useful going forward.

My advice to prospective students is to find something that interests you regardless of how unqualified you are for it, you'll learn on the job. You can also contact someone and get them to create a project just for you. If you're both driven and interested, they'll be happy to have you. I'm happy to be contacted by prospective students but remember that my BMedSc (Hons) was not a holiday so I did a lot of work.

Abstract

Background: In 2017, technology dominates our interactions with the world. This has allowed massive increases in connectivity with family, research and working efficiency. Interactions with technology are currently dominated by voice, cursor and keyboard control. A substantial population who are unable to utilise these technologies are those with motor paralysis. Brain-computer interfacing (BCI) is a technique that enables a user to control a computer or machine using their neural signals, consciously or unconsciously. At the same time exponential increases in computing power and the collection of big data have made CPU heavy machine learning techniques a viable research direction. BCIs can capitalise on this development in machine learning to better recognise complex and abstract neural patterns and empower those with motor paralysis.

Objectives: Determine the electroencephalographical (EEG) signal decoding differences between imagined and executed movements and investigate which imagined and executed movements are most readily decoded.

Methods: 7 healthy controls and 1 participant with partial paralysis secondary to multiple sclerosis had their EEG signals recorded while they executed and imagined a variety of tasks. Sessions were completed from June 2017 to September 2017 at University of Melbourne. Participants were instructed to clench their right/left hand, plantarflex their right/left foot and imagine walking. Limb movements were performed as both executed and imagined tasks. The power spectral densities produced after each task were used as the feature set and a support vector machine classifier was used to classify between different classes.

Results: Analysis of healthy controls shows that all executed and imagined movement tasks can be reliably decoded from rest with higher accuracy than chance. In general, executed accuracy is significantly higher than imagined accuracy with a mean accuracy of 75% and 71% respectively. Inter-task classification accuracy was lower than task-rest classification accuracy and 3+ task classification could be achieved significantly above chance level.

Conclusion: EEG can be used to classify executed and imagined tasks from rest however more trials are needed for higher inter-task classification accuracy. Analysis showed that the partially paralysed participant's decoding accuracy lay within the range of non-paralysed participants' however more participants are needed to confirm this phenomenon. Further work should be done in validating classification differences in those with total and partial paralysis.

Gowri Shivasabesan

Missing Data in Trauma Registries

Associate Professor Gerard O'Reilly, Professor Biswadev Mitra, National Trauma Research Institute,
School of Public and Preventive Medicine

After four years of medicine, I wanted to do something a bit different that combined my interests in research and public and global health. I had heard great things about my supervisors and was really interested in my project, which was under a much larger collaboration between Australia and India to help develop trauma systems in India (the AITSC).

I had a fantastic experience and learnt so much. Doing a BMedSci has given me new skills in understanding, appraising, and conducting research. I was also able to learn a lot about health in another country, and visit India to gain some 'on the ground' perspectives on my project. I'd like to thank my supervisors, everyone at the NTRI, and all those involved with the AITSC for making my year unforgettable.

I would highly encourage people to consider doing research; If you have any questions please feel free to shoot me an email at gsgowri16@gmail.com

Abstract

Background: Trauma registries play an important role in monitoring and improving trauma care. Registry data can inform a range of processes including clinical and policy interventions. However, missing data in registries can bias results and data interpretation if not appropriately managed. India faces a very high injury burden; to help alleviate it, a trauma registry has been developed across four hospitals as part of the Australia-India Trauma Systems Collaboration (AITSC). Previous studies on trauma registries have found varying levels of data completeness and have established that certain variables are more likely to be abnormal when missing. Hence, this thesis aims to examine how missing data are addressed in contemporary research based on trauma registries, and then to assess the extent and predictors of missing data in the AITSC trauma registry. Specifically, the relationship between mortality and missing data on key "first-taken" physiological variables will be examined.

Method: The thesis consisted of two main parts. Firstly, a systematic review was conducted, assessing the extent that contemporary manuscripts based on trauma registries quantify missing data and the methods used to manage such observations. Secondly, a study was conducted to evaluate the extent of missing data in the new AITSC trauma registry, and examine the association between patient hospital mortality and other predictors of missing physiological data [systolic blood pressure (SBP), heart rate (HR), Glasgow Coma Scale (GCS), respiratory rate (RR)].

Results: The systematic review included 539 manuscripts; more than half of these (295, 54.7%) did not quantify the extent of missing data for any variables. Out of those studies where the method of managing missing data could be identified, the majority used complete case analysis (almost 80%). The study of the AITSC registry found most variables missing less than 20% of observations (54 variables, 73.0%), with high rates of missingness in pre-hospital, hospital arrival, in-hospital complications, and 'time' variables. 808 (18.1%) patients were missing first in-hospital SBP, HR, GCS and/or RR observations. Hospital death was found to predict missing physiological data. Other predictors identified were: patient arrival time out-of-hours, hospital of care, 'other' place of injury, and blunt force or sharp force mechanism of injury (as compared to road traffic incidents). Assault/homicide as intent of injury (compared to unintentional intent), and occurrence of chest x-ray were predictors of not missing complete first-physiological data.

Conclusions: This first assessment of missing data in the AITSC registry found most variables well-collected with only a small number showing high rates of missing data. Hospital death, a proxy for more severe injury, predicted missingness of first in-hospital physiological variables. The completeness of these variables would likely be improved by: the adoption of data collectors 24 hours a day, implementation of data collection procedures used in assault (police/medico-legal) cases; and the sharing of recording processes and lessons between hospital sites. Better data collection will help improve the quality, validity, and usefulness of the registry to improve the care and outcomes of injured patients in India.

Neda So

Accident and Emergency presentations for Adverse Events Following Immunisation in the second year post-introduction of the 4CMenB vaccine: an observational study in Oxfordshire

Prof Jim Buttery, Professor of Paediatric Epidemiology. Departments of Epidemiology and Preventative Medicine & Paediatrics, School of Public Health and Preventive Medicine & School of Clinical Sciences, Monash University; Infection and Immunity, Monash Children's Hospital; Monash Immunisation, Monash Health; Murdoch Children's Research Institute; Ritchie Centre, Hudson Institute; Clayton, Victoria, Australia.

Dr Matthew Snape, NIHR Oxford BRC Consultant in Paediatrics and Vaccinology, Oxford Vaccine Group, Department of Paediatrics, University of Oxford; John Radcliffe Hospital, Oxford University Hospitals NHS Trust; Oxford, UK.

Department of Biomedical Engineering

During fourth year of the MBBS(Hons), I decided to intermit the following year to complete a BMedSc(Hons) in paediatrics. I wanted to explore the world of research, gain new skills, and experience a year studying abroad, and was fortunate enough to take on a project commenced by Viveka Nainani and under the joint supervision of Dr Matthew Snape in Oxford and Professor Jim Buttery in Monash. In Oxford, I had the pleasure of joining Green Templeton College, and working within the renowned Oxford Vaccine Group and the A&E Department of the John Radcliffe Hospital.

This experience has become the most challenging, rewarding and enjoyable academic year I have ever had. Not only was Europe at my doorstep for travelling, but I also lived and worked in a historic centre of global academic and research excellence. The best highlights were presenting our research at the EMGM and MRF conferences in Prague and London respectively, and meeting students and colleagues from all over the world.

If you're interested in clinical research in paediatrics, vaccinology, or doing a BMedSc(Hons) in the UK, please feel welcome to contact me on Facebook or via email at nedaso(at)gmail(dot)com. I would highly recommend a BMedSc(Hons) year abroad.

Abstract

Background: Invasive Meningococcal Disease is a major infectious cause of death in childhood, of which meningococcal B is a major cause. From September 2015, a meningococcal vaccine (4CMenB) was introduced into the United Kingdom routine immunisation schedule for infants, with booster doses at 12 months beginning in May 2016. However, an increase in presentations to Oxfordshire Accident and Emergency (A&E) departments for acute vaccine reactions was observed in the year following the introduction of 4CMenB into the UK routine infant immunisation schedule in September 2015. This increase (from an annual average of 12 infants with vaccine reactions in 2013/2015, to 38 infants in 2015/2016) was observed at 2 months (increase from 1.03 to 3.4 per 1000 immunisations) and 4 months (0.14 to 1.13 per 1000 immunisations) but not at 3 months, when 4CMenB was not given.

Aims: To ascertain whether this increase in infant A&E presentations would continue into the second year post-4CMenB introduction, and whether this would be apparent in the first cohort of toddlers receiving a 12-month booster dose from May 2016 (an age at risk of febrile convulsions). To also determine rates of prophylactic paracetamol use in children who present.

Methods: A retrospective review of electronic hospital records identified all 1- to 6-month olds presenting to Oxfordshire A&E departments between September 2016 and August 2017, and all children aged 11-18 months presenting between January 2015 and August 2017 (i.e. 16 months before and after the 4CMenB booster for 12-month olds). The presentations of potential vaccine reactions occurring within 48 hours of immunisation were classified as 'probable' or 'possible' vaccine reactions or as 'not related'.

Results: A sustained increase was observed in the 1-6 month infant population in the second year (2016/2017), with 43 presentations for vaccine reactions (24 at the 2 month immunisation episode, 3 at 3 months and 22 at 4 months). At 2 and 4 months combined the rate increased from 0.574 per 1000 doses of vaccine pre-4CMenB, to 2.702 post-4CMenB (OR=4.714, $p<0.001$), but there was no significant change at 3 months (OR=1.478, $p=0.425$).

In the 16 months pre-4CMenB immunisation of 12-month olds, there were 9 AEFI-related A&E presentations for vaccine reactions at that age, including one case of febrile convulsion. In the 16 months following, there were 14 presentations, including three cases of febrile convulsion. However the change was not significant, with the rate at 0.877 per 1000 doses pre-4CMen, and 1.578 post-4CMenB (OR=1.799, $p=0.163$).

49.0% of infants and 30.4% of toddlers were admitted for further management.

In a pilot study of paracetamol use, 8 of 8 children who presented had been given the 1st dose prophylactically.

Conclusions: Presentations, admissions and invasive management of infants to A&E for vaccine reactions remain higher in the second year post-4CMenB compared to the pre-4CMenB era, despite following prophylactic paracetamol guidelines. However, rate of presentation at 12 months showed no significant change. While this does not detract from the success of the 4CMenB campaign, it highlights the need for a safer and less-invasive approach to managing 4CMenB-related AEFIs.

Ashleigh Spittle

The effect of lipids on atherosclerotic burden as quantified by carotid intima-media thickness

Professor Walter Abhayaratna, The Canberra Hospital

I decided to do a BMedSc at the end of fourth year to take a break from clinical studies and learn more about medical research. I chose to relocate to Canberra for the year to make some new contacts outside the Monash circle and get out of my comfort zone. This proved to be very rewarding as I got to know lots of people working in clinical trials in Canberra and was able to brush up on my clinical knowledge while living and working with some preclinical ANU medical students. My supervisor, while very busy and sometimes hard to schedule time with, was very enthusiastic and encouraging all year, and pushed me to have a clear understanding of the theory behind epidemiological studies and statistics; something I didn't realise I knew so little about until I started the year. I've learned that I don't really enjoy sitting at a desk all day and am looking forward to getting back into the clinical setting next year, but that research is something I hope to continue one day alongside clinical practice, particularly expanding on the public health and preventative medicine aspects of paediatrics and cardiology that I studied this year.

Abstract

Background: Cardiovascular disease (CVD) is a major burden of disease in Australia. Atherosclerosis is the pathological disease process behind CVD, and has its origins in childhood due to the combined effects of cardiovascular risk factors: dyslipidaemia, hypertension, obesity, diabetes mellitus, smoking, age, sex, poor diet, and physical inactivity. Carotid intima-media thickness (CIMT) is a validated surrogate outcome measure for subclinical CVD, correlating with the early stages of atherosclerosis. There is no one lipid variable that is most predictive of subclinical disease in previous studies. No studies have investigated the longitudinal effect of lipids on childhood or adolescent CIMT.

Aims: This study aimed to investigate if lipid levels are related to CIMT in children, and to examine if and how cardiovascular risk factors modify the relationship between lipids and CIMT in children.

Methods: Children aged 7-8 were allocated to control and intervention groups for physical education intervention by school. Repeated measures were taken of fasting serum total cholesterol (TC), LDL cholesterol, HDL cholesterol, and triglycerides (TG) over four observation periods in 2005, 2007, 2009, and 2013 (ages 8, 10, 12, and 16). CIMT was measured in 145 children in 2013. Repeated measures of blood pressure (BP), height, weight, physical activity, cardiorespiratory fitness, percentage body fat, and percentage visceral fat were also taken at each study observation. A summary "load" measure of each lipid component and other risk factors was calculated as an average of the four observations, and binary risk categories created from risk factor continuous data.

Results: Significant trends in lipids were observed over four years; TC, LDL, and HDL decreased, TG increased. Analysis of mean CIMT by quartile of lipid load variables showed CIMT to be significantly higher among the top quartile of TG compared with lower three quartiles (0.442mm v. 0.424mm, $p<0.03$). No other lipid variables were associated with CIMT. Linear regression analysis showed a weak positive relationship in females between TG load and CIMT and the TG/HDL ratio and CIMT (α=0.33 and 0.36 respectively, $p<0.05$). A weak linear relationship between the TG/HDL ratio and CIMT was found in children with "low risk" systolic BP below published risk levels, body mass index (BMI) >85th percentile according to WHO references, and physical activity <25th percentile (α= 0.35, 0.37, 0.27 respectively, $p<0.05$), and a strong linear relationship was shown in the high risk systolic BP group (α=0.96, $p<0.05$). No significant associations between lipid load variables and CIMT were shown in logistic regression analysis adjusting for sex, BMI, and physical activity.

Conclusion: This study was the first to examine the longitudinal impact of lipids on childhood CIMT. TG and the TG/HDL ratio are predictive of increasing CIMT levels and therefore subclinical disease in our cohort. This is in line with evidence showing that high TG is atherogenic, particularly when associated with low HDL in overweight and obese populations. Due to limitations from relatively low sample size and use of summary variables, this study may have lacked sufficient power to assess the relationship between other lipid variables and CIMT in children.

Myuran Sritharan

Interrelationship among different muscle measurements and the association of muscle properties with knee pain and function in people with knee osteoarthritis

Dr Yuanyuan Wang, Dr Monira Hussain – School of Public Health and Preventative Medicine – Musculoskeletal Epidemiology Unit
Department of Biomedical Engineering

I completed my project at the School of Public Health and Preventative medicine, after my fourth year of MBBS. I have a keen interest in bones, muscles and pain and found the perfect project to undertake.

Throughout the year, I have learnt a great deal about evidence based medicine and epidemiology. My supervisors were both very supportive and tutored me in a range of different aspects including MRIs, statistical analyses and scientific writing. Conducting a project in the in a musculoskeletal field of research has also given me the opportunity to complete extensive reading and be well versed in topics which I am keen to pursue in the future.

I have thoroughly enjoyed my honours year and would encourage who is thinking about it to take the leap and go for it.

Abstract

Background: Knee osteoarthritis is one of the leading causes of disability worldwide. Current management is centred around symptomatic relief rather than a cure. Research shows that local muscle properties are associated with knee pain and functional decline. Further clarity into what specific muscle properties are relevant in the pain mechanism of knee osteoarthritis may prompt development of more targeted interventions. Commonly assessed muscle properties in knee osteoarthritis include quadriceps cross-sectional area (CSA), quadriceps strength, fat infiltration and fat-free mass. However, no study has examined all four muscle properties within the same project.

Aims: The aims were (i) to examine the interrelationship among vastus medialis CSA, quadriceps strength, vastus medialis fat infiltration and fat-free mass; (ii) to investigate the relationship between each muscle property and knee pain/function; and (iii) to examine the association of demographic/lifestyle factors with each of the four muscle properties, in those with symptomatic knee osteoarthritis.

Methods: A cross-sectional study was performed in 174 participants with symptomatic knee osteoarthritis. Height and weight were measured and body mass index calculated. Data on demographic and lifestyle factors were collected using questionnaires. Knee pain and function were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index. Quadriceps strength and fat-free mass were measured using dynamometry and bio-impedance analysis respectively. Vastus medialis CSA and vastus medialis fat infiltration were measured from magnetic resonance imaging. Spearman's correlation and multiple linear regression analysis were conducted.

Results: Vastus medialis CSA was positively associated with quadriceps strength ($r=0.404$, $p<0.001$) and fat-free mass ($r=0.622$, $p<0.001$). Quadriceps strength was also positively associated with fat-free mass ($r=0.537$, $p<0.001$). These correlations remained significant after adjustment for age, gender, body mass index and physical activity. Vastus medialis fat infiltration was not significantly associated with vastus medialis CSA, quadriceps strength, or fat-free mass.

Greater vastus medialis CSA was associated with lower WOMAC pain (B-coefficient=-8.662; $p=0.013$) and function (B-coefficient=-41.795; $p<0.001$) scores. Quadriceps strength, vastus medialis fat infiltration or fat-free mass were not significantly associated with WOMAC pain or function score. ($p>0.05$)

Males had greater vastus medialis CSA (B-coefficient=2.992; $p<0.001$), quadriceps strength (B-coefficient=52.568; $p<0.001$) and fat-free mass (B-coefficient=19.151; $p<0.001$) than females. In males, age was negatively related with vastus medialis size (B-coefficient=0.086; $p=0.021$) and quadriceps strength (B-coefficient=-1.939; $p=0.011$). Additionally, BMI was positively associated with vastus medialis CSA (B-coefficient=0.095; $p<0.001$), vastus medialis fat infiltrate (B-coefficient=0.108; $p<0.001$) and fat-free mass (B-coefficient=0.700; $p<0.001$).

Conclusions: This study found that vastus medialis CSA, quadriceps strength, and fat-free mass were moderately interrelated. Also, vastus medialis CSA was associated with knee pain and function, however other muscle properties were not. This study has identified vastus medialis CSA as the specific property relevant to knee pain and function in symptomatic knee osteoarthritis. Targeted invention which increases vastus medialis CSA may be beneficial in those with symptomatic knee osteoarthritis to reduce knee pain and improve function. This may provide a backbone for research into further management approaches.

Jessica Stark

Human amnion epithelial cell derived exosomes as a treatment for perinatal brain injury

Dr Bryan Leaw and Dr Rebecca Lim, The Ritchie Centre, Hudson Institute of Medical Research

I chose to do a Bachelor of Medical Science (Hons) after fourth year as I needed a break from clinical studies and wasn't yet ready to finish up with med school. I'm interested in Obstetrics and Gynaecology and wanted to do a lab based project, so I decided to undertake my research at The Ritchie Centre. With so many fellow medical students always around, this was the best decision I could have made. I chose my project as I wanted to unlock the potential of placental-derived stem cells and thought I could cure cerebral palsy, how naïve I was. However, I gained an enormous amount of knowledge about research and developed new skills in the laboratory. Throughout all the challenges of the year I learnt how to deal with different (and difficult) people and that I can achieve more than I thought possible of myself. I also was fortunate enough to obtain a first author publication in the course of the year. Feel free to contact me if you have any questions via email at jessicaclarestark@gmail.com

Abstract

Background: Perinatal brain injury can result from inflammation, hypoxic-ischaemia, haemorrhage or a combination of these processes, though evidence describes inflammation as most responsible for long-term injury. Currently, there is a lack of treatment options available to those who suffer brain injury during the perinatal period. However, in recent years there has been increased research into stem cell therapy.

Amnion membranes have been used in wound healing since as early as 1910, and the epithelial cells derived from the amnion of human placentae has become a focus in regenerative medicine. These cells have been shown to be anti-fibrotic and anti-inflammatory, improving outcomes in a range of diseases including but not limited to bronchopulmonary dysplasia and perinatal brain injury. Recent findings indicate conditioned medium from these cells may be responsible for the improved outcomes seen, hence greater research into the extracellular vesicles released by the amniotic epithelial cells (hAEC) is warranted.

In this study, I investigated the modulation of astrocyte activation and proliferation by hAEC derived extracellular vesicles (hAEC-EV) during inflammatory stimulation. Previous studies showed hAEC-derived conditioned media reduced astrogliosis, thus I sought to elicit further information about the effect of hAEC-derived exosomes on astrocytes stimulated with an inflammatory cytokine.

Method: This study explored the effect of inflammatory stimulation on astrocyte reactivity, proliferation and behaviour, and the ability of exosome treatments to modulate this. hAEC-derived exosomes were isolated from the placentas of six women by differential centrifugation. These samples were subsequently verified and quantified by BCA, electron microscopy and nanoparticle tracking analysis. Astrocytes and neurons were isolated from healthy mice, and cultured prior to the in vitro experiments. Following stimulation with IL-1α, exosomes were immediately added to pure astrocyte cultures, in doses of 1αg or 5αg. Immunocytochemistry was performed to assess astrocyte reactivity, an MTS assay investigated proliferation and the xCelligence RTCA SP system measured the adherence and proliferation of the astrocytes in real time.

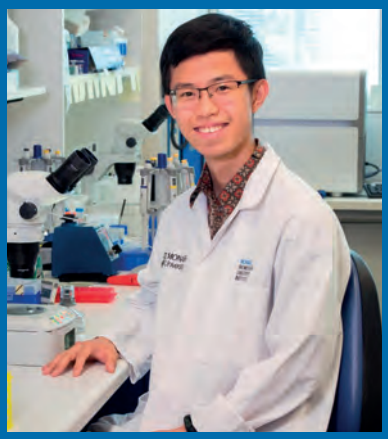
Results: A significant portion of my year was spent developing and optimising protocols critical to the success of my experiments, thus limited data was collected. Also, due to inadequate numbers of technical replicates and large variability between hAEC donors, I was unable to draw conclusions from the results obtained. However, despite clinical significance, it was observed that exosomes may decrease reactivity of the cells as evidenced by decreased GFAP area coverage and intensity, compared to no treatment. Furthermore, exosomes appeared to decrease proliferation of the cells as measured by the MTS assay. However, the xCelligence results varied across three experiments and thus no conclusion could be drawn.

Conclusions: Whilst it appears exosomes may be able to modulate astrocytes during inflammation, it is also possible the exosomes elicit their effect on other glial cell types or on neurons directly. Further investigations are required to better understand hAEC-derived exosomes and their therapeutic potential. The ultimate long term goal is a safe and efficacious cell-free treatment to improve outcomes related to perinatal brain injury.

Andre Elton Heryanto Tan

Deciphering the Fundamental Functions of Syndecan in the C. elegans Germline

Supervisor: Associate Professor Roger Pocock
Co-supervisor: Dr Sandeep Gopal



I am a medical student from Indonesia that took a one-year Honours research program in Monash University in my fourth year. I have taken interest in encrypting mechanistic functions of biological molecules as I find them very interesting and challenging to be able to understand how these molecules interact with the environment to carry out their functions in the system. Moreover, such knowledge can be further used in future studies to explain certain medical situations where the molecules are involved in diseases and help in creating new potential medicines. It was one of the most difficult year in my studies, but it taught me precious lessons that help me learn to think with a broad perspective, confronting problems in various ways, and learn the importance of a team in research.

Abstract

Background: Syndecan is a type-I transmembrane proteoglycan and a member of the cell surface heparan sulfate proteoglycan family. In C. elegans, syndecan (SDN-1) is a homologue of syndecan-2 in mammals and regulates multiple development processes such as vulval development, neuronal migration and axon guidance. In the absence of syndecan, the brood size of C. elegans is also significantly reduced, indicating a germline defect.

Method: To study the role of syndecan in germline development, we performed DAPI and phospho-histone H3 (pH3) staining on wild type and sdn-1 mutant germlines. We also performed germline-specific RNA-sequencing followed with qPCR validation to identify genes that are regulated by syndecan signalling. In addition, we examined the requirement of the heparan sulfate (HS) chains of syndecan during germline development.

Results: Our results show that the absence of syndecan leads to significant reduction in mitotic region length and in the number of pH3 positive cells in the germline. From the gene expression analysis, we found that gld-1, gld-3, gld-4, glp-1, and lag-1 were downregulated in the germline of sdn-1 mutant animals. We also found that the lipid transport and lipid metabolism genes vit-5, vit-4, elo-5 were downregulated and lipl-1 was upregulated.

Conclusions: Our results highlight a HS-dependent function of syndecan during germline stem cell development possibly through regulating the rate of proliferation of germline stem cells by GLP-1/Notch signalling and the meiosis pathway through gld-1, gld-3, and gld-4 that are involved in oocytes maturation to produce progeny. In addition, syndecan is also involved in mediating lipid transport for the maturation of oocytes through modulating vit-4 and vit-5 lipid transport family members.

Sarthak Tandon

Skin Closure Techniques in Children Undergoing Elective Paediatric Surgical Procedures

Mr. Ramesh Nataraja – Monash Children's Hospital, Monash University
Mr. Peter Ferguson – Monash Children's Hospital

I undertook my BMedSc(Hons.) this year after completing my fourth year of medicine. Having always had an interest in research and academic medicine, I hoped to gain formal experience in clinical research and also explore a field of medicine I was interested in. I was fortunate enough to complete my BMedSc(Hons.) in the Department of Paediatric Surgery at Monash Children's Hospital, under the supervision of Mr. Ramesh Nataraja and Mr. Peter Ferguson. With their guidance, I had the opportunity to design and conduct a randomised controlled trial which allowed me to experience the various facets of clinical research – from completing the initial ethics application, to recruiting patients, to following up study participants.

I have throughly enjoyed this year and have learnt a lot about clinical research whilst also developing my research skills and gaining an insight into paediatric surgery as a specialty. I felt very well-supported by my supervisors and Department and am extremely grateful to them for all of their guidance, advice and teaching throughout the year. I would highly recommend the BMedSc(Hons.) program to any student with an interest in clinical research.

Abstract

Background: The closure of a surgical wound is usually completed in layers from deep to superficial. Wound closure has traditionally been achieved using sutures, however, closure of the skin can also be achieved using various alternatives including adhesive glue, adhesive tape and staples or a combination of these techniques. The evidence comparing these techniques in paediatric surgical cohorts is limited. Only one prospective study has compared adhesive tape with adhesive glue. It has also not been assessed whether combination closure with sutures and adhesive glue or adhesive tape alters outcomes compared to wound closure with sutures alone.

Method: We designed a randomised controlled trial comparing outcomes in children undergoing elective procedures following skin closure of surgical incisions with sutures and adhesive glue, sutures and adhesive tape or sutures alone. Our aims were to determine:

1. Which technique yielded optimal outcomes
2. Whether skin closure with adhesive glue achieved better results compared to skin closure with adhesive tape
3. Whether combination closure with sutures and adhesive glue or adhesive tape improved outcomes compared to skin closure with sutures alone

Evaluated endpoints included wound cosmesis at 6 weeks post-operatively (assessed by parents using a visual analogue scale and two clinicians using a visual analogue scale, the Hollander Wound Evaluation Scale and Stony Brook Scar Evaluation Scale), parental satisfaction with the technique used 2 and 6 weeks post-operatively as assessed using a 5- point Likert scale and rates of wound infection or dehiscence.

Children (age ≤18 years) presenting to Monash Children's Hospital for an elective general surgical or urological procedure were eligible for the study. Participants were randomised to either skin closure of wound/s with sutures and adhesive tape, sutures and adhesive glue or sutures alone. Wound closure materials and technique were standardised. Follow-up was conducted 2 weeks post-operatively via phone call and email, and at 6 weeks post-operatively in the Outpatients Clinic.

Results: Recruitment is still ongoing, however, we conducted an interim analysis with 82 patients – 24 patients (n=26 wounds) in the adhesive glue group, 28 patients (n=34 wounds) in the adhesive tape group and 30 patients (n=35 wounds) in the sutures-only group. There were no significant differences in median patient age, gender, type of surgical procedure or location of surgical wounds between groups. We found no significant difference in parent- or clinician-rated wound cosmesis between the groups 6 weeks post-operatively. Parents tended to rate satisfaction highly, with no differences between groups at 2 weeks (p=0.0914) or 6 weeks (p=0.5461). There were no confirmed cases of wound infection or dehiscence.

Conclusions: Results from our preliminary analysis demonstrated equivalence between techniques in terms of evaluated endpoints. Adhesive tape and adhesive glue yielded similar outcomes when used for skin closure. Combination closure did not improve results when compared to skin closure with sutures alone. Based on our findings, all three techniques can continue to be suitably used for skin closure in children undergoing elective general surgical and urological procedures. However, completion of recruitment and future studies are required to confirm these findings.

Tanya Tang

Effects of Inflammation on Human Umbilical Cord Blood: Implications for Therapy

Dr Courtney McDonald: The Ritchie Centre, Hudson Institute of Medical Research
Dr Suzie Miller: Department of Obstetrics and Gynaecology, Monash Health

As a would-be-final year student, I had decided to forgo the safety known as Ward Rounds As A Medical Student and set out to conquer the dark land of Research. First, I needed a companion. After careful month or so of deliberation, I settled on Umbilical Cord Blood to help me on my journey of mastering the Pipette. With UCB and INF-γ by my side, I thought I was ready for all the beasts that resided in Research.

I was wrong.

But with the help of my mentor and supervisor Dr Courtney McDonald, I battled and successfully defeated the horrors known as Late Nights At The Lab, Poor Cell Recovery, Why Is There A Fold Change Of 7 Million+, and Falling Asleep 3 Hours After Drinking Red Bull. I have become a more experienced Medical Student and more world-weary (although that might just be an age thing). You can now find my bitter heart at ttan48@student.monash.edu if you seek further advice for defeating Research.

Abstract

Background: Hypoxic ischemic (HI) injury results in neuroinflammation and leads to brain injury. Currently there are limited therapy options. Umbilical cord blood (UCB) and its individual components has been proposed as a potential treatment for HI injury, with many animal studies supporting its benefit. However, given cells are transplanted into a highly inflamed environment that may affect the function of the cells, this may have implications for the optimal timing of cell administration. Currently there is no data on the effect of inflammatory stimulation of different UCB cell types. Our study aimed to observe the effects of inflammation on UCB and to determine if there were any changes in cell surface markers and gene expression.

Method: UCB was obtained from healthy human term caesarean sections and isolated into: mononuclear cells (MNCs), T regulatory cells (Tregs), endothelial progenitor cells (EPCs), haematopoietic stem cells (HSCs) and monocytes. Each cell lineage was cultured under four conditions: media, media with TNF-α, media with IFN-γ, and media with TNF-α & IFN-γ. After 16 hours in culture, cells were harvested and processed to analyse cell surface markers and gene expression using quantitative real-time PCR.

Results: The main finding of this study was no overall changes in cell viability or the expression of HLA-ABC was observed in UCB cells when stimulated with inflammatory cytokines. However, we did find a significant increase in HLA-DR expression when HSCs were stimulated with TNF-α (79.4±3.9% vs 95.77±0.55%, $p<0.01$) or TNF-α and IFN-γ (79.4±3.9% vs 98.3±0.27%, $p<0.005$), compared to controls. This was similar for monocytes where HLA-DR expression increased when stimulated with IFN-γ (8.18±1.24% vs 51.42±4.99%, $p=0.0001$) or TNF-α and IFN-γ (8.18±1.24% vs 41.63±4.45%, $p<0.001$), compared to controls. No statistically significant difference was detected in gene expression. However, there was a trend towards increased expression of chemokine receptor genes in MNCs and EPCs after inflammatory stimulation. Inflammatory gene expression also trended towards an increase in MNCs, EPCs and HSCs when stimulated with all cytokines. Growth factors, BDNF and VEGF, were increased in EPCs and HSCs although Tregs downregulated their expression when these cell types were stimulated with inflammatory cytokines.

Conclusions: Our results show that in an inflamed environment UCB cell viability is not affected. However, the increase of HLA-DR on HSCs and monocytes could potentiate a rejection of UCB, which requires consideration. The increase in chemokine receptor genes we observed could mean the if cells were stimulated in the inflamed environment after transplantation, their ability to home to the sites of injury may be increased, but the increased expression of inflammatory genes, such as IL-1α and MCP-1 may further add to the initial HI injury. As a future direction, we still need to analyse the protein expression after stimulation to confirm these changes in gene expression. From this study, we suggest that UCB transplantation during a time of peak inflammation may have consequences for the markers expressed by the cells and the cytokines they produce. Therefore, we believe that UCB transplantation should be avoided in a period of high inflammation.

Louisa Thong

Epidemiology of Episcleritis and Scleritis in Metropolitan Melbourne

Associate Professor Lyndell Lim, Centre for Eye Research Australia, The Royal Victorian Eye and Ear Hospital, University of Melbourne
Associate Professor Anthony Hall, Department of Ophthalmology, Alfred Health

I completed my BMedSci at the Centre for Eye Research Australia (CERA) following the completion of my fourth year of placement. I've always had a key interest in ophthalmology but quickly realised that there was limited exposure to this field during medical school. I chose to do a clinical project at CERA because it is an institution that constantly strives to be at the forefront of eye research and has many subspecialty research units. My work with the Clinical Trials Research Unit primarily involved data collection and retrospective analysis, and this also provided me with a unique opportunity to develop and improve my practical skills in ophthalmology during my time at The Royal Victorian Eye and Ear Hospital. The support and level of excellence at CERA is unparalleled, and I especially gained valuable skills through one-on-one statistical guidance and training. If you are interested in ophthalmology please do get in touch if you have any further questions.

Abstract

Background: Episcleritis and scleritis are two distinct but commonly confused forms of ocular inflammation. However, population-based studies on the epidemiology of episcleritis and scleritis are sparse. The aim of this retrospective study was to determine the incidence and prevalence of episcleritis and scleritis in a well-defined population of Metropolitan Melbourne, and describe the clinical characteristics of both conditions. This study also evaluated the accuracy of diagnosis and appropriateness of management of episcleritis and scleritis.

Method: All patients with episcleritis or scleritis seen at the Emergency Department (ED) and Ocular Immunology Clinic (OIC) of The Royal Victorian Eye and Ear Hospital (RVEEH) were identified from November 2014 through to October 2015. Retrospective chart review was conducted to confirm the diagnosis, establish time of onset and disease subtype. Additional data collected included underlying aetiology and ocular complications. Age and gender-stratified population data from the Australian Bureau of Statistics 2015 were used to calculate incidence and prevalence. Diagnostic accuracy was assessed in all identified episcleritis and scleritis patients, by comparing the initial diagnosis in the ED to the final diagnosis in the OIC or by independent chart review. Investigations ordered were reviewed and compared between initial visits to the ED, the Acute Ophthalmology Service (AOS) and the OIC within the RVEEH.

Results: The adult population of Metropolitan Melbourne was 3,500,331 people. During the study period, there were 147 new-onset and 23 prior-onset cases of active episcleritis, and 34 new-onset and 20 prior-onset cases of active scleritis. For episcleritis, this yielded an incidence of 4.2 per 100,000 person-years and a 12-month period prevalence of 4.9 per 100,000 persons. For scleritis, the incidence was 1.0 per 100,000 person-years and the 12-month period prevalence was 1.5 per 100,000 persons. There was 1 case of infectious scleritis. Of those with non-infectious scleritis, diffuse scleritis was the most common (62.3%), followed by nodular (29.5%) and posterior scleritis (8.2%). Most cases of episcleritis were simple (86.4%) with the remaining being nodular. One-third (33%) of scleritis patients had an associated systemic disease compared to 10% of those with episcleritis. Ocular complications were seen in 3% of episcleritis eyes versus 46% of scleritis eyes, with the most common being anterior uveitis and ocular hypertension. At presentation, the diagnostic error rate was 13% for those given an initial diagnosis of episcleritis and 48% for those who received a diagnosis of scleritis. The majority of presumed episcleritis patients (94%) did not receive any investigations in the ED, as appropriate. Investigations judged to be appropriate for presumed scleritis were not ordered in a significant proportion of patients in the ED (33%) and AOS (21%), but ordered in all scleritis patients seen in the OIC.

Conclusions: In this first Australian study, population rates of episcleritis and scleritis were lower compared to previous US studies. Clinical characteristics of this population confirmed that episcleritis often remained benign, whereas scleritis was more severe in nature. Finally, the study highlighted the ongoing difficulty in making the initial diagnosis of episcleritis or scleritis, as well as the varied investigation of these patients.

Tiffany Tie

A brief intervention for obesity in a tertiary hospital

Supervisor: Professor Wendy Brown
Centre of Obesity Research and Education, Monash University
Department of Upper Gastrointestinal Surgery, The Alfred Hospital
Co-supervisor: Kirstan Corben

My honours year with the Centre of Obesity Research and Education (CORE) was an amazing experience. Having spent two clinical years rural as an ERC student, I was excited to be at The Alfred. I was given the opportunity to coordinate a clinical trial on using brief interventions to promote obesity management. This was a challenging and exciting undertaking which helped me to develop a range of skills, build confidence and gain more perspective of the healthcare system.

A huge number of incredible people across many disciplines and teams were involved in the trial. I cannot thank them enough for their support and for making the project possible. In particular, I would like to express my gratitude to my supervisors Professor Wendy Brown and Kirstan Corben, and to Dr Geraldine Ooi for her mentorship over the year.

Feel free to get in touch if you have any questions!

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Abstract

Background: Obesity is a complex and prevalent condition with significant health and economic impact. In the tertiary hospital setting, discussing weight management with overweight and obese patients is often neglected. Brief interventions, defined as time-limited interactions aiming to promote behaviour change, are potential strategies to address this. They are effective in hospitals for smoking and heavy alcohol use and show promising results for obesity in primary care. However, brief interventions for obesity have not yet been studied in the hospital setting.

This study investigates the prevalence of obesity amongst inpatients and occurrence of opportunistic screening. We then aimed to determine the efficacy and practicality of implementing a brief intervention to encourage weight loss.

Methods: To assess the prevalence of obesity and opportunistic screening amongst the inpatient population, we conducted two cross-sectional studies on separate single days: the weight and the screening audits. The weight audit involved weighing all inpatients. The screening audit involved assessing bedside charts for evidence for formal screening for obesity with body mass index (BMI). Obesity is defined as BMI≥30kg/m2.

To evaluate efficacy of the brief intervention for obesity, we conducted a single-blinded randomised controlled trial at a metropolitan tertiary hospital. Participants were randomised into 'brief intervention' or 'standard care' groups. Junior doctors on the treating teams delivered the brief intervention, involving the following steps: a short discussion on obesity, provision of information pamphlets, recommendation to speak further with their general practitioner (GP), and communication from the hospital to the GP requesting weight management support. Three months post-randomisation, we contacted all participants to complete a follow-up questionnaire. Primary outcomes were based on behaviour change, and included (1) weight loss attempts and (2) follow-up discussion with GPs regarding weight management. Outcomes were assessed blinded to treatment allocation. To assess practicality and facilitate improvement of the programme, participants, hospital doctors and GPs were asked to provide feedback. Follow-up is ongoing, thus 55 participants are included in this thesis for preliminary analysis.

Results: The prevalence of obesity amongst inpatients was 21.5%. The screening audit identified that only 23.2% of inpatients were formally screened for obesity.

For the trial, we recruited 173 participants, of which 87 were allocated to standard care and 86 to brief intervention arms. Fifty participants (28.9%) were 'missed' by the doctors, meaning that trial protocol was not completed. The major barriers to delivery were time and discomfort with having the conversation.

The preliminary per-protocol analysis of 55 participants demonstrated that participants who received the brief intervention were 17.2% more likely to attempt weight loss compared to participants who received standard care (66.7% vs 83.9%, p=0.202). The brief intervention group was also 22% more likely to discuss weight management with their GP (16.7% vs 38.7%, p=0.133).

Conclusion: Obesity is a significant issue in our community which affects many hospital patients. Preliminary results suggest that a brief intervention delivered in hospital may be effective at increasing weight loss attempts and community follow-up for weight management. Follow-up for this study needs to be completed to determine final results.

Darcy Tupper-Creed

Perioperative changes in creatinine production rate in patients undergoing cardiac surgery

Dr. David McIlroy & Professor Paul Myles (Department of Anaesthesia and Perioperative Medicine, Alfred Health and Monash University)

I undertook my BMedSc with the Department of Anaesthesia at the Alfred Hospital after having completed my fourth year of medicine. My project was a prospective study looking at the detection of acute kidney injury in patients undergoing cardiac surgery, which I chose having an interest in anaesthesia and hoping to gain both some research and clinical experience. On the whole I've had a thoroughly enjoyable year, learnt a great deal, and gained invaluable insights into the world of clinical research.

Abstract

Background: Acute kidney injury (AKI) is a common complication of cardiac surgery and is independently associated with significant morbidity and mortality. A major barrier to managing and researching the syndrome is our present inability to detect renal injury in a timely manner. Serum creatinine (SCr) is the current diagnostic standard for AKI, however it is widely held to be flawed, due to it being a slow and imprecise measure of injury. Recent studies have demonstrated that early, and very small changes in SCr after cardiac surgery portend serious adverse clinical outcomes consistent with more conventional diagnostic criteria for AKI. However, a mechanism by which SCr may provide such early detection of evolving renal injury is unclear. An increase in creatinine production rate during cardiac surgery is one plausible mechanism by which an acute perioperative decline in glomerular filtration rate (GFR) may produce an earlier than expected rise in SCr. Importantly, although creatinine production rate is typically considered to be constant this has never been evaluated in the context of cardiac surgery. Thus the primary aim of this study was to test whether the rate of creatinine production changes in the perioperative period in patients undergoing cardiac surgery.

Method: We conducted a prospective observational study of patients undergoing cardiac surgery. Three distinct perioperative epochs were defined, a baseline preoperative period, an intraoperative and early postoperatively period, and a late postoperative period. Creatinine production rate was then calculated for each time period, based on the principle of mass conversation. Additional data on patient demographics and perioperative variables was collected. Differences in creatinine production rate were compared using paired, non-parametric testing. Univariate and multivariate associations between perioperative variables and the proportionate change in creatinine production rate from baseline until 24 hours postoperatively were also explored.

Results: To date, 20/50 participants have been recruited. Of these, four were excluded from this preliminary analysis due to incomplete data. All patients underwent coronary artery bypass grafting surgery with the use of cardiopulmonary bypass, the median patient age was 65 years and the median baseline weight was 85 kg. There was no significant change in creatinine production rate from the preoperative period to the intraoperative/early postoperative period, with a median proportional increase of 15% (IQR -2 to 34, $p = 0.06$). There was an increase in creatinine production rate from the preoperative period to the late postoperative period, with a median absolute increase of 1.2 µmol/kg/hr (IQR 0.7-1.7, $p = 0.01$) and a median proportional increase of 23% (IQR 12-30, $p = 0.006$).

Conclusions: Our results showed a tendency for creatinine production rate to increase in patients undergoing cardiac surgery from preoperatively through 48 hours postoperatively. This is the first study to measure creatinine production rate changes in the context of cardiac surgery. These findings may explain how an early creatinine based signal of renal injury is possible and support further research into perioperative creatinine production changes and the role of SCr in the wider search for a timely, accurate marker of AKI.

Jennifer Volaric

Interferon Epsilon in the Human Gastrointestinal Tract

Dr Edward Giles, Department of Paediatrics, Monash Children's Hospital; Department of Paediatrics, Monash University; Centre for Innate Immunity and Infectious Disease, Hudson Institute of Medical Research

Professor Paul Hertzog, Centre for Innate Immunity and Infectious Disease, Hudson Institute of Medical Research
Population Health and Health Promotion, Alfred Health

I completed my BMedSc(Hons) after my fourth year of medicine. I chose this project because I wanted to gain practical science skills, a better understanding of statistics, and see how lab work can translate to clinical medicine.

From this year I have gained not only technical skills performing experiments, but more importantly trouble shooting and problem solving skills when trying to decipher why things didn't work. I've benefitted greatly from the knowledge and experience of my supervisors and fellow lab colleagues and would like to thank them again for their patience and generosity of time. It's been a whirlwind of a year made so much better by supportive friends, family and new lab friends.

Abstract

Background: Interferon-ε (IFNε) is a novel type 1 interferon with anti-viral and anti-inflammatory properties. Unlike other type 1 interferons IFNε is not significantly upregulated in viral infection, instead in the female reproductive tract (FRT) IFNε is hormonally mediated. Current literature of human tissue is limited to the FRT. Animal studies have shown the presence of IFNε in the epithelial cells of the lung and gastrointestinal tract, and areas of the male reproductive tract. Investigations into IFNε knockout models have shown an impaired ability of tissue to respond and recover from inflammation. Inflammatory bowel disease is a chronic relapsing remitting disorder of uncertain aetiology, however type 1 interferons and their signalling pathway have been identified as significant cytokines of interest in the process of the disease.

Aim: We aim primarily to determine the presence of IFNε and its receptors (IFNAR1 and IFNAR2) in normal and inflamed human gastrointestinal tract tissue. Additionally we compared and identified differences in the pattern of IFNε in control and inflamed samples.

Method: Patients undergoing colonoscopy requiring tissue sampling were approached to request a number of additional samples to be taken. Separation into control or IBD cohort was decided based upon clinical pathology reports and medical history. Immunohistochemistry was used to localise IFNε, and IFNAR1 and IFNAR2 presence in paraffin-embedded tissue samples of the terminal ileum, caecum and rectum. Aperio Imagescope© (Leica Biosystems) Positive Pixel Count v9 was used to quantitatively assess staining. mRNA was extracted from tissue samples stored in RNAlater to perform RT-qPCR, with normalisation to the housekeeping gene 18S. RT-qPCR data was used to determine expression levels of mRNA of IFNε, IFNAR1, IFNAR2 and other related cytokines present in inflammation. mRNA expression was used to compare between IBD and control cohorts, between tissue sites, and assess correlations in expression.

Results: 16 Patients were included in this study (8 IBD and 6 Control) with a total of 40 samples. We found the IFNε was expressed constitutively and in inflammation. IFNε was localised to the epithelium and crypts in tissue samples of all sites. Quantification of staining indicated no difference in IFNε expression in sample sites or between IBD and control cohorts. Of measurable samples, RT-qPCR also showed no significant difference. However, the incidence of undetermined samples was significantly higher in the control cohort and in rectal samples. This suggests a difference between IBD and control samples exists but which we were unable to quantify.

We also observed IFNε and IFNβ expression correlates ($R=0.700$, $p<0.05$), in normal conditions, a relationship lost in inflammation. Additionally, IFNε presented as a potential mediator of the proinflammatory cytokine CXCL10, correlating significantly in inflammation ($R=0.654$, $p<0.001$).

Conclusions: We established that IFNε is expressed by the human gastrointestinal tract, primarily localised to epithelial cells. No quantifiable difference was observed comparing inflamed and 'normal' samples, however a trend of increased expression was noted in IBD samples. From correlations potential relationships between IFNε and ISGs in IBD were also identified.

Patrick Walker

Using intermittent pulse oximetry to guide oxygen therapy in neonates: a validation study

Dr Kenneth Tan, School of Clinical Sciences, Monash University
Dr Hamish Graham, Department of Paediatrics, University of Melbourne

Doing a BMedSc is a chance to complement your medical degree with an introduction to the complex and sometimes confusing world of research. I was wary of doing a research year for the sake of doing research, and wanted to make sure the project I did properly reflected my interests. I was fortunate enough to meet my supervisor at a global health research seminar early in my fourth year, and had the opportunity to marry two of my interests – global health and paediatrics – into the one project.

My project was about oxygen saturation monitoring in newborn babies, but it was also about how to design health interventions that benefit the people that need them most – and making sure those interventions don't cause unintended harm. I got to go to Nigeria and experience a beautiful country and culture, I learnt how to carry out a research project from beginning to end, and I learnt a huge amount about research, health, and health equity. I loved my project and loved my year, and would encourage anyone considering a similar style project to go for it. It's an opportunity that doesn't come round too often, and is one you'd be sore to miss.

Abstract

Background: Oxygen is an essential medical therapy that can save the lives of many neonates around the world. However, it must be used judiciously in preterm and small neonates, due to the risk of retinopathy of prematurity and bronchopulmonary dysplasia. To balance the risks and benefits of oxygen therapy, SpO2 of these infants should remain between 90-95%, requiring monitoring via pulse oximetry. Continuous monitoring is the gold standard monitoring method, but remains unavailable in much of the world, where intermittent monitoring is used instead. This study aims to evaluate the ability of intermittent monitoring to keep neonates' SpO2 within the desired range.

Method: This was a prospective, quantitative validation study with user feedback. We recruited 41 neonates admitted to the nursery of a secondary-level hospital in south-west Nigeria during a six week study period in June-July 2017. We performed concealed continuous pulse oximetry, in addition to the normal practice of intermittent monitoring three times daily. This allowed us to measure the proportion of time neonates spent within different SpO2 ranges. We also obtained user feedback from nursing and hospital management staff regarding barriers and facilitators to effective oximetry use, and how it could be improved.

Results: While receiving oxygen, preterm/small neonates spent 15.35% (95% CI 6.7-18.7%) of time within the target range of 90-95%, 78.45% (62.3-88.9) of time in hyperoxia (SpO2 >95%), and 3.25% (0.4-15.4) in hypoxia (SpO2 <85%). Term neonates and neonates not receiving oxygen therapy spent 98.9% (97.0-99.2) of time within the target range of 90-100%, and 0.3% (0.1-0.8) of time in hypoxia (SpO2 <85). Preterm/small neonates also experienced a significantly higher frequency of desaturation episodes than term neonates (9.7 v 4.3 episodes per hour; p = 0.01). Barriers to effective oximetry use included financial, equipment, and staffing constraints. Facilitators included integration of pulse oximetry into routine care, good availability of oxygen, and accessible oxygen therapy guidelines.

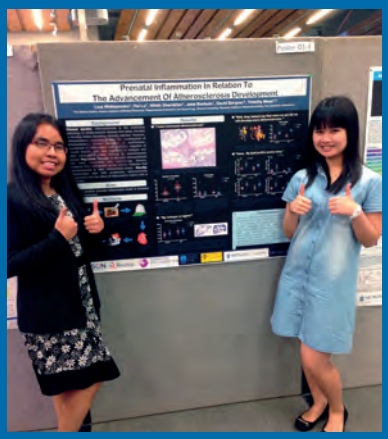
Conclusions: In this study, preterm and small neonates who required oxygen therapy spent only a small proportion of time within the target range of 90-95%, and spent a very high proportion of time in hyperoxia. This suggests that these neonates may be being subjected to an increased risk of hyperoxia-related harm. However, term neonates (in and out of oxygen) and neonates (including preterm neonates) not on oxygen spent almost all of their time within the target range of 90-100%, suggesting that the current practice of monitoring SpO2 three times per day may be appropriate in these patients.

In resource-constrained environments where continuous monitoring is not available, more frequent monitoring of neonates targeted at 90-95%, coupled with frequent training for nurses on SpO2 targeting and oxygen titration, may be beneficial. Further, in settings where continuous monitoring is possible for only some patients, it should be used preferentially in preterm/small neonates while they are receiving oxygen.

Lisa Kurnia Widiasmoko

Prenatal Inflammation In Relation To The Advancement of Atherosclerosis Development

A/Prof Timothy Moss (Hudson Institute) and Professor David Burgner (Murdoch Children Research Institute)



Hi, my name is Lisa. Im a 4th year medical student in Universitas Indonesia, however currently taking my second degree (honours) from Monash University. My honours year here was superb. Ups and downs, laugh and tears, I had them all although mostly through sleepless nights. My project was to look at atherosclerosis in relation to the presence of prenatal inflammation. It was intriguing for me why atherosclerosis was investigated in such an early age, while the disease was manifested in elders mostly. My honours project faced many difficulties just like many research would be, however I am thankful for the presence of my supervisors, research assistant, seniors, and friends who were with me through it all. I realized that it is the journey that coloured and encouraged us to walk till we reach the goal.

Abstract

Background: Atherosclerosis is the underlying pathology of cardiovascular disease that takes decades to develop before becoming clinically relevant. However, atherosclerosis originates in early life. Development of atherosclerosis involve disruption of endothelium, recruitment of inflammatory cells and lipid, migration of smooth muscle cells, and deposition of collagen and other extracellular matrix, forming an atherosclerotic plaque. Although for decades atherosclerosis has been associated with lipid-storage disease, evidence from animal and human studies indicates that atherosclerosis is often inflammatory-driven. Inflammation after birth accelerates atherosclerosis progression but the effect of inflammation before birth is unknown.

Method: To investigate the development of atherosclerosis after prenatal exposure of lipopolysaccharide (LPS, 1ng/fetus)-induced inflammation at embryonic day 15.5 by looking at collagen deposition, intima media thickness, lesion number and area, plasma lipid profile, and inflammatory cell counts in the aortic sinus and brachiocephalic artery of 13-week-old ApoE-/- mice. Data were analysed statistically using analysis of covariates. Fourteen mice received intraamniotic (IA) injection of LPS, and 14 received IA saline (for control).

Results: There was higher collagen deposition (77.50 ± 0.50% in LPS group, 77.50 ± 0.50% in control group; p=0.010) and lesion number (5.64 ± 0.68 in LPS group, 3.09 ± 0.56 in control group; p=0.004) in LPS-treated mice. Aortic lesion area (2.78 ± 0.54% in LPS group, 3.14 ± 0.22% in control group; p=0.395) and plasma lipid profile including total cholesterol (7.20 ± 1.51 mmol/L in LPS group, 8.06 ± 1.76 mmol/L in control goup; p=0.440), HDL cholesterol (0.47 ± 0.19 mmol/L in LPS group, 0.96 ± 0.37 mmol/L in control group; p=0.161), LDL cholesterol (6.20 ± 0.51 mmol/L in LPS group, 6.00 ± 0.55 mmol/L in control group; p=0.732), and triglyceride (2.00 ± 0.68 mmol/L in LPS group, 2.06 ± 0.60 mmol/L in control group; p=0.598) were not different between the two groups. Intima media thickness and inflammatory cell counts were unable to be completed due to some technical problems.

Conclusions: Prenatal inflammation appears to increase atherosclerosis. However, further studies should confirm findings in this study by doing more specific marker evaluation of atherosclerotic lesion development stage.

Kishan Wijesinghe

Examining the Inflammatory Profile of Adipose Tissue in Oesophageal Cancer

Mr. Paul Burton[1,2], Professor Matthew Watt[3], Professor Wendy Brown[1,2]
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[3]Department of Physiology, Monash University, Clayton, Victoria, Australia

After finishing fourth year of medicine in 2016, I decided to undertake a BMedSc(Hons). This year provided a perfect opportunity to gain significant skills and knowledge, as an introduction to the research world.

I was involved with a lab based surgical project, spending my time between the Alfred Hospital and Department of Physiology, Monash University. This year I was given the opportunity to spend plenty of time in theatre, as well as be involved with a diverse range of laboratory work. As a result, I gained a thorough appreciation of fundamental science and its translation into the clinical context.

I cannot thank my supervisors, the surgeons and my colleagues, both at CORE and the Biology of Lipid Metabolism laboratory enough. I have appreciated all your unwavering assistance and encouragement to make this year a success.

I would strongly recommend prospective students to pursue a BMedSc(Hons). It is a steep learning curve, however you will gain an immense amount of amazing skills and experiences. Finally, it is incredibly rewarding to be able to personally contribute something meaningful to science.

Abstract

Background: Oesophageal adenocarcinoma (OAC) carries a poor prognosis, with treatment costly and highly invasive. In the last 40 years, the incidence of OAC has risen 400%, and this is parallel to the obesity trend.

Adipose tissue, contains a dense immune cell population and secretes pro-inflammatory cytokines. There are two structurally different adipose tissue depots; visceral (abdominal) and subcutaneous (femoro-gluteal). Most of these inflammatory factors are through to originate from visceral adipose tissue, and visceral obesity is independently linked with OAC.

As the correlation between chronic Inflammation and carcinogenesis is well established, it is proposed that secreted inflammatory factors from visceral adipose tissue adjacent to the oesophagus may contribute to the development of oesophageal adenocarcinoma. However, this has never been studied.

Method: Case patients undergoing surgery for oesophageal adenocarcinoma and controls undergoing non-cancer related surgery were recruited from Alfred Health, Melbourne, Australia.

Adipose tissue was obtained from three locations; 1. Peri-oesophageal visceral (OFAT), 2. Distant visceral from the omentum (VAT), and 3. Subcutaneous (SAT).

Immune cell populations were characterised by fluorescence activated cell sorting (FACS). The cytokine expression was assessed through real time polymerase chain reactions (qRT-PCR), and enzyme-linked immunosorbent assays (ELISA).

OE33 oesophageal adenocarcinoma cells were cultured in an adipose conditioned medium from each of the tissue depots and proliferation was assessed at 24 and 48 hours.

Results: 15 case patients and 4 controls were recruited. In case patients, both visceral depots expressed a greater immune cell profile when compared to subcutaneous. This was observed in; total leukocytes (OFAT 37.9%, VAT 32% vs. SAT 21.3%, p=0.047, p=0.007), neutrophils (OFAT 8%, VAT 4.1% vs. SAT 2.2%, p=0.007, p=0.009) and non-classical monocytes (OFAT 22.3%, VAT 8.9% vs. SAT 5.2%, p=0.001, p=0.05). Total monocytes, plasmacytoid dendritic cells, CD8+ T Cells were significantly increased in distant visceral compared to sub-cutaneous.

Differences in cytokine expression were also observed in the case group. mRNA expression of IL-8 was increased in OFAT compared to SAT (8-fold vs. 2.2-fold, p=0.007). While mRNA expression was increased in VAT compared to SAT for IL-6 (p=0.04) and IL-1α (p=0.04). Increased cytokine secretion of IL-6 was recorded in OFAT and VAT when compared to SAT (OFAT 19670pg/mL, VAT 19072pg/mL vs. SAT 9714pg/mL, p=0.002, p=0.004)

mRNA expression of VEGF was significantly increased in the case population compared to control in VAT (p=0.04) and SAT (p=0.04). There were no significant differences between depots within the control population for any parameters.

At 48 hours, proliferation of OE33 oesophageal adenocarcinoma cells in adipose conditioned media were significantly increased in OFAT when compared to both VAT and SAT (OFAT 3.5-fold vs. VAT 2.4-fold, SAT 2.6-fold, p=0.02, p=0.04).

Conclusions: In OAC patients, peri-oesophageal adipose tissue does secrete factors that are promoting cancer proliferation. Visceral adipose tissue both proximal and distal to the tumour microenvironment exhibits an increased inflammatory profile when compared to subcutaneous. While this inflammation can mechanistically influence cell proliferation, the precise causative factors are yet to be elucidated.

These results justify an exploratory project to conclusively identify the exact secreted factors from peri-oesophageal adipose tissue that is directly promoting this carcinogenesis.

Jonathan Woliansky

Steroid absorption in Serial Intralesional Steroid Injections for Subglottic Stenosis

Dr. Debra Phyland – Monash Health, Mr. Paul Paddle – Monash Health

I've always wanted to be involved in medical research, which is why I chose to do a BMedSc. Being involved in prospective and retrospective clinical research has given me a unique perspective on what it means to do clinical research and the importance of evidence-based medicine. I've gained so many skills this year and feel that I've expanded my horizons.

My project was with the Department of Otolaryngology/ Head and Neck Surgery at Monash Health. Not only was I able to take part in research but I also was exposed to a variety of surgical and clinical cases and have finished this year with a deeper understanding of the specialty.

A BMedSc year isn't always easy, but it is definitely rewarding. In all, I've had a great experience, thanks in no small part to my supervisors and the Department.

Abstract

Background: Subglottic stenosis (SGS) is a pathological fibroinflammatory repair process, resulting in recurrent and excessive scarring and luminal narrowing of the upper airway. Greater understanding of its aetiology and pathophysiology has led to a paradigm shift away from surgery, towards medical therapy. One such therapy is serial intralesional steroid injection (SILSI). To date, the systemic effects of SILSI have not been studied.

Aims:

- To characterise an Australian SGS population and analyse treatment outcomes
- To study the systemic effects of SILSI for the first time.

Methods: A retrospective chart review of adult patients with SGS presenting over a 16-year period, from 2001-2017 was conducted. Demographics, comorbidities, disease morphology and treatment burden were described among aetiologies and comparisons between iatrogenic and idiopathic groups were performed. Subsequently stepwise logistical regression was employed to examine the association between clinical/surgical factors, and treatment outcome, as measured by tracheostomy incidence and dependence. Second, a prospective, single-arm, non-blinded, observational pilot study was conducted to detect the systemic effects of steroid absorption among SILSI patients. HPA axis, white cell counts and inflammatory markers were assessed pre and post procedure. Participants underwent 3-4 rounds of testing per protocol: at baseline (day 0), day 1, 7 and 28. Results: 75 patients were identified over a 16-year period. Patients with iatrogenic aetiology were significantly older ($p=0.002$), more morbid ($p<0.001$) and had worse disease, with significantly greater percentage stenosis ($p=0.015$), shorter procedure interval ($p=0.019$) and increased incidence of tracheostomy ($p<0.001$) and tracheomalacia ($p=0.003$). Meanwhile idiopathic patients were almost entirely female (97.3%, $p=0.001$) and had significantly higher rates of reflux ($p=0.029$) than their iatrogenic counterparts. When adjusted for age, sex and iatrogenic aetiology, patients with an 'American Society of Anaesthesiologists' score >2 had significantly higher odds of undergoing tracheostomy (Adjusted odds ratio [AOR]=11.23, 95% confidence interval [CI]=1.47- vi 86.17). The same was true for iatrogenic aetiology (AOR=17.33, 95%CI=1.93- 155.66) and Cotton-Myer grade 3-4 (AOR=9.84, 95%CI=1.36-71.32). Meanwhile, stroke conferred higher odds of tracheostomy dependence (AOR=9.03, 95%CI=1.01- 81.08). Surgical technique was not significantly associated with either outcome when adjusted.

Simultaneously, we recruited 4 patients for our prospective study. Despite a small sample size, cortisol levels and white cell counts changed quite dramatically. Plasma cortisol levels at baseline were 313±105.6nmol/L (mean ± SD) and dropped to 15±3.4nmol/L, 1 day following triamcinolone injection to the subglottis. 1 week later levels returned to within the normal range (269.3±47.5nmol/L) and rose further to 373.5±78.2nmol/L at 28 days. A similar effect was observed in urine creatinine- adjusted cortisol, total white cell count, neutrophils, eosinophils and lymphocytes. There was seemingly no effect on C-reactive protein and erythrocyte sedimentation rate.

Conclusions: Our SGS cohort comprised of distinct subgroups. Iatrogenic patients tended to be more morbid, with more severe disease. Idiopathic patients were demographically homogenous and had more mild disease. Further we concluded that patient rather than surgical factors affect treatment outcome.

Although statistical and therefore clinical significance could not be concluded from a sample size of 4, our preliminary findings suggest that SILSI has a short-lived systemic effect and is unlikely to result in any clinically relevant sequelae.

Vincent Wong

Early interventions and acute kidney injury in high risk in hospital patients

Professor Yahya Shehabi, Department of Medicine, School of Clinical Sciences, Monash University.
Associate Professor David Ernest, Department of Medicine, School of Clinical Sciences, Monash University.

I did my BMedSc(Hons) after my fourth year of medicine, I thought this would have been the best time to have some exposure to research after the treacherous VIA exams but before graduating. I specifically sought out a prospective clinical project in critical care as a challenge and I had the privilege of working with Prof. Shehabi and A/Prof. Ernest at the School of Clinical Sciences over the year. Although I ran into some difficulties, with the support of my supervisors and the critical care research team I was able to learn more than I had ever imagined possible.

The prospective nature of my project meant that I faced a significant learning curve in obtaining informed consent from participants and identifying specific variables of interest. Despite this, the breadth of clinical experience and exposure I had this year is irreplaceable and I thoroughly enjoyed dabbling in the world of clinical research.

If you've got any questions feel free to contact me at vhwon3@student.monash.edu

Abstract

Background: Acute kidney injury (AKI) is a condition affecting up to 25.6% of hospitalised patients. It carries a significant mortality rate and is associated with chronic kidney disease (CKD) and other extra-renal comorbidities. Patients with CKD, diabetes mellitus, advanced age, sepsis, shock or who undergo cardiac surgery and other major surgeries are known to be at high risk for developing an AKI. Despite this, preventative measures and treatments are limited. Early interventions, particularly in the first 48 hours, have the potential to reduce the burden of AKI as patients often receive a large number of interventions early in their admission.

Aims/Objectives: The primary aim of this study is to identify potential candidate interventions and risk factors in high risk patients in the first 48 hours of an admission that may modify the burden of an AKI and quantify the impact of AKI in the transition to CKD.

Methodology: A single centre observational longitudinal study was conducted at Monash Medical Centre, Clayton. High risk participants, with CKD, insulin requiring diabetes mellitus, >70 years old, sepsis, a prolonged ICU admission and complex surgery, were recruited during their admission. Observational data identifying interventions and risk factors for AKI were extracted for the first 48 hours of their admission. Participants were then followed during their admission to identify AKI incidence as defined by the Kidney Disease: Improving Global Outcomes (KDIGO) work group. At discharge and at 90 days participants were then assessed for Major Adverse Kidney Events (MAKE), defined as mortality, new dialysis or persistent KDIGO stage II or III AKI. Secondary outcomes included length of stay and change in serum creatinine.

Results: 72 participants have currently been recruited for this study. A total of 25 (34.7%) developed a KDIGO defined AKI of whom 6 (8.3%) developed a stage two or three AKI. An overall MAKE event rate of 2.8% was observed at hospital discharge. Identified interventions and risk factors revealed that the number of hyperglycaemic episodes in the first 48 hours had an OR of 1.47 (95%CI 1.03-2.09, p=0.02) for AKI. The number of pre-admission nephrotoxic agents were seen to increase the odds of AKI (OR=1.75, 95%CI 1.04-2.95, p=0.03), in particular the use angiotensin converting enzyme inhibitors or angiotensin receptor blockers (OR=3.54, 95%CI 1.28-9.76, p=0.01). Finally, patients undergoing cardiac surgery had an odds ratio of 5.07 (95%CI 1.19-21.51, p=0.02) for developing an AKI.

Conclusion: In this high-risk population, AKI is a common complication. It was associated with the risk factors of pre-admission nephrotoxic agents, as well as cardiac surgery. A potential candidate intervention identified that may influence AKI incidence is control of hyperglycaemia in the first 48 hours of an admission. These data suggest that the avoidance of hyperglycaemia and consideration of pre-admission use of nephrotoxic medications have the potential to influence AKI morbidity. However larger studies with long term follow up should be conducted to evaluate the significance of these associations.

Teresa Wulandari

Maternal obesity-associated hyperactivity in the hippocampus: Can the effects be rescued by diet reversal?

Prof. Helena C. Parkington, Dr. Harold A. Coleman
Department of Physiology, Clayton

I love analysing people's behaviour on a non-intentional daily basis as well as listening to people's way of thinking and this interest landed me into this cognitive and behaviour neuroscience research! I aspire to learn and contribute as much towards studies that aims at preventing, alleviating and rehabilitating various neurodevelopmental and behaviour disorders. I had a very packed yet enjoyable time throughout my honours year as I learned more than I initially expected. From doing hands-on experiments to analysing data, I learnt one very important lesson from my supervisor, that is… when things don't go as planned, no matter how much time, energy and money you've put in, move on! There's nothing much we should be regretting about when we have put in our best. Work towards what's scientifically beneficial for as much people and (with lots of prayers) we would get there eventually! ;) I'll be happy to be contacted through teresawlim@gmail.com.

Abstract

Background: Literatures have shown that exposure to early-life obesogenic condition is linked to hippocampal hyperactivity, a similar observation as with dementia patients. We hypothesize that maternal obesity gives rise to neuroinflammation in the offspring that impairs inhibition and thus results in hippocampal hyperactivity that affects memory and learning. Rescue by a good diet during weaning period onwards was assessed to observe the extent to which it could improve neurodevelopmental problems mentioned earlier.

Method & Results: A rat model was used. Dams on high fat (HF) diet were found to be metabolically challenged compared with those on control chow (CC) in terms of body mass (12% higher, $p<0.0001$) and insulin sensitivity ($p=0.007$) as determined by glucose tolerance test. Half of the offspring remained on their dam's diet while the other half were switched over to the other diet from weaning onwards (late diet). Only male offspring were included in this study. Early HF diet increased body mass mildly (10.5%, $p=0.0216$) while late HF diet increased retroperitoneal fat strongly (76%, $p=0.0001$). Behaviourally, an early obesogenic diet anxiety (23%, $p=0.016$) according to the elevated plus maze test. The radial arm maze showed a clear reduction of memory by 27% ($p<0.0001$) in rats on early HF diet. Further analysis revealed that late HF diet decreased working (3.2 folds, $p<0.0001$). and reference memory (2.75 folds, $p<0.0001$). A reversal to CC since weaning could rescue working but not reference memory. Working memory is highly dependent on the ventral hippocampus due to its location and interplay with the prefrontal cortex (decision making) and amygdala (fear and anxiety). Multielectrode arrays was used to measure extracellular electrical activity. Hyperactivity of ventral hippocampal slice superfused with zero magnesium aCSF was found in rats that took on late HF diet as marked by an increase of frequency (1.5 folds, $p=0.021$) and amplitude (2.9 folds, $p=0.003$) as well as a decrease in burst latency (1.8 folds, $p<0.0001$). All the 3 parameters could be rescued by a change to a late CC diet. Immunohistochemistry using ventral hippocampal slices showed a late HF diet influence in the reduction of GABA inhibitory nerve terminals (GAD 65 marker) by 13.7 folds ($p<0.0001$), which could be rescued with late CC diet switch. Increased astrocytic activation (GFAP marker) was shown in both early and late HF diet which could not be rescued by CC.

Conclusions: Dam obesity has shown to have a substantially vibrant impact on the offsprings' reference memory performance and state of astrocytic activation. However, more aspects such as retroperitoneal fat, blood glucose level, working memory performance, hippocampal activity and amount of GABA inhibitory nerve terminals were plastic, as indicated by improvements found through a late CC rescue. Thus, we need to emphasize on the importance of obese mothers to ensure good postnatal diet is given as early as possible for their children.

Cecilia Xu

Effect of vitamin D supplementation on insulin resistance and physical function in overweight and obese older adults

Dr David Scott (School of Clinical Sciences at Monash Health, Monash University / University of Melbourne, St Albans)
Professor Peter Ebeling AO (School of Clinical Sciences at Monash Health, Monash University / University of Melbourne, St Albans)

I did my BMedSc after 4th year. I was keen for a break from medicine and I knew I enjoyed research, which is why I decided to do it. I chose this project because I had an interest in preventative medicine and geriatrics. I had a wonderful year, mostly owing to the incredibly supportive team I was with. Although I didn't have much in the way of results, I got to understand the ins and outs of an RCT, present at a conference, and take a cheeky vacation to Europe!

I had a lot of trouble deciding what I wanted to do, and ended up changing my project multiple times for various reasons, so if anyone is having a similar experience I'd be more than happy to chat about it. My email is clxu1@student.monash.edu.

Abstract

Background: Obesity, insulin resistance, and physical disability are major issues in the ageing population. An important component in the management of these is exercise; however, a substantial proportion of overweight and obese older adults have poor exercise responsiveness resulting in blunted functional and metabolic improvements. We hypothesise this may be mediated by high levels of pro-inflammatory intramuscular adipose tissue (IMAT) resulting from vitamin D deficiency. Previous studies examining the effect of vitamin D with exercise have been inconclusive due to low vitamin D doses, inclusion of vitamin D replete participants, and small sample sizes. Furthermore, no studies have investigated the role of IMAT in this context.

Aims: To quantify and compare changes in calf IMAT, physical function, and insulin sensitivity in 50 overweight and obese older adults with vitamin D insufficiency treated with vitamin D or placebo 12 weeks prior to, and also throughout, a 12-week exercise program.

Methods: In 2017, we recruited 25 out of 50 participants for this ongoing pilot, double-blinded, randomised, placebo-controlled trial of community-dwelling overweight and obese adults aged 50-80 years. All participants have completed baseline (T1) assessments and been randomised to receive 4,000 International Units per day (IU/d) of vitamin D3 or identical placebo for 12 weeks. Ten participants have completed midpoint (week 12; T2) assessments. One participant has completed endpoint (week 24; T3) assessments. At all time points, we measured insulin resistance (HOMA IR), C-reactive protein (CRP), body composition, IMAT, physical function, and 25-hydroxyvitamin D (25(OH)D) and physical activity levels. We compared outcomes in the vitamin D and placebo groups and determined associations between change in vitamin D and change in study outcomes. We also report outcomes for the single participant who completed the study.

Results: There were no significant differences between the vitamin D and placebo groups at baseline. The average pill compliance rate was 93%, and no adverse events related to vitamin D supplementation were reported. The increase in 25(OH)D from T1 to T2 was significantly greater in the vitamin D group than in the placebo group (33.2 ± 6.5 nmol/L vs. - 9.8 ± 6.7 nmol/L; $p<0.001$), leading to a significantly greater mean vitamin D level in the vitamin D group than in the placebo group at T2 (75.8 ± 11.1 vs. 36.8 ± 10.9; $p=0.001$). There were no significant differences for any outcome between groups at T2, nor were there any significant correlations between change in vitamin D and change in any outcome, including HOMA IR, IMAT, or physical function (all $p>0.05$). However, clinically meaningful improvements in physical function at both T2 and T3 were observed for the single participant who completed the study.

Conclusion: 4,000 IU/d of vitamin D3 over 12 weeks is a safe and effective way of treating vitamin D insufficiency in overweight and obese older adults. However, our results so far provide no evidence that raising serum 25(OH)D improves insulin resistance, calf IMAT, or any measure of physical function. Completion of the trial is necessary to determine potential benefits of vitamin D alone or synergistically with exercise.

Hannah Youn

Therapeutic Potential of Stem Cell Therapy in Ventilation Induced Lung Injury of Growth Restricted, Preterm Lungs

Beth Allison & Suzie Miller - Ritchie Centre, Miller Group & Hooper Group

I commenced my honours year after completing my fourth year of medicine, as was the case for many of the other honours students. I was drawn to this project chiefly because of the lovely people in the research group, it revolving around women's/neonatal health and the laboratory work. Over the year I learnt a lot about what research is about, what it involves, all the hard work that it requires and thus the inherent value of research. I learnt that manual counting is punishing, data analysis is confusing and writing a thesis sometimes makes you question life. But I also learnt that everyone is incredibly supportive and people are happy to help when asked. An honours year is quite a nice introduction into research for interested students and I am happy to be contacted with any questions.

Abstract

Background: Fetal growth restriction (FGR) imposes significant pulmonary morbidity and mortality on growing fetuses and newborns. Early delivery and supportive ventilation are designed to ensure survival of these infants, however many go on to develop ventilation induced lung injury (VILI). Thus rising interest has surrounded using stem cell therapy to treat this adverse outcome, where specific stem cell types have demonstrated attenuation of inflammation and injury associated with VILI in preterm animals. Whole umbilical cord blood (UCB) is a highly accessible source of stem cells, however there has been little research into whether UCB is also effective in treating VILI and additionally whether it is equally effective in FGR infants.

Objectives: The purpose of our study is to establish the ability of UCB to attenuate acute inflammation in the first 24 hours of ventilation, and whether effects are equal in both appropriately grown (AG) and FGR contexts.

Methods: Lamb fetuses were left as controls (AG) or FGR was induced by single umbilical artery ligation in twin-bearing Border Leicester Ewes at 88 days gestation. Lambs were delivered preterm at 125 days gestation, where they were either unventilated controls (AGUVC = 9, FGRUVC = 4) or commenced on 24 hours of gentle supportive ventilation (AGV = 5, FGRV = 4), or commenced on 24 hours of ventilation with UCB treatment (AGVUCB = 7, FGRVUCB = 4). Lung tissue from unventilated controls were collected at delivery, whilst tissue from ventilated animals were collected at the end of 24 hours, to be assessed for histological outcomes.

Results: FGR induced no detectable differences in lung weight (adjusted for body weight), tissue density, septal crest density, elastin and collagen density or ventilatory requirements. Ventilation caused a statistically significant rise in peak inspiratory pressure that was not different between AG and FGR lambs. Ventilation caused a 57.6% and 44.6% reduction in septal crest density, in AG and FGR lambs respectively, with qualitative heterogeneity of lung injury and thickening of alveolar walls. No differences in elastin and collagen density were detected with ventilation. Whilst inflammatory marker CD45 and cell proliferation were increased by ventilation in AG lambs, there was no significant difference in CD45 positivity and cell proliferation was reduced after ventilation in FGR lambs. UCB had no significant effect on ventilation but significantly reduced inflammation and partially preserved lung morphology and septal crest density in AG lambs. Contrastingly, FGR lungs did not demonstrate the same degree of inflammation attenuation or lung structure preservation and cell proliferation remained low after UCB treatment.

Conclusion: This is the first study to explore the therapeutic potential of UCB in the first 24 hours of ventilation, in both AG and FGR lambs. UCB demonstrates promising anti-inflammatory effects, thus presenting UCB as an easily accessible source of stem cells with therapeutic potential. Unexpected results of UCB therapy in FGR lambs suggest further investigation is required to ascertain its effects with FGR.

Angela Yu

The association between early childhood infection burden and childhood vascular parameters.

Professor David Burgner, Murdoch Children's Research Institute, Department of Paediatrics, School of Clinical Sciences.

Associate Professor Cuno Uiterwaal, Department of Epidemiology, Julius Center for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, The Netherlands.

Dr Gerdien Dalmeijer, Department of Public Health, Julius Center for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, The Netherlands.

I decided to do a BMedSc to give research a proper try, for a bit of a break, and to live in Europe. Learning how to conduct epidemiological research was frustrating, difficult, and sometimes isolating; but incredibly rewarding in the end. It wasn't easy at the start, or at end, but I have come away with an unexpected love for this field.

If you have even the slightest desire to do a BMedSc, just do it! I was never certain that I would love it, but I really did! Not only do you get introduced to the amazing world of research that is out there, but you meet inspirational mentors, colleagues and friends along the way. If you can do it overseas, I highly recommend it. It expands your medical world from Clayton, Melbourne, to Europe, North America, and beyond. The world becomes smaller and bigger at the same time. I will always be thankful for my decision to do a BMedSc, and to my supervisors for guiding me through it. I can't wait to see where research takes me and each of my BMedSc and UMCU friends. Feel free to contact me at: angelayu7@hotmail.com.

Abstract

Background: Inflammation plays a significant role in atherosclerosis development. Infections are ubiquitous in early childhood and result in inflammation that may affect the vasculature. Whether these infections cause changes to the vasculature at an early age is unknown. We investigated the relationship between early childhood infection burden and children's vasculature parameters.

Method: 778 five-year-olds in the WHISTLER (Wheezing-Illnesses-Study-Leidsche-Rijn) birth cohort were assessed for carotid intima-media thickness (CIMT) and carotid distensibility using ultrasonography. The number of general-practitioner (GP) diagnosed infections from birth to assessment date were summed and grouped into quartiles. Specific infection types, early childhood (first 12 months of life) and recent infections (in the preceding three and six months) were also investigated for their relationship with vascular parameters. General linear regression was used to measure this association. The correlations between parent-reported upper respiratory tract infections (URTIs) and febrile episodes, and GP-diagnosed URTIs and febrile episodes were investigated.

Results: 711 (91.4%) children had at least one lifetime GP-diagnosed infection (median=3, inter-quartile range 1-6). Children in the highest infection number tertile (6-33 infections) were more likely to be of non-Western background compared to children with fewer GP-diagnosed infections (no infection – 7.5% from non-Western backgrounds, tertile 1 – 5.8%, tertile 2 – 6.9%, tertile 3 – 13.8%, p=0.04). Overall, there was no significant association between total infection burden and vascular characteristics at age 5 years. Children with other viral infections only (n=49) showed a significant increase in distensibility compared to the no infection overall group (α=64.0MPa-1, 95%CI: 11.8, 116.2, p=0.02). There was no association between other specific infection types nor the infection timing and vascular parameters. There were weak correlations between parent-reported and GP-diagnosed URTIs and febrile episodes (Kendall's tau=0.15, p<0.001 and =0.070, p=0.025, respectively).

Conclusions: No association was found between early childhood infection burden and children's carotid vascular parameters at age 5. This study attempted to accurately quantify healthy children's total infection burden, however, parental health-seeking behaviour may have affected these results. As such, more robust infection measures are required to test this association.

Saffanah Zahra

Evaluating The Effects of Tranexamic Acid on Fibrinolysis and Immune Response in Cardiac Surgery

Robert Medcalf, Dominik F. Draxler
Australian Centre for Blood Diseases

Hi! I'm an Indonesian student coming for a one-year abroad. I'm in my fourth year out of a total of 6 years of my medical school. I was interested in this project because it was one of what were available for me lol, and also I think it's cool to be getting samples from a large clinical trial, and somewhat contribute to the trial too. My advice is to enjoy your honours year! Gain as much as possible and just have fun!

Abstract

Background: Cardiac surgery involving cardiopulmonary bypass (CPB) influences the hemostatic system resulting in bleeding abnormalities leading to morbidity and mortality. The hemostatic system can be compromised and result in excessive activity of the fibrinolytic system during and after surgery. Antifibrinolytic drugs, particularly tranexamic acid (TXA) as a lysine analogue, has been found to reduce bleeding outcomes in cardiac surgery. Another effect of CPB is systemic inflammatory response syndrome, which is also known to be modulated by the fibrinolytic system. While TXA effectively inhibits fibrinolysis and reduces bleeding, the duration of its antifibrinolytic effect following CPB is not clear and it also likely to affect anti-inflammatory mechanism in cardiac surgery.

Method: 41 patients undergoing elective cardiac surgery were randomized to placebo or TXA. Citrated and EDTA plasma were taken at preoperatively (Pre-Op), immediately posoperatively (Post-Op; 4-6 hours), at the 24-hour, and at 72-hour time points. Citrated plasma was subjected to clot lysis assays with the addition of either t-PA or u-PA to induce fibrinolytic activity. Plasma samples were also tested for t-PA, u-PA, plasmin-α2-antiplasmin (PAP) complex, and D-dimer to analyze fibrinolysis using commercially available enzyme- linked immunosorbent assay (ELISA) kits. Proinflammatory cytokines (TNF-α, IL-1β, and IL-6) and complement system products (C3a and C5a) levels were also measured using enzyme- linked immunosorbent assay.

Results: t-PA levels was increased after cardiac surgery both in the placebo group ($p = 0.011$) as well in TXA group ($p = 0.0002$). u-PA levels did not change after cardiac surgery in the placebo group but levels were significantly reduced in patients administered TXA at the 72h points ($p = 0.0303$). t-PA induced fibrinolysis was significantly decreased in TXA group, at post- op ($p = 0.0173$) and 24-hour ($p = 0.0053$) time point, consistent with the expected effects of this antifbrinolytic agent. PAP complex levels were increased at post-op time point in the placebo group ($p = 0.0424$) and TXA group ($p < 0.0001$), and surprisingly was further increased in the TXA group at the post-op time point ($p = 0.0039$). D-dimer levels significantly increased after surgery in placebo group ($p < 0.0001$), but were markedly suppressed in the TXA group, consistent with the anti-fibrinolytic effect of TXA. TNF-α, IL-1β, and IL-6 levels were all increased after cardiac surgery in both groups, but the increases were less in the TXA group. C3a and C5a level did not show any differences after cardiac surgery nor after TXA administration.

Conclusions: We have found that TXA inhibit t-PA induced fibrinolysis in cardiac surgery until 24 hours after surgery, and that t-PA level is increased after cardiac surgery. TXA administration causes an almost significant lower level of proinflammatory cytokines in cardiac surgery patients.

Karen Zhang

Cough in Cancer – The Methadone Trial and Local Cough Patterns

Associate Professor Peter Poon, Director of Supportive and Palliative Care at Monash Health
Adjunct Associate Professor Michael Franco, Supportive and Palliative Care at Monash Health
Dr Leeroy William, Supportive and Palliative Care at Monash Health

I took on my BmedSc after completing fourth year. Despite being interested in research, getting involved during med school had been difficult for me as I just didn't have the time or skillset. I hoped to dedicate this year to building a solid foundation in scientific writing, statistical analysis and running a clinical trial. Given that I am interested in cancer research and improving patient quality of life, choosing my project was a no-brainer!

In the end, the honours year has been entirely worthwhile both academically and personally. I'm glad to say I come out of this year not just a better researcher but also a more resilient and critically-thinking individual. Lastly, I'm so very grateful for my amazing supervisors – it is absolutely true that your supervisors can be the making point of a project!

Abstract

Background: The literature establishes that cough is prevalent within both palliative care and general patient cancer populations although cough as a pathology is not well characterised. Evidence for the efficacy of treatments for cough is poor, especially in cancer. Methadone has been found to improve cough anecdotally but has never been studied for this purpose.

Method: Patients with a cancer diagnosis were screened for cough and recruited at multiple sites at a tertiary centre. Once consented for the trial, the patient would receive three days of either methadone 5mg twice daily or a matched placebo tablet twice daily, followed by a one-day period for washout, and then three days vice-versa of the alternative. Cough severity as measured by the visual analogue scale (VAS) and Leicester cough questionnaire (LCQ) was recorded at baseline and then following each round of medications.

In response to encountering low eligibility rates while screening, we collected data on the prevalence of cough seen at trial screening sites. To investigate potential causes of this, we then compared cough presence to patient demographic information. Patients with cough at our major site were asked to complete cough questionnaires and we analysed the responses to explore cough severity and the quality of life effects of cough on patients.

Results: To date, 6/40 patients have been enrolled onto trial. Recruitment is ongoing. One patient passed away before the first endpoint and two passed before the second, all due to expected and unrelated causes. A preliminary t-test comparing the difference in effect of methadone and placebo on LCQ and VAS cough scores was not statistically significant (p=0.36, p=0.88), as expected due to the limited data size. Unexpectedly, the LCQ and VAS scores appeared to show incongruous changes to cough.

Cough prevalence at screening sites were significantly lower than expected. The cough prevalence of lung cancer patients at two main sites, McCulloch House – a palliative care ward – and the Chemotherapy Day Unit were 21.4% (95% CI 5.2% to 37.6%) and 38.9% (95% CI 27.3% to 50.4%) respectively. The prevalence of cough in general cancer patients at these sites were 11.2% (95% CI 5.0% to 17.4%) and 8.8% (95% CI 6.0% to 11.6%). Cough was not associated with any disease or patient factors we collected data for except for smoking status (p=0.02). Patients who were interested in the cough trial had more severe cough than those who were not (p=0.01, p=0.046).

Conclusions: This is the first trial to study the efficacy of methadone as an antitussive agent and thus far no significant results have been found. We encountered unexpected low eligibility rates within the patient population. On investigation we found that cough rates in our population were significantly lower than what has been reported. Further analysis also revealed that presence of cough was not associated with extent of disease or patient factors except smoking. These findings suggest cough may be a diminishing health care problem within the cancer population, and further research on why this is the case is needed.

Kevin Zhang

Predictors of damage transition in systemic lupus erythematosus

Professor Eric Morand, School of Clinical Sciences
Doctor Sarah Boyd, Department of IT, Monash University
Doctor Hieu Nim, Department of IT, Monash University
Doctor Francois Petitjean, Department of IT, Monash University

Having completed four years of medical school, I chose to undertake a year of research. For me, research has always been something that I wanted to do, even before deciding to study medicine. I chose to do my BMedSc(Hons) project jointly with the department of IT at Monash University because of my interest in data analysis, programming and bioinformatics.

I believe that in the future, as medicine becomes increasingly digitalised, the use of computers to aid decision making and process vast amounts of data will become vital. Doing a project with the department of IT has allowed me to develop skills that are not routinely taught in medical school and ultimately, I would like to continue with this research in the future.

Abstract

Background: Systemic Lupus Erythematosus (SLE) is a heterogeneous, autoimmune disease that affects many Australians. A major goal of lupus treatment is to prevent the accrual of organ damage. Currently, tone of the few good predictors of short term risk of organ damage accrual is disease activity, often measured by the SLEDAI-2k. The SLEDAI-2k is a potentially flawed index, because of its subjectivity and the lack of consideration of damage outcomes in its conception. Routinely measured clinical pathology data, however, is objective and does not suffer from inter-observer bias. The Australian Lupus Registry and Biobank is the only database in the world that contains routine pathology data and represents a unique opportunity to study the utility of routine pathological data in relation to as a predictor of damage accrual in SLE patients.

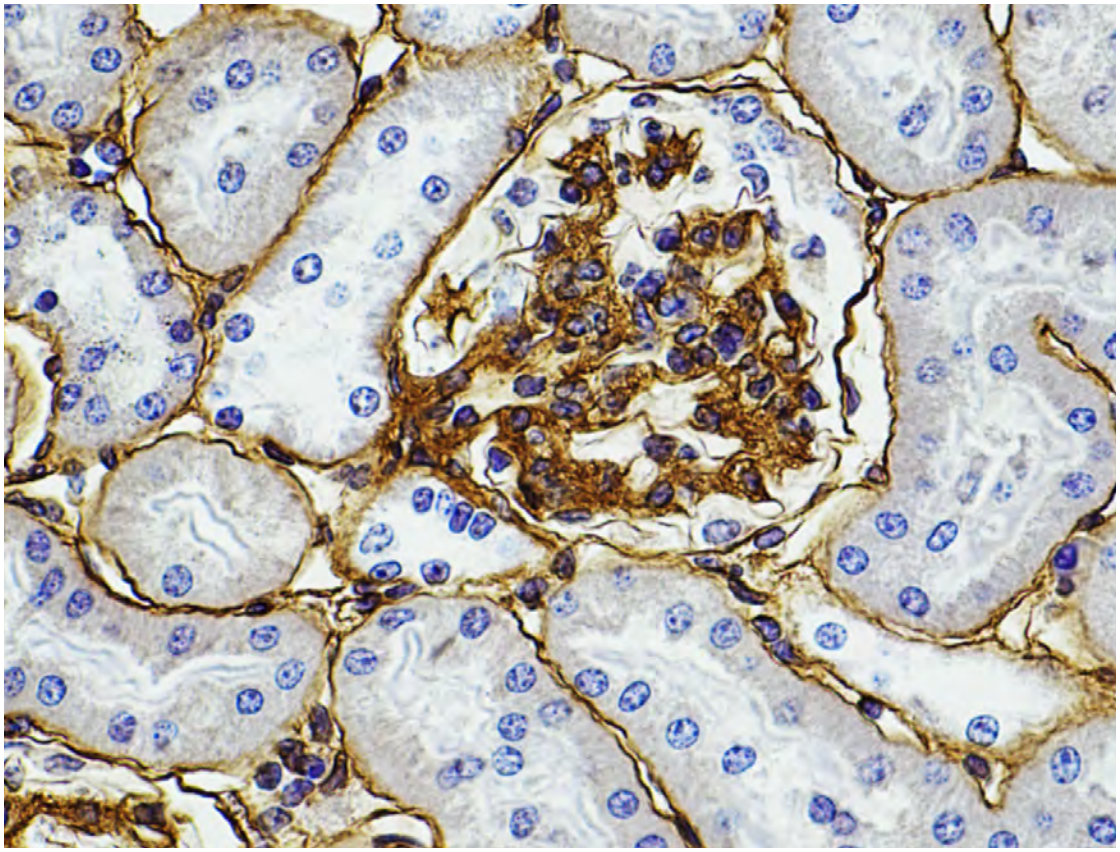
Aims: To find objective, routine pathology measurements that are associated with organ damage accrual.

Method: Data from the Australian Lupus Registry and Biobank was utilised and analysed ac- cording to the concept of organ damage transition. Domains of the SLEDAI-2k and sixteen routine pathology parameters were analysed for their association with organ damage transition. Univariable and multivariable analysis was performed with logistic regression and odds ratio trends were generated with bootstrapping.

Results: The SLEDAI-2k domains have different associations with risk of damage transition. Pericarditis, pyuria, alopecia and rash were the most strongly associated with increased risk. However, the relative weighting of the SLEDAI-2k domains is not proportionate to the degree of associated risk. Moreover, contrary to expectation, there was no clear trend of increasing SLEDAI-2k score and increasing odds ratio of risk of damage tran- sition. Scores of a threshold greater than 4 conferred risk of organ damage transition relative to a score threshold of less than or equal to 4. However, score thresholds of greater than 5, 6, 7, 8 and 9 do not confer additional risk when compared to a score threshold of greater than 4.

Aberrant values of creatinine, eGFR, urine protein:creatinine ratio, ESR and haemoglobin were all correlated with damage transition. Unlike the SLEDAI-2k, they showed progressive increases in risk as time adjusted mean values became more deranged from normal.

Conclusions: Whilst the SLEDAI-2k can predict organ damage transition, it does so unreliably. The weights of the SLEDAI-2k need to be readjusted for it to be a reliable predictor of organ damage. Routine pathology variables can predict organ damage transition and are more reliable in doing so than the SLEDAI-2k.



Donna Almira “Stains Speak Damage”

Collagen IV deposition as one of the extracellular matrix components can be used as a marker of renal injury, as shown in the picture with dark brown staining inside the glomerulus of a diabetic kidney using immunohistochemical labelling.

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