MONASH University
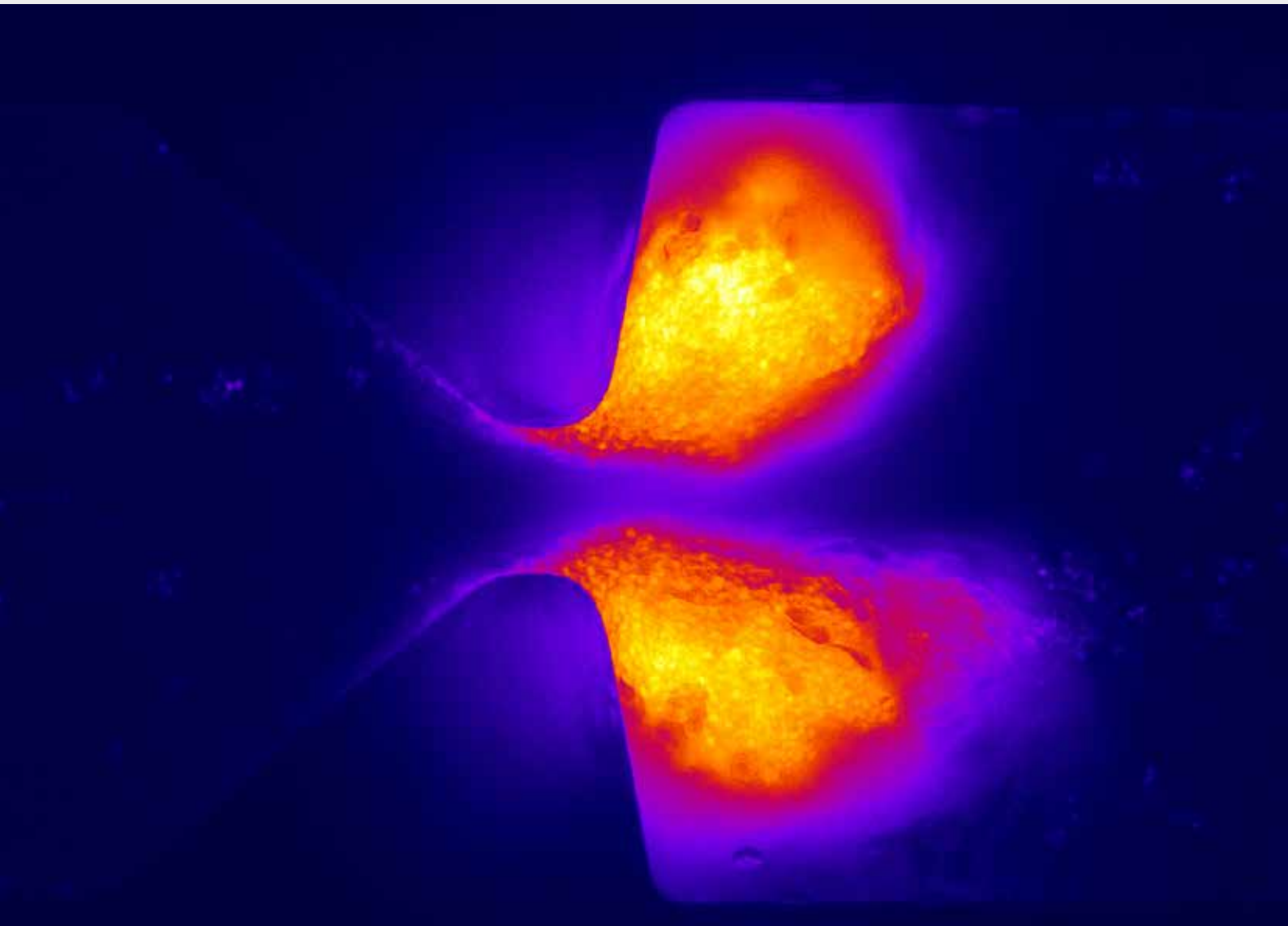
**MONASH
MEDICINE,
NURSING AND
HEALTH SCIENCES**

**MRSS ANNUAL
BMEDSC (HONS)
YEARBOOK 2016**

GROUP
OF EIGHT
AUSTRALIA

"The dark side of platelet aggregation" by Rose Brazilek

Thrombosis in stenosed vessels is the leading cause of cause of morbidity and mortality, particularly in industrialised nations. This epifluorescent microscopy image depicts platelet aggregation in an artificial stenosis.

MESSAGE FROM THE BMEDSC(HONS) COURSE MANAGEMENT COMMITTEE

Dear Students,

Congratulations for completing your BMedSc(Hons) degree. Well done!

The BMedSc(Hons) year is a transformational year, one that challenges you both personally and academically. A year that gives you a new appreciation of: how much more there still is to discover and learn, 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 firmly believe that the BMedSc(Hons) degree will enhance your capacity to practice evidence-based medicine. For many of you it will also have instilled the desire to continue with research and we look forward to hearing and reading about your many achievements. It may also be the first step of your development into a future leader and opinion-maker in the profession.

The Course Management Committee would like to thank each and every one of you for undertaking BMedSc(Hons). We would also like to acknowledge the contributions of your MRSS committee, particularly your Co-Chairs; Aidan Kashyap and Eshwar Yogakanthi, who 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, I wish you all the very best for a bright future.

Dr Megan Wallace – Director of Medical Student Research

MESSAGE FROM MRSS

Congratulations on an incredible year!

Whether it has been spent pipetting in the confines of Clayton or exploring ethical theories overseas, we are confident this year has led to new experiences and skills, and hopefully like us, a similar disdain for statistical analysis programs.

This yearbook represents the incredible dedication and commitment that has been placed into this year by us all, and provides evidence of our achievements to look back on in years to come. We know that for all of us, this year has become not so much about the answers, but about the questions unearthed and new directions to follow (Figure 1). We hope that this year has left you inspired and passionate about pursuing research in your future careers, and look forward to hearing about your achievements long into the future.

Eshwar Yogakanthi and **Aidan Kashyap**

Co-Chairs, Medical Research Students' Society

Figure 1 – "What Will We Discover Next"

"I feel like this exciting, empowering question, which is at the entrance to the Murdoch Children's Research Institute, applies to us as a BMedSci cohort as well. We are all dedicating months of our lives researching different areas and discovering things which no one has ever discovered before and I'm sure that all of us would have made a huge contribution to science and discovery by the end of this year." Masad Alfayadh.

MASAD ALFAYADH

Do Vaccinations Trigger Flares in Juvenile Idiopathic Arthritis?

Professor Jim Buttery, Professor of Paediatric Epidemiology, Monash University, Head, Infection and Immunity, Director of Research, Monash Children's Hospital, Head, Monash Immunisation, Monash Health Director, SAEFVIC, Murdoch Children's Research Institute. Dr Peter Gowdie, Paediatric Rheumatologist and General Paediatrician, Department of Paediatric Rheumatology and Department of General Medicine, Monash Children's Hospital Department of Rheumatology, Royal Children's Hospital, Department of Paediatrics, Monash University. Dr Jonathan Akikusa, Lecturer, University of Melbourne, Paediatrics, Paediatric Rheumatologist, Royal Children's Hospital Researcher, Murdoch Children's Research Institute.

I completed my BMedSci after 4th year. I met one of my supervisors in clinic during my paediatrics rotation, who spoke to me about a project that he'd been thinking about for three years. I was really interested in the project and loved the supervisors, who were really kind and supportive, and so I decided to do it!

The project was about immunisation safety in children with Juvenile Idiopathic Arthritis. Many parents and healthcare providers were concerned about the possibility of vaccinations causing flares in JIA, and so my task was to determine whether there was any increase in the rate of flares after immunisation. The project was a joint one between Monash Children's and The Royal Children's Hospitals. I worked mainly at the Murdoch Children's Research Institute and the Paediatric Rheumatology Department at the RCH.

If you're interested in doing research in paediatrics, I am happy to be contacted via Facebook or on my email: masadalfayadh@gmail.com. I loved the BMedSci year and would encourage everyone to think about doing research before the end of med school!

Background: Juvenile Idiopathic Arthritis (JIA) is a complex, heterogenous group of conditions. It is the most common disease encountered in paediatric rheumatology. JIA has a relapsing-remitting course, so flares are an inherent part of the disease process. Flares have been attributed to viral infections or changes in medication. Some parents and healthcare providers fear that vaccination could also be a cause of flares. As a result, significant disparity exists in current clinical practice. Despite this being a common disease, the safety of vaccinations in patients with this diagnosis has not been assessed in the Australian immunisation schedule. This study aims to achieve this-to assess the safety of vaccinations in children aged 0-6 with JIA.

Method: The patient population included in this study were all children aged 0-6 seen in the Rheumatology Department at the Royal Children's Hospital from 2010-2016. Using the patients' Medicare numbers, we linked their immunisation data from the Australian Childhood Immunisation Register (ACIR) with their clinical data from the Rheumatology Database. Subsequently, we employed the self-controlled case series methodology (SCCS), which is a novel methodology in the area of pharmacovigilance research where patients act as their own controls, to analyse whether the risk of flares in the three months following immunisation was greater than the baseline risk of flares in JIA. We used a risk interval of 90 days.

Results: 138 patients were included in the study, with a mean age of 3.37 years. 70% were female and 56% had a diagnosis of oligoarticular JIA. In these patients, 32 flares were observed in the risk window of 90 days following immunisations. The risk of flares during the 90 days following immunisation was reduced compared with patients' baseline risk of flares (RR 0.59 [95%CI 0.39-0.89, p=0.012]).

Conclusions: Our results indicate that the risk of flares in the 90 days following vaccination is significantly less than the baseline risk of flares for that same patient. These results do not support vaccinations increasing the risk of flares in patients with JIA.

ROSE BRAZILEK

Development of a novel shear micro-gradient system for the diagnosis of von Willebrand Disease.

Dr Warwick Nesbitt, Microplatforms Research Group, School of Engineering, RMIT University, Melbourne, Victoria, Australia

Professor Harshal Nandurkar, The Australian Centre for Blood Diseases, Monash University, Alfred Medical Research and Educational Precinct, Melbourne, Victoria, Australia
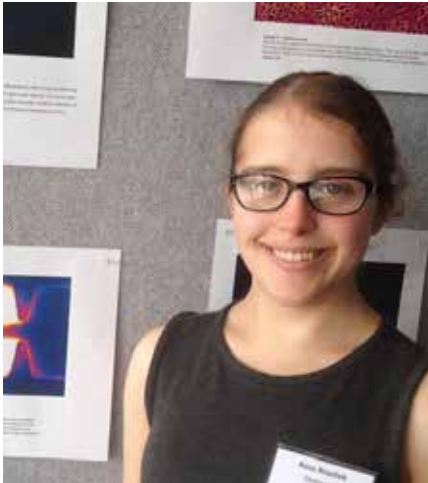
I chose to undertake a Bachelor of Medical Science (Hons.) following completion of my fourth year of MBBS. I have an interest in haematology, and hoped to enhance my laboratory and analytical skills. My project was an amazing opportunity to experience the basic science that underpins medical treatment in a supportive environment. I'm thankful for my supervisors at the Australian Centre for Blood Disease and all the laboratory staff for assisting in my project, and offering me guidance and support.

Background: Von Willebrand's Disease (VWD) is the most common inherited bleeding disorder, and is caused by deficiencies or defects of Von Willebrand factor (VWF) and platelet GPIba. VWF function is dependent on the physiological effects of high shear blood flow. Given this haemodynamic sensitivity, the Biorheology Subcommittee of the International Society on Thrombosis and Haemostasis recommended the development of flow-incorporating assays for VWD assessment. Many available devices are not optimal clinically, as they lack reproducibility, have long waiting periods, require large blood volumes, and do not incorporate physiological blood flow. It is anticipated that this microfluidic device will more accurately model blood flow, allowing for more sensitive VWD screening. The device has the advantage of reducing blood volumes to less than 200µL, and allows for rapid VWD screening. In addition, because platelet aggregation can be monitored in real-time, the device may lead to insights into how haemodynamic factors affect platelet function.

Method: Whole blood samples from 11 adults with suspected or confirmed VWD (4 type 1 patients, 5 type 2 patients and 2 type 3 patients) aged 18-62 years, with mean VWF levels of 46.67% (SD 38.8) was perfused through the device incorporating stenosis that generate well defined blood shear gradients. Resulting aggregate size was monitored in real-time using high-speed epifluorescence microscopy. Maximal aggregate area for control donors and samples taken from patients with confirmed or suspected VWD was assessed to determine the device's diagnostic potential and performance. This project used blood samples from control subjects and subjects with VWD. Microfluidic channels with a number of shear geometries were trialled. Platelet aggregation was determined using epifluorescence microscopy. Platelet aggregation dynamics were quantitatively assessed using developed image analysis algorithms. Device derived data was compared against clinically available platelet function analysis methods including VWF antigen, VWF-collagen binding, and Ristocetin cofactor analysis. Device performance was compared against "gold standard" light aggregometry and the Siemens Healthcare PFA200®.

Results: Parameters that have been found in the literature to alter thrombus growth, such as increased shear force, platelet count and haematocrit and amplification loop blockers, consistently influenced aggregation in the device. Data suggested that von Willebrand Factor (vWF)/GPIb/IX/V binding has a critical role in the device, with minimal contribution from fibrinogen. There appeared to be a clear threshold cut-off for diagnosis of vWD through analysis of smaller aggregate size. Limited correlation existed between aggregation in the device and current pathology testing.

Conclusions: It was determined that thrombogenesis in the device was influenced by a number of parameters, including haematocrit, platelet count, channel pre-coating, addition of amplification loop blockers or adhesion receptor blockers, and channel dimensions. Results appeared encouraging in achieving the aims of characterising a device that could accurately differentiate between samples from vWD patients and healthy controls. Despite difficulties in fabrication standardisation and up-scaling production, this novel prototype device is potentially a clinically useful, rapid and high throughput screening tool for vWD, as well as other shear dependent platelet and blood disorders.

MATTHEW CHAN

Evaluation of the effect of targeted therapeutic mild hypercapnia during cardiopulmonary bypass on cerebral oxygenation and neuropsychological outcomes.

Prof Rinaldo Bellomo & A/Prof Glenn Eastwood (Department of Intensive Care, Austin Hospital; The Australian and New Zealand Intensive Care Research Centre, School of Public Health and Preventative Medicine, Monash University)

I was lucky enough to work under the esteemed Prof Bellomo at the Austin Hospital ICU for my BMedSci this year, after completing 4th year in 2015. In particular, it was a privilege to be involved in such a high level project for my honours year, having the opportunity to help design and carry out a randomised controlled trial. I'd like to thank my supervisors and all members of the research team and affiliated departments for welcoming me and making the year such a great experience for me. I had a fantastic time working with the team and getting involved in the multitude of research projects being undertaken, and would highly recommend the year and this team for any future prospective students!

Background: Post-operative cognitive dysfunction (POCD) is commonly experienced by cardiac surgical patients requiring cardiopulmonary bypass (CPB). Intra-operative cerebral oxygen desaturation (COD) may be a causative factor in the development of POCD. Near-infrared spectroscopy (NIRS) provides the ability to monitor regional cerebral tissue oxygen saturation (SctO2) and detect episodes of COD. Presently, no clear intervention, supported by robust evidence, exists to optimise peri-operative SctO2 in these patients. Targeted therapeutic mild hypercapnia (TTMH) is an emerging intervention for SctO2 optimisation for resuscitated cardiac arrest patients who, like cardiac surgical patients, experience a period of cerebral hypoperfusion. Investigation of TTMH in cardiac surgical patients therefore appears warranted. Consequently, we aimed to test the feasibility, safety, and physiological effects of TTMH during cardiopulmonary bypass in cardiac surgical patients.

Methods: In an exploratory single centre randomised controlled trial involving adult cardiac surgical patients requiring CPB, participants were allocated to receive targeted normocapnia (TN) (PaCO2: 35-45mmHg) or TTMH (PaCO2: 50-55mmHg) from intubation to extubation in the intensive care unit (ICU). NIRS-assessed SctO2 was recorded at baseline, continuously throughout the intra-operative period and the first 12 hours in the ICU, and periodically on days two and three post-operatively. Neuropsychological testing was performed pre-operatively at baseline and on day five post-operatively. Additional data on patient demographics, physiological variables, and outcomes were also collected. SctO2 was analysed using repeated measures analysis of variance; other variables were compared using non-parametric statistics (medians reported).

Results: To date, 18/40 participants have been recruited. Of these, ten patients were allocated to TN, eight to TTMH, the median patient age was 67.5 years, and 83% were male. Patient comorbidities, smoking status, and type of surgery were similar between groups. Separation in mean intra-operative PaCO2 for each patient was achieved between the TN group and the TTMH group (39.4 mmHg vs. 53.1 mmHg; p<0.001). However, achievement of the TTMH target was less successful during mandatory ventilation in the ICU (48.8mmHg; p<0.001), and there was no significant difference once pressure support ventilation was initiated (p=0.289). Median pre- operative baseline SctO2 was 66.1% and 65.8% for the left and right hemispheres respectively, and was similar in both groups (left/right: p=0.408/0.203). The mean percentage SctO2 change from baseline was significantly different between groups over the pre-CPB and CPB operative periods (left/right: p<0.001 each) and on the left side in the post-CPB operative period (p=0.021), but remained similar between groups through the first 12 hours in ICU (left: p=0.127; right: p=0.728). COD from baseline was evident on day three post-operatively (left/right: -19.4%/-18.8%). Patient mortality, complication rate, neuropsychological test scores and POCD rates were similar between groups.

Conclusions: In cardiac surgical patients requiring CPB, TTMH was a feasible and effective intervention for prevention of intra-operative COD, but was difficult to achieve in the ICU. TTMH did not lead to any difference in neuropsychological outcomes, mortality, or morbidity. Post-operative follow-up of SctO2 revealed persistent COD at day three post-operatively. These findings support further research into the relationship between PaCO2 and SctO2, as well as post-operative changes in SctO2.

SAHAN CHANDRASEKARA

Autophagy and Chemoresistance in Multiple Myeloma

Professor Andrew Spencer[1,2], Dr Tiffany Khong[1]
[1]Australian Centre for Blood Diseases, Alfred Hospital, Monash University
[2]Department of Clinical Haematology, Alfred Hospital

I chose to undertake a BMedSc to delve into the unfamiliar world of research. As a medical student I have developed a particular interest in the fields of Haematology and Medical Oncology, both of which rely heavily on molecular diagnostic techniques and basic and translational laboratory research. During the course of the year I learnt a great deal about medical research and developed valuable critical thinking, writing and presentation skills. Most importantly though, I discovered a passion for translational medical research and am compelled to integrate research into my future career.

I owe particular thanks not only to my supervisors but also the whole Myeloma Research Group at the Alfred, who have helped me to find my feet in the laboratory and have provided continued support and mentoring.

Background: Two contemporaneously derived human myeloma cell lines (HMCLs) [TK-1 (bone marrow), TK-2 (peripheral blood)] from a patient with primary plasma cell leukaemia, the terminal phase of multiple myeloma (MM), provide a model of disease progression. Preliminary characterisation suggested upregulation of autophagy, a pro-survival pathway implicated in tumour growth and chemoresistance, in TK-2 compared to TK-1.

Aim: To further characterise differences in autophagy in a model of disease progression and explore the role of autophagy-induced resistance to bortezomib in multiple myeloma in a panel of HMCLs and a MM patient cohort.

Methods: HMCLs derived from the bone marrow (TK-1, KMS12-BM, TK-4), peripheral circulation (TK-2, LP1, U266) and pleural effusions (KMS26, KMS12-PE, NCI-H929) were cultured. TK-1 paired TK-2 and KMS12-BM paired with KMS12-PE provided a model of disease progression. Proliferation of TK-1, TK-2, KMS12-BM and KMS12-PE was monitored over a period of 1 week. Basal autophagy was characterised by measurement of static SQSTM1/p62 expression, LC3B turnover and SQSTM1/p62 turnover by immunoblot. Autophagy modulation in response to bortezomib treatment was determined by measuring SQSTM1/p62 expression using flow cytometry. Cell viability in response to treatment was measured using propidium iodide and flow cytometry. Additionally, examination of LC3B immunohistochemistry in a cohort of relapsed/refractory MM patients was conducted.

Results: Basal autophagy was significantly higher in TK-2/KMS12-PE compared to TK-1/KMS12-BM respectively. Immunoblotting demonstrated 7-fold greater baseline SQSTM1/p62 expression in TK-2 compared to TK-1 (p=0.014). Turnover of LC3B was 2.9 times greater in TK-2 compared to TK-1 (p=0.01) and 2.6 times greater in KMS12-PE compared to KMS12-BM (p=0.02). Turnover of SQSTM1/p62 was 2.4 times greater in TK-2 compared to TK-1 and 2.3 times greater in KMS12-PE compared to KMS12-BM. Bortezomib treatment induced autophagy (determined by decrease in SQSTM1/p62 expression) in both TK-1 and TK-2, but did so to a much greater degree in TK-2.

Despite differences in autophagy, TK-1 and TK-2 demonstrated similar sensitivity to bortezomib. Pharmacological autophagy inhibition with chloroquine resulted in an additive but not synergistic effect on cell death (synergy quotient (SQ) = 1.11 for TK-1 treated with 5nM bortezomib + 40µM chloroquine at 48 hours, SQ < 1 for all other doses and time points in TK-1 and TK-2). KMS12-PE was significantly more sensitive to bortezomib compared to KMS12-BM at 24 (p=0.02) and 48 hours (p=0.03). SQ values between 1 and 1.5 were obtained for KMS12-BM at 24 hours, however this was lost for clinically significant doses after 72 hours incubation. Overall, additive but not synergistic cytotoxicity was observed in both pairs of cell lines. Quantification of LC3B immunoreactivity in bone marrow trephines failed to correlate with bortezomib response in relapsed/refractory MM patients.

Conclusions: Upregulation of autophagy in extramedullary derived HMCLs compared with bone marrow derived HMCLs may represent an important event in MM disease progression. Inhibition of autophagy did not synergise with bortezomib therapy, suggesting that autophagy may not be implicated in mediating bortezomib resistance. Furthermore, expression of LC3B in the bone marrow of MM patients does not appear to predict for bortezomib treatment response.

FIONA CHEN

SOX2 Expression in the Fallopian Tube Epithelium in Patients with Ovarian Cancer

Professor Ahmed Ashour Ahmed, The Weatherall Institute of Molecular Medicine, Nuffield Department of Obstetrics and Gynaecology, Oxford University.
Professor Stephen Kennedy, Professor of Reproductive Medicine & Head of Department, Nuffield Department of Obstetrics & Gynaecology, University of Oxford. Dr Jim Tsaltas, School of Clinical Sciences, Monash University

I conducted my research at the Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, University of Oxford, UK. It was an incredible year getting to know the world of research whilst also getting to live in a different country. Living in Oxford was an experience unique to anything I had encountered. Whether it was chilling out in the Exeter MCR or listening to a speech at the Oxford Union, I enjoyed every moment of my time this year. Being able to go to a different European country for weekend trips was also a bonus!

Background: Ovarian cancer is a disease of high mortality. There is lack of clarity over the natural history and origin of the disease. It is thought serous tubal intraepithelial carcinomas (STICs) may be the preneoplastic origin of high-grade serous ovarian carcinomas (HGSOCs), since its discovery in the asymptomatic high-risk population after risk-reducing salpingo-oophorectomy. However, the rate of association between STICs and HGSOCs has remained unclear.

Sex determining region Y-box 2 (SOX2) is a transcription factor that maintains stem cell properties and differentiation restriction. It has been found to be overexpressed in the fallopian tube epithelium (FTE) of cases with HGSOC compared to benign conditions. The overexpression of p53, an important tumour-suppressor gene, and Ki-67, a marker of increased proliferation, has also been identified in HGSC cases and in STICs.

Aims: To appraise the literature describing the association between STICs and established HGSOCs. Also, the expression of SOX2 in the normal FTE of various ovarian diseases will be investigated. The association of SOX2 expression with Ki-67 and p53 expression will be explored in HGSC cases as well as those with STICs.

Hypotheses: STICs will be identified frequently in the FTE of women with HGSOCs. There will be increased expression of SOX2 in the FTE of HGSCs compared to other ovarian diseases. As expression of SOX2 increases, so will the expression of Ki-67 and p53 in HGSC FTE. There will be increased expression of p53, Ki-67 and SOX2 in the normal FTE of those with STICs compared to those without.

Method: *Systematic Review*

Ovid MEDLINE and EMBASE were searched. Studies were included if they evaluated the frequency of STICs in HGSOCs and were published in an English peer-reviewed journal. Studies were evaluated with the 'Strengthening and Reporting of Observational Studies in Epidemiology' criteria.

SOX2 Expression in Ovarian Disease and Association with p53 and Ki-67

This case-control study includes the FTs of 74 women with HGSOCs. 2 control groups include the FTs of 33 women with cystadenoma in one and 24 with borderline tumours or low-grade serous ovarian carcinomas (LGSOCs) in the other. Immunohistochemistry for SOX2 was performed on all cases, whilst Ki-67 and p53 was reserved for only HGSC cases. Quantification of the magnitude of expression was analysed. Participant ages, chemotherapy and STIC status was collected.

Results: *Systematic Review*

Ten articles met the selection criteria. The reported coexistence between STICs and HGSOCs was 28%-61%. Small sample size, lack of objective STIC diagnosis and the retrospective study design contributed to variability in rate.

SOX2 Expression in Ovarian Disease and Association with p53 and Ki-67

There is increased SOX2 expression in the FTE of HGSCs compared to those of other ovarian diseases. There is no apparent correlation between SOX2 and p53 or Ki-67 expression in the FTE of HGSCs. No differences in expression of SOX2, Ki-67 and p53 have been identified between cases with and without STICs.

Conclusions: STICs are common in women with HGSOC. SOX2 overexpression occurs in the normal FTE of HGSCs, but not in other ovarian diseases. SOX2 expression has no apparent association with STICs, p53 or Ki-67 in HGSC cases. The exact role of SOX2 and its mechanisms in carcinogenesis in the FTE of women with HGSC is yet to be determined.

NATASHA CHING

Epidemiology, clinical features and management of invasive group A streptococcal disease

Primary – Associate Professor Andrew Steer[1,3,4], OTHER: Monash University Primary – Dr Samar Ojaimi[56], Associate Professor Jim Buttery[2,5,6], Dr Nigel Crawford[2,3,4]

[1]Group A Streptococcus Research Group and [2]SAEFVIC, Murdoch Children's Research Institute. [3]Department of General Medicine, Royal Children's Hospital. [4]Department of Paediatrics, University of Melbourne. [5]Department of Paediatrics, Monash University. [6]Department of Infection and Immunity, Monash Children's Hospital.

I'm a first year advanced training paediatric registrar who is dual training in General Paediatrics and Paediatric Infectious Diseases. During my medical school years, I didn't take the year off to do a BMedSc when many of my peers did. Last year as I was planning my advanced training research project it was suggested that I should consider doing a BMedSc at the same time.

Passionate about Paediatric Infectious Diseases, I've always been fascinated by meningococcal disease and previously have wanted to do further research into the disease. There is already substantial research in this disease, and in addition, since the introduction of the vaccination the disease burden has significantly declined. Invasive group A streptococcal disease can be just as devastating, and doesn't have a clinical vaccination yet. This topic and project really attracted me due to the clinical impact the information in the long run has the potential to have.

It's been a real experience doing a BMedSc alongside clinical work. It's definitely demanded a great deal of forward planning, but I've thoroughly enjoyed it also. I'd be more than happy to speak to any trainees who were interested in doing the same thing in the future.

Background: Group A beta-haemolytic streptococcus is a common infective organism that can cause serious invasive illness in children, with potential to cause death or significant disability. It causes a wide spectrum of disease; from the common less significant infections such as pharyngitis and impetigo to more severe presentations including streptococcal toxic shock syndrome and necrotising fasciitis.

Surveillance and understanding of the epidemiology of this infection is important to enable preventative measures, as well as provide further advice on appropriate early management interventions that may impact on outcomes.

Method: We aimed to describe the clinical and microbiological epidemiology of invasive group A streptococcus (iGAS) disease. To establish a cost-effective ongoing surveillance system for iGAS disease at the Royal Children's Hospital Melbourne and Monash Children's Hospital.

Data were prospectively collected through active surveillance of iGAS at Royal Children's Hospital Melbourne (October 2014 – June 2016), and Monash Children's Hospital (March 2016 – June 2016). In addition, retrospective data collection was done at MCH from 1st January 2015 until 31st December 2015.

Cases were included if GAS was isolated from a sterile site. Patients and their families were approached for informed consent to be included in the study. Demographic and clinical data were collected using a standardised and comprehensive data collection form entered directly into a REDcap database. Severe IGAS disease was defined as requiring either of mechanical ventilation or inotropic support, and very severe disease was defined as requiring extracorporeal membrane oxygenation. GAS isolates were stored at the GAS laboratory at the Murdoch Children's Research Institute, and emm-typing was subsequently performed following the Centre of Disease Control GAS emm-typing protocol.

Results: There were 30 cases of iGAS disease flagged and recruited following the identification of GAS from a normally sterile site. Five cases were excluded upon review as they did not meet the case definition for iGAS so that 25 cases were included in the final analysis. The median age of children was 3.2 years, ranging from 4 days to 11.3 years. There were seven cases (28%) of severe disease, and two cases of very severe disease. There were nine children (36%) who had presented to an emergency department during the illness prior to their admission presentation, with four of these cases having severe disease. There was a wide-spectrum of clinical disease observed with the most common disease being bacteraemia without focus (n=9, 36%), followed by cellulitis (n=7, 28%), and osteoarticular disease (n=5, 20%). emm types were known in 22 (88%) with two serotypes contributing to 50% of cases: emm1 was the most common identified (n=6, 27%), followed by emm4 (n=5, 23%). There were three children with ongoing disability at 6-months follow-up in the setting of iGAS disease complications.

Conclusions: There is considerable morbidity associated with iGAS disease in children. Microbiology-based identification is a relatively low-resource surveillance system. This system could feasibly be implemented at other Paediatric Active Enhanced Disease Surveillance (PAEDS) sites around Australia to establish a nation-wide surveillance system.

RU DEE CHUNG

Process mapping in the intraoperative period

Associate Professor Warren Matthew Rozen, Associate Professor David Hunter-Smith; Department of Surgery, Peninsula Health

I'm Dee, and I decided to complete a BMedSci after my 4th year of medicine to get a firm grounding in research. I chose my project as I am passionate about surgery and public health. This field of quality improvement in healthcare is essential in our fast expanding world, and I believe all clinicians have a duty to continuously improve their skills and service delivery.

This project was undertaken at Frankston Hospital, which serves as a major healthcare provider for the metropolitan and regional areas of Victoria's Mornington Peninsula. The project investigated the use of process mapping, a quality improvement tool, in the improvement of surgical efficiency across different surgical specialties.

My project was very hands-on from the start, and much time was spent in the operating theatre. This kept my clinical skills sharp and I learnt the skills needed to execute good clinical research. I have also had the privilege to work with outstanding surgeons, anaesthetists, nurses and technicians. My advice for future students is to choose an area you are passionate about, and a supervisor who is too. Feel free to ask me any questions via email at rudeechung@gmail.com.

Background: Inefficiencies within surgical care contribute to long elective surgery waitlists. Identifying potential areas of improvement in the intraoperative period is the first step towards improving efficiency. Process mapping has been identified as a strategy to improve surgical efficiency. However, there is limited evidence of its applicability and benefits when applied to the individual surgical steps of various surgical specialties – and no Australian studies have done so. This study aims to establish the feasibility and effectiveness of process mapping as a tool in the improvement of surgical efficiency during the intraoperative period across different surgical specialties in an Australian context.

Method: A cohort of surgeons based at a tertiary referral centre (Peninsula Health) were recruited, with all procedures performed across two hospital campuses – Frankston Hospital (public hospital) and Beleura Private (private hospital) between March and September 2016. Process mapping was applied to the intraoperative period (defined as period on-the-day of surgery) of laparoscopic cholecystectomies, total knee replacements, deep inferior epigastric perforator flap (DIEP flap) breast reconstructions, and total thyroidectomies. This study's process mapping approach identified the operation step via discussions with consultants and real-time pathway observation of each operation with timing of each step. Any additional steps and/ or delays, and the position of the main surgeon (consultant or registrar) was recorded. Types of additional steps and delays that occurred were collated into similar themes. Process maps for cases with the longest and shortest surgical time in each operation group were created. Mean time taken (± standard deviation) for each intraoperative component and surgical step was found. A sub-group analysis comparing consultant and registrar mean operating time and time taken for completion of surgical steps was conducted.

Results: The number of cases observed were: 32 laparoscopic cholecystectomies, 33 total knee replacements, 5 DIEP flap breast reconstructions, and 12 total thyroidectomies. The intraoperative component that had the greatest variance in time was identified for each surgery type. Step(s) with large variability in time taken were found for each surgery. Sub-group analysis on the laparoscopic cholecystectomy and total knee replacement groups revealed some steps that took significantly longer for registrars to complete compared to consultants. Delays accounted for 4.77% of intraoperative time in the laparoscopic cholecystectomy group; 2.24% in the total knee replacement group; 1.71% in the DIEP flap breast reconstruction group; and 1.81% in the total thyroidectomy group. Different types of delays and additional steps were described. Process maps of the surgical period for the cases with the longest and shortest surgical time for each group depicted the process flow, step times, delays and parallel steps.

Conclusions: This is the first Australian study to demonstrate different ways process mapping can aid in the improvement of intraoperative efficiency. Process mapping can: classify delays; identify which component of the intraoperative period needs to be targeted for improvement; determine variability in surgical step time; and enables the identification of factors that affect surgical time. The same process mapping approach can also be applied across multiple surgical specialties.

KATHERINE COLMAN

Current practices and priorities surrounding haemoglobin thresholds to define anaemia: an exploration of current haemoglobin reference ranges and priorities for reconsideration

Associate Professor Erica Wood – School of Public Health and Preventive Medicine, Department of Epidemiology and Preventive Medicine, Monash University, Australia. Dr Sant-Rayn Pasricha – MRC Human Immunology Unit, Weatherall Institute of Molecular Medicine, University of Oxford, UK. Dr Simon Stanworth – National Health Service Blood and Transplant, John Radcliffe Hospital, University of Oxford, UK

I studied my BMedSci this year in the NHS Blood and Transplant division of the John Radcliffe Hospital at the University of Oxford. I had an amazing year and enjoyed taking ownership over my research project, and feeling useful for the first time in medical school. I am very thankful for the great support and advice I received all year from my supervisors and all the staff at NHSBT. I was also fortunate enough to work in collaboration with the World Health Organization, including visiting WHO headquarters in Geneva in March for a conference.

My BMedSci was an amazing opportunity to live overseas for a year, and meet and live with like-minded people from all over the world. Being an Associate Member at Exeter College allowed me to experience a thriving college environment, from relaxing in the MCR to attending formal halls, to meeting other colleges at wine and cheese nights. We also became involved in university life including trying (and failing at) rowing, and hearing inspirational international speakers at the Oxford Union. Oxford has so much history and tradition to offer, plus with Europe on our doorstep, we had a truly unforgettable year.

Background: Anaemia is a significant problem, particularly affecting pregnant women (estimated 32.4 million, 38.2%, affected worldwide in 2011), and children under 5 years (estimated 273 million affected worldwide, 42.6%). Anaemia prevalence ranges from under 25% in the Western Pacific Region, to half those in South-East Asia and Africa.

In 1968, WHO proposed anaemia be defined as Hb<13g/dL in males, <12g/dL in females, and <11g/dL in pregnancy based on four studies that, according to current standards, are considered biased by limited data and inadequate methodology. Yet this definition has since been maintained with only minor adjustments.

Consequently there are concerns this threshold is not universally appropriate. As Shields described in 2011, there are "currently no widely acknowledged reference range[s] for haematinics." To optimise health outcomes, clear haemoglobin (Hb) thresholds are required to define, and therefore diagnose, anaemia.

Method: We surveyed laboratories to document current Hb thresholds used, the degree of consensus between laboratories, source of laboratory ranges, and confidence in current WHO anaemia guidelines. We also conducted a worldwide scoping exercise, asking experts and clinicians their views as to research priorities concerning Hb thresholds to define anaemia.

Results: The questionnaire of 208 laboratories largely encompassed UK (67% respondents) and European (28%) laboratories. It found significant variation in Hb thresholds used, with under 10% of laboratories applying specific Hb ranges for pregnancy, pre- and post-menopausal women, and the elderly. No laboratory applied ethnic-specific thresholds. Mean Hb thresholds to define anaemia fell below the value recommended by WHO for all population subgroups except males. Few laboratories (11%) referenced WHO values, with more opting for textbook values (39%). Only 18% of respondents expressed full confidence in the accuracy and applicability of current WHO values to their populations,

with 22% having concerns and 49% not having considered this.

In the scoping exercise, 123 respondents proposed 553 research priorities. Commonly raised themes included clarifying what is meant by anaemia, which population subgroups require separate Hb thresholds, and approaches to redefining anaemia.

Conclusions: Laboratories are inconsistent in Hb thresholds used to define anaemia, this variation greatest for females, including pregnant women, and young children. Laboratories are generally waiting longer (i.e. using lower Hb thresholds) to diagnose and treat anaemia than WHO recommends, risking under-diagnosis of anaemia. Such disparity of Hb thresholds risks complications and financial and societal costs of mismanaging anaemia, and creates unacceptable inconsistencies in healthcare. Varying Hb thresholds to define anaemia also affects the 'apparent' anaemia prevalence.

The confidence level in, and uptake of, WHO anaemia guidelines are low. Populations with poorly defined Hb ranges by laboratories – including pregnant females, children and those of different ethnicities – were frequently mentioned in the research scoping exercise, suggesting these are well-recognised knowledge gaps. These results highlight the need for reconsidering Hb thresholds to optimise anaemia diagnosis and management. This is an important process given the need for evidence-based guidelines.

BEN CROCK

Investigating the eye health of refugees in South East Melbourne

Professor Grant Russell, Dr. I-Hao Cheng, Dr. Joanne Enticott and Dr. Riki Lane
Southern Academic Primary Care Research Unit (SAPCRU), in collaboration with Monash Health Department of Ophthalmology

I decided to undertake a BMedSci after my fourth year of MBBS to gain an insight into the world of research. I chose to do a project in refugee health, an interest of mine, and with the help of my supervisors I was able to design my own project, which also incorporated an element of ophthalmology, another field I'm interested in. My project looked at the prevalence of eye disease in refugees and Australians attending Monash Health's Ophthalmology outpatient clinic, and compared the two cohorts.

I chose to do a secondary data project, rather than a lab-based or clinical project, because I wanted the experience of designing a research project and the freedom to thoroughly explore a specific population in the time frame of only one year. My supervisors were incredibly supportive, and the experience of building and conducting my own project from the ground up was very rewarding, despite the steep learning curve. If you have any questions about working with SAPCRU, in the field of refugee health, or the experience of designing your own project, please feel free to contact me at benjcrock@gmail.com.

Background: Refugees are at risk of poorer health outcomes internationally and in Australia across a broad range of areas of physical and mental health. While refugee eye health has been shown to be poor in international studies, there is little published literature about the eye health of refugees in Australia. Other population subgroups, such as indigenous or rural Australians, have benefited from focussed research into eye health, and in an Australian context the same could be expected of refugees. An important early step in understanding the epidemiology of eye problems within the refugee population would be to compare the prevalence of common eye conditions and visual impairment in this community to that of other Australians.

Aim: To determine whether refugee status influences the prevalence of common eye conditions or visual impairment among people accessing tertiary ophthalmological care in South-East Metropolitan Melbourne.

Method: For this quantitative, retrospective cross-sectional observational study, patient data from Monash Health Ophthalmology outpatient clinic were collected. Two cohorts were selected from those attending the clinic between 2011 and 2015 inclusive; a refugee cohort, using country of birth as a proxy measure of refugee status, and a comparative Australian-born cohort of twice the size. Patients under the age of 4 were excluded. Demographic variables were obtained from Monash Health's Outpatient Database, while the presence or absence of eye diseases and visual impairment was extracted by a patient note audit.

Demographic characteristics were compared between the two cohorts using odds ratios (OR) for binomial variables and mean differences for continuous variables. The prevalence of common eye diseases and visual impairment (defined as a best corrected visual acuity <6/12) were recorded as binomial variables. Prevalence was compared between cohorts using unadjusted odds ratios followed by multivariate analysis adjusting for refugee status, age, gender, smoking, and socio-economic status.

Results: The refugee cohort had a distinctly different demographic profile; refugees were on average 6.35 years younger than Australian patients (95% CI 2.90-9.80), more likely to be male (OR 1.74, 95% CI 1.31-2.31), less likely to smoke (OR 0.54; 95% 0.40-0.74), and were more likely to be in the lowest socio-economic quintile (OR 3.18; 95% CI 2.30-4.41) and to speak a language other than English (OR 128; 95% CI 65.8-252). Multivariate analysis demonstrated that refugees were more likely to have cataract (OR 1.69; 95% CI 1.07-2.70), visual impairment or blindness (OR 1.89; 95% CI 1.21-2.97) and pterygium (OR 6.91; 95% CI 3.48-13.7). We found no significant difference in risk for glaucoma, macular degeneration, diabetic retinopathy, eye trauma or refractive error.

Conclusions: Refugees accessing public hospital outpatient eye care in South-East Melbourne are a demographically distinct group compared to other Australians accessing the same service. The data suggests that eye health practitioners consider refugee status as an independent risk factor for cataract, visual impairment and pterygium, although further research into refugee eye health in the wider community would be needed to generalise these results to the broader population of refugees in Australia.

KEVIN CULHAM

Modulation of Plasmalogens to Prevent Metabolic Disease

A/Prof Peter Meikle – BakerIDI - Supervisor
Prof Bronwyn Kingwell – BakerIDI – Co-supervisor

I'm a fourth year medical student from Indonesia; parts of my course requirements dictate that I study abroad for my honours year. I was set on becoming a doctor and pursuing my interest in cardiology so undertaking a scientific project at Baker IDI whilst completing my study at Monash University was initially a means to an end.

Given my interest area, and a recommendation about Baker IDI from a friend, I found my way to Associate Professor Peter Meikle's laboratory. One of the primary goals of the Metabolomics laboratory is to understand the difference between stable and unstable coronary disease, which includes the examination of changes in lipid metabolism associated with coronary artery disease.

When I started my honours project in early 2016, it was the first time that I set foot in a scientific laboratory and I loved it. So much so that it has opened my eyes to the possibility of a career as a clinician scientist.

Background: Metabolic syndrome is a significant risk factor for cardiovascular disease. It is especially common in individuals who consume excessive nutrients and are physically inactive. Metabolic syndrome is associated with a number of states that contributes to the development of cardiovascular disease. These include atherogenic dyslipidemia, increased blood pressure, impaired glucose tolerance, increased thrombosis and increased inflammation. Dysfunction in lipid metabolism can cause increased levels of oxidative stress and inflammation, which contributes to the development of atherosclerosis. Previous studies from our lab have identified that plasmalogens (a type of membrane phospholipids) are negatively associated with coronary artery disease.

Our study aims to see if the supplementation of alkylglycerol (in the form of shark liver oil) can increase the level of circulating plasmalogens in humans, and to see if there are beneficial effects to health.

Method: This study was a randomized, double-blind, placebo-controlled (methylcellulose) cross over study. The study population consisted of 10 males from 25-60 years of age with a BMI of 28-40 kg/m2. The participants had no evidence of diabetes or CVD, were not taking any lipid lowering or antihypertensive medication, and were not taking any fish oil supplementation. The participants had normal liver function. Mass spectrometry is used to measure the lipid concentration in plasma, lipoproteins, erythrocyte membranes and leukocytes. Monocyte subsets population and their activation of the participants were measured by the Canto II flow cytometer and the clinical measurements were performed by the Alfred Pathology.

Results: The supplementation of alkylglycerol in blood plasma displayed an increase in ether lipids with decreasing dyslipidemia. In leukocytes and erythrocytes, we observed an increase in choline plasmalogen and its precursors. The modulation of plasmalogen was also associated with a significant reduction of intermediate monocyte subset. In addition, there was a reduction of the level of inflammatory marker (hsCRP), triglyceride, cholesterol and total white blood cell count (mainly neutrophils) following the supplementation of alkylglycerol.

Conclusions: The supplementation of alkylglycerol (in the form of shark liver oil) increases the level of plasmalogens in human plasma, lipoprotein fractions, white blood cells and erythrocyte membranes. The modulation of plasmalogens in humans was associated a reduction in the obesity related dyslipidemia (a decrease in total cholesterol and triglycerides). We also observed a decreased white blood cell count, due primarily to a reduction in the number of neutrophils. Further to this, the levels of intermediate monocytes were decreased following alkylglycerol supplementation as was the level of hsCRP.

These results suggest that plasmalogen modulation leads to a reduction in obesity related dyslipidemia, which is associated with chronic inflammation in atherosclerosis.

AMANDA DHARMANINGPUTRI

Collaboration between Platelets and Neutrophils to Prolong Inflammatory Response

Dr Elizabeth Gardiner and Robert K. Andrews of Australian Centre of Blood Diseases of Central Clinical School.

I was a fourth year medical student when I took the middle-year intake program for BMedSc(Hons). I was interested in taking a project that enables me to have newer and better knowledge in the field of haematology and oncology, thus Australian Centre of Blood Diseases seemed to be the best place to help me achieve my goal. In my honours year, I aimed to look for the result of collaboration between platelets and neutrophils in the form of neutrophil extracellular traps that can enhance inflammation using flow cytometry. Before I was on board with this course, many people had told me that honours year is not going to be easy. Boy, did I sweat blood and tears during that year! Up to this day, I still remember that satisfaction when I had a good result in front of the flow cytometry machine and crying on the laboratory bench when I failed an experiment. I hope other prospective students will be able to enjoy this life-changing yet exciting journey in life because I know I wouldn't trade that time for anything else in the world! I really love to share my experience with other, so don't be hesitant to contact me at amanda.dharmaningputri14@gmail.com!

Background & Aim: Neutrophil Extracellular Traps (NETs) release is a novel neutrophil defensive mechanism. NETs take forms of DNA lattice-like structures that can interact with pathogens to decrease their virulence factors and possibly kill them. There have been several postulates to address the formation of NETs in inflammation-associated conditions and one of them being the interaction between neutrophils and platelets. Increasing studies have shown that activated platelets can induce neutrophils to generate NETs. Interaction between these vascular cells could be studied using several approaches. However, some of them still have some limitations. This project aims to establish a rapid and convenient experimental approach to study NETs formation using platelet-leukocyte suspension with a flow cytometry-based methodology.

Methods: Human whole blood samples were processed in order to obtain platelet/leukocyte suspensions. Platelets were activated using the generic agonist phorbol-12-myristate-13-acetate (PMA), to induce/enhance platelet-leukocyte aggregates in cell suspensions to mimic an inflammatory condition in healthy blood. Immunostaining techniques using antibodies targeting platelet-specific markers, a pan-leukocyte marker and releasate molecules from activated neutrophils were employed to quantitate cell and molecular responses. Analysis by flow cytometry enabled monitoring of platelet-leukocyte aggregates and cell-surface associated neutrophil elastase, a marker of NETs formation. Data were assessed using FlowJo software with back-gating analysis.

Results: In platelet/leukocyte suspensions, treatment of platelets with PMA resulted in increased levels of platelet-leukocyte aggregates. Within leukocyte subsets, the highest number of platelet-positive events was associated with the neutrophil/granulocyte subpopulation. We established a protocol to detect and quantify the soluble marker of NETs formation, neutrophil elastase, in PMA-treated suspensions of platelets and leukocytes.

Conclusion: These findings suggest that flow cytometry is a promising approach to monitor and quantitate NETs formation in platelet-leukocyte suspensions. Using this assay may improve assessment of blood samples from patients with dysregulation in immune responses, thus it should be considered to bring this experimental approach into use in clinical settings.

KEYUR DOOLABH

Zika: ethical questions in the South American outbreak

Dominic Wilkinson – Oxford Uehiro Centre for Practical Ethics
Julian Savulescu – Oxford Uehiro Centre for Practical Ethics
Michael Selgelid – Monash University
Lucius Caviola – Oxford Uehiro Centre for Practical Ethics

I was lucky enough to be selected for the Oxford Bioethics BMedSc programme after finishing third year, and had an absolutely great time! I'm interested in philosophy and public health, so mapping the ethical terrain around the Zika virus in this project was a very rewarding experience. I'd advise future students who go to Oxford to throw themselves into the student culture as much as they can, and use the research as a springboard into other philosophical pursuits. I'm happy to be contacted for advice about how to get into the programme.

Background: The outbreak of Zika virus in 2015/2016 has affected millions of people in South and Central America, and was declared a Public Health Emergency of International Concern by the WHO in February 2016. Zika has been associated with a pattern of severe microcephaly and neurological injury in fetuses, (Congenital Zika Syndrome, CZS). Since Zika is poorly understood and its worst effects are felt by fetuses, it raises a range of ethical issues.

Method: This thesis combined empirical data with ethical analysis. A short online survey gathered responses from the US public, measuring their prioritization and evaluation of different hypothetical and actual interventions to tackle Zika/CZS. These included mosquito control, antiviral treatment, vaccination and abortion. Interventions were presented in pairs, and preferences were tested with Likert scales and with 'willingness-to-pay' style questions. The survey also tested participants' moral intuitions on the non-identity problem, both with a Zika-based question and with an adaptation of Derek Parfit's '14 year old girl' thought experiment.[1]

The ethical analysis systematically reviewed the literature, outlined the ethical issues around Zika and identified any novel ethical features of the disease. It critically appraised arguments in the literature and put forward suggestions in some areas, comparing its findings with the results of the empirical survey to establish a level of reflective equilibrium.

Results: The survey had 98 valid responses. Participants preferred preventative interventions like mosquito control or vaccination over contraception (63% and 54% respectively), and had a strong aversion to termination of pregnancy (83% preferred contraception). In the willingness-to-pay questions, participants were divided: a proportion of those who preferred one intervention would easily change their preferred intervention to avoided a few additional cases of CZS; however, some respondents would never prefer the alternative intervention, or would only prefer it if it avoided many extra cases. There was no change in preferences (for prevention of Zika compared with birth control) after explanation of the non-identity problem.

The ethical analysis gave an overview of Zika's more familiar ethical issues, including proportionality, surveillance, quarantine, resource allocation, and the testing of novel interventions. For the issues more particular to Zika, I argued that: we should favour more stringent cut-offs when screening for CZS; that advice on global travelling and events like the Rio Olympics should be based on empirical risk analysis; that the non-identity problem should not rule out contraception for tackling CZS; that termination of pregnancy should be made accessible in Zika-affected areas; and that novel mosquito control techniques should be used but need to be monitored for human and ecological harms.

Conclusions: Analysis and attention to the ethical issues raised by Zika is an important part of the public health response. This thesis has identified a broad range of ethical issues around Zika, as well as being the first study to measure the relative value placed by the public on different interventions to tackle Zika and their views on the non-identity problem.

JOEL FERNANDEZ

Does placental telomere length differ by maternal region of birth: A biological driver of increased adverse outcomes in South Asian born women

Professor Euan Wallace – The Ritchie Centre, Hudson Institute of Medical Research, Monash university, Monash Health, Department of Obstetrics and Gynaecology
Dr. Miranda Davies-Tuck – The Ritchie Centre, Hudson Institute of Medical Research.

I chose to do a BMedSci because I wanted a change of pace after the stress of 4th year. I chose to do an obstetrics project after I listened to one of Prof. Wallace's lectures in my women's health rotation in 4th year. I just emailed him and within a couple of weeks we'd had it all sorted. The idea was that my project would give me a taste of everything from recruitment of patients to lab work to data collection. Overall I'd say we've achieved the goals we set out with (i.e. don't die in the lab and don't make a complete fool of yourself).

What a massive learning curve this year has been. Doing a research year has definitely altered the way that I see my medical career unfolding. My advice to future students is that lab-based projects are difficult but rewarding. Naturally I've bumped into a lot of expensive lab equipment, I've inhaled more than my fair share of harmful chemicals and my fingertips no longer sense cold because of not wearing the protective gloves when handling stuff in the minus-80°C fridge. Nonetheless I've learned so much this year and couldn't have enjoyed it more.

Background: Women of South Asian origin have an increased risk of adverse pregnancy outcomes compared to Caucasian women whilst South-East/East Asian women have better outcomes. South Asians have also been found to have smaller babies than Caucasians and are more likely to require obstetric intervention in labour due to fetal compromise. Many studies blame social factors such as education or socioeconomic status as the reason for these differences in outcomes. However, these racial differences in outcomes have been shown to persist across generations and in both high and low income countries, suggesting a biological factor plays a role.

Methodology: Using the TeloTAAG Telomere Length Assay kit, I digested genomic DNA extracted from placentae of women born in South Asia, Australia and South-East/East Asia. These were run through a gel electrophoresis and transferred onto a nylon membrane via Southern Blotting. The nylon membrane was treated with a telomere probe that fluoresces under X-Ray light. I analysed the membrane and was able to determine the mean telomere length of each sample in kilobases. In total I analysed 21 South Asian placentae, 20 Australian placentae and 17 South-East/East Asian placentae.

Results: There was no statistically significant difference between the different ethnic groups and their telomere lengths. BMI was positively correlated with telomere length and gestation was positively correlated with telomere length in our South-East/East Asian women.

Conclusion: It appears that there is the length of telomeres does not differ by ethnicity in the placentae of women born in South Asia, Australia and South-East/East Asia. Further investigation is warranted to identify the biological driver for ethnic differences in pregnancy outcome.

LUKE FLETCHER

The design, creation and validation of a computerised decision support system for haemodynamic monitoring and management in intensive care

A/Prof Geoffrey Parkin, Intensive Care Unit, Monash Medical Centre;
A/Prof Christopher Wright, Faculty of Medicine, Monash University

My name is Luke. I completed by BMedSc(Hons) at end of my fourth year of medicine. I have an interest in intensive care and anaesthetics. I also have an interest in the way that technology can intersect with medicine to improve health care delivery and health outcomes for patients. Intensive care provides a unique environment where physiological parameters are more readily available, and are thus amenable to integration with technology. My project is in building a computerised decision support system for monitoring and managing the circulatory system of patients.

My research was undertaken at the Monash Medical Centre Intensive Care Unit. I was primarily supervised by A/Prof Geoffrey Parkin, who has been an incredible teacher and mentor. My project has taught me an amazing amount about circulatory physiology, assessment and management. I have also learnt a lot about electronics, hardware and software engineering.

If you are interested in discussing my project further, or interested in discussing other projects of a similar nature, please feel free to contact me at lukefletcher@mac.com.

Background: The circulatory system is of paramount importance in sustaining life. It is responsible for delivering oxygen to the tissues for consumption. Protuberances to the balance of this system may result in haemodynamic instability and circulatory shock, which are common and are major causes of morbidity and mortality in intensive care. Haemodynamic monitoring and assessment is used to detect and guide management of haemodynamic instability, however exactly which physiological variables to monitor is the subject of debate. Further, many variables are not readily available at the time of clinical decision making. In other disciplines, clinical decision support systems have been shown to improve clinical practice, and invite an innovative solution to circulatory management.

The aims of this research were to design, build and validate a decision support system capable of monitoring and guiding management of the circulatory system of patients in intensive care. It also seeks to quantify important variables, including oxygen consumption, cardiac output, and aortic pressures continuously. Circulatory assessments, and resulting management plans would be displayed in an intuitive interface readily available to the clinician at the time of decision making. It was hypothesised that the calculated variables would be sufficiently accurate against alternative means of measurement, and that assessment and management plans would be similar to those produced by clinicians.

Method: A hardware and software platform was created, called Circulate™. It connects with existing intensive care equipment to obtain physiological variables, and measures other variables with inbuilt sensors.

Oxygen consumption and delivery targets were estimated mathematically. This permitted cardiac power and systemic vascular resistance targets to be produced to assess the sufficiency of the hydraulic work of the heart, and the circulatory resistance, respectively. A better means of assessing volume responsiveness was also developed. As haemodynamic instability occurs, Circulate™ produces assessments and management plans, which are wirelessly transmitted to an iPad app, where it can be viewed with a simple and easy to use interface by the clinician.

Oxygen consumption, continuous cardiac output, and aortic pressures were calculated with: the ventilatory inspired-expired difference in oxygen; the Liljestrander-Zander formula; and radial-to-aortic Fourier transform functions, respectively. These variables were measured in cardiac post-surgical patients and compared against alternative means of measurement. Assessment and management plans were to be compared against those produced by clinical staff.

Results: The decision support system described above was successfully designed and built. The validation studies were not powered sufficiently to draw formal conclusions to support the hypotheses. Initial results from the validation of oxygen consumption, continuous cardiac output and aortic pressures look promising. Data supporting the quality of assessments and management plans produced is pending.

Conclusions: Circulate™ is a simple, cheap and powerful tool in circulatory assessment and management. Further samples must be obtained to validate the variables calculated by Circulate™, and the resulting assessments and management plans produced. It is hoped that, if successfully validated, Circulate™ could be tested as an intervention in a randomised control trial to determine if it improves clinical outcomes for patients in intensive care.

HUGH GAO

In silico analysis of IFN-ε in ovarian cancer and its correlation with immune signatures

Professor Paul Hertzog

Dr Helen Cumming, Centre of Innate Immunity and Infectious Diseases, Hudson Institute of Medical Research

I chose to undertake the honours year to understand what research is about. I chose a project in bioinformatics because I wanted to understand how computational methods are being applied to analyse biological problems.

Background: Ovarian cancer is the seventh most common female cancer, accounting for 3.6% of all female cancers worldwide. The low five-year survival rate of 43.0% prompts the need to understand the mechanism of ovarian cancer initiation and progression. Type I interferons are a family of cytokines. Interferon epsilon (IFN-ε) is a novel member of this family, and is constitutively and highly expressed in the female reproductive tract epithelium. Its expression, however, is downregulated in patients with high-grade serous ovarian cancer. Other members of the type I interferon family have known anti-microbial and anti-tumour functions. While IFN-ε has a known anti-microbial function, it has no known anti-tumour functions.

Method: Serous ovarian cancer cohorts with oligonucleotide microarray data were downloaded and analysed to determine if IFNE expression was correlated with disease progression by stage or metastasis, or overall survival. Robust k-means clustering was applied the transcriptome profiles of the tumours to assign patients to 1 of 4 clusters. The analysis was repeated and stratified by cluster.

Results: IFNE expression is not correlated with serous ovarian cancer disease progression by stage or metastasis, nor was it correlated with overall survival. However, high IFNE expression is correlated with longer overall survival in tumours characterised by low immune cell infiltration (log-rank p-value < 0.05).

Conclusions: This study is the first to identify IFNE expression as being associated with longer overall survival in serous ovarian cancers characterised by low immune cell content. Hence, secreted IFN-ε may play an important tumour-suppressing role in tumours with low immune cell content or after immune cell exhaustion. Further wet lab studies are necessary to establish IFN-ε as playing a causal role in prolonging overall survival in serous ovarian cancer.

KEVIN ARISTYO GUNAWAN

Modulation of Plasmalogens in Humans: A Potential New Therapy for Atherosclerosis

Associate Professor Peter Meikle and Professor Bronwyn Kingwell – Baker IDI Heart and Diabetes Institute

Honours year was a truly outstanding experience for me. I was fortunate enough to take part in a therapeutic human RCT project at Baker IDI Heart and Diabetes Institute, with the Metabolomics Lab. I chose this project, as I have always been interested in lipidomics and its therapeutical value. I firmly believed the research knowledge that I have acquired will be very useful during the rest of my clinical years. I would definitely encourage potential students to undertake an honours year. Know what your passion is and be wise in choosing your project. Overall, this year proved to be amazing and an absolutely rewarding experience. Feel free to contact me on kevin.aristyo@gmail.com if you have any questions.

FIDINNY IZZATURRAHMI HAMID

Investigating Arg2 as a Novel Target of IL-10/MiR-155 Signaling Pathway in Macrophages

Dr. Claire McCoy, Dr. Jonathan Ferrand & Prof. Bryan Williams
Center of Cancer Research at Hudson Institute of Medical Research
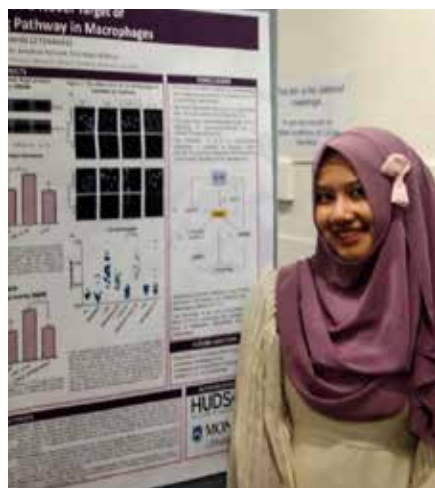
It's amazing how one small decision can lead to major life-changing experiences on your life. Back home I'm studying medicine at University of Indonesia, where I had a few experiences on looking at mRNAs relating to cancer and knowing how such small molecules can bring huge impacts on our homeostasis is quite intriguing for me. Hence I looked up some Monash affiliated research institute websites where I came across Dr.Claire McCoy's project on mRNA signalling in inflammation and cancer. That moment when she responded positively I knew it was going to be a big year for me. Great hands-on experience, friendly and supportive working and living environments made me really sure that I had the best moments of my life which I can't be anymore grateful for. At the end of the year I got to work as her technical assistant which greatly boost my confidence and my love for the field. Don't be hesitant to go blunt, it's okay to face the challenges on pursuing what you like. It's going to be worth it.

Background & Aims: Inflammation is a complex yet important process requiring a broad range of mechanisms and mediating proteins. It is vigilantly controlled by a number of feedback mechanisms to ensure a robust and effective function on killing pathogens. One way to prevent excessive inflammation is through the action of the anti-inflammatory cytokine IL-10. A previous study has identified that IL-10 is a potent inhibitor of miR-155 in cells of the immune system. To uncover unique downstream targets of the IL-10/miR-155 signalling axis and the role of these targets in macrophage function, an Affymetrix microarray revealed a possible target gene, arginase type 2 (Arg2), to play a role and merits further exploration. Moreover IL-10 has been found to lower inflammation through a process known as autophagy, a process which is possibly mediated by Arg2 and to our knowledge has yet to be clearly investigated. Therefore, this study seeks to probe whether Arg2 is a novel target of IL-10/miR-155 signalling and thus mediates IL-10 function in controlling inflammation as well as cellular processes such as autophagy.

Methodology: Primary bone marrow derived macrophages (BMDM) cells were stimulated with a potent bacterial agonist LPS to stimulate an inflammatory response. The anti-inflammatory effects of IL-10 were investigated by the administration of IL-10 alone or in the presence of LPS for 24 hours. RNA from the stimulated cells was extracted and converted to cDNA. Using primers specifically designed for Arg1, Arg2 and 18s mRNA, mRNA expression was measured using semi-quantitative and Real-time PCR. Cells from the same model were lysed for protein and analysed by western blotting for Arg2 and control -tubulin protein. Arginase activity was measured on total cell lysates from stimulated BMDM and the production of urea was observed. To identify the functional effect of IL-10 on autophagy, LC3 punctuation was visualised on stimulated green fluoresecent protein-Light chain 3 (GFPLC3) immortalised BMDM (iBMDM) under fluorescent miscropscopy. To investigate if the IL-10 inhibition of LC3 punctuation observed by immunofluorescence and LC3 punctuation

was dependent on arginase, the arginase inhibitor nor-NOHA was employed.

Results: IL-10 was found to induce Arg2 mRNA on semi-quantitative PCR and RT-PCR, as well as protein expression on western blot and immunofluorescence analysis. Arginase enzyme activity was also induced by IL-10. An LPS stimulation causes a great induction of autophagy, and the administration of IL-10 decreases the amount of puncta, which indicates autophagosome formation has been inhibited. IL-10 itself doesnt promote autophagy which may indicate the autophagy is based on inflammatory setting. Conversely, when the cells were pre-treated with nor-NOHA, a well-known inhibitor of arginase, IL-10 could no longer decrease the LC3 puncta, which to our knowledge has never been established by other studies.

Conclusion: In this study, we identified Arg2 as a novel target of IL-10 in the context of activation by LPS. Furthermore, the inhibition of IL-10 on LPS-induced autophagy is mediated by arginase

GRYSELDA HANAFI

Does Tranexamic Acid Change the Cellular Immune Response after Cardiac Surgery and Traumatic Brain Injury?

Prof. Robert Medcalf – Australian Centre for Blood Diseases, Central Clinical School
Dr. Dominik Draxler – Australian Centre for Blood Diseases, Central Clinical School

I have always been intrigued with the brain and the heart, two of the most important organs in the human body. For quite some time, I was looking for an opportunity to do experiments in a laboratory setting as I missed my chance to do so during my study in Indonesia. I think that choosing the subject that you are interested in, combined with excellent learning environment, will provide the best quality of learning experience one can get, and I believe, my honours year was just that. Under excellent teaching from my supervisors at Australian Centre for Blood Diseases, I learned many things from basic handling of laboratory equipment to how to conduct an experiment independently. Although the year when I did my honours year was one of the most challenging year, I also believe that it is the most memorable and fun year of my live. I highly encouraged future students to try doing a research year to further challenge yourselves.

Background: The immune system is important in the prevention of infection as the fibrinolytic system in the prevention of bleeding. These two systems appear to be unrelated, but recent studies showed a potential linked between them. Patients with high risk of hemorrhage, such as in condition of trauma or those who will undergo major surgery are commonly given an anti-fibrinolytic drug tranexamic acid to minimize bleeding. This study aimed to find a potential benefit of tranexamic acid in the alteration of immune response in patients undergoing cardiac surgery and in trauma.

Method: This study is divided into two parts: the clinical study of cardiac surgery patients and in traumatic brain injury (TBI) mice model with or without an induced infections. The patients and mice were administered to either tranexamic acid or placebo (saline). Flow cytometry was conducted from the blood of forty-one cardiac surgery patients with three time points: pre-surgery, 24h, and 72h time points. Myeloid and lymphoid cell populations were assessed for comprehensive evaluation of the immune response. In the mouse TBI model, the spleen was extracted and cells stained for flow analysis with two time points: 3 days and 7 days post-trauma. Myeloid and lymphoid cell populations were assessed in addition with the complete blood evaluation.

Results: In the human clinical setting, it was found that tranexamic acid does not have significant effect on monocyte or conventional dendritic cell numbers. However, an increase in plasmacytoid dendritic cells levels in addition to a partial switch of conventional dendritic cells to a tolerogenic phenotype was found that may afford protection against apoptosis. On the other hand, in traumatic brain injury mice models, no changes were found in the proportion or cell count of the myeloid and lymphoid cell subsets after the administration of tranexamic acid compared to placebo.

Conclusions: The results suggest that tranexamic acid treatment may protect cardiac surgery patients against infection. On the other hand, tranexamic acid does not improve the immune status in traumatic brain injury mice models.

SOPHIE HOY

Reducing caesarean section: An in-depth analysis of the care of women undergoing induction of labour

Professor Euan Wallace,[1,2,3] Dr Annie Kroushev[3]
[1] The Ritchie Centre, Hudson Institute of Medical Research, [2] Monash University Department of Obstetrics and Gynaecology, [3] Monash Health

I completed my project at Monash Medical Centre looking at opportunities to reduce rates of medically unnecessary caesarean section in first time mums undergoing induction of labour. I had a great year together with many other students at the Ritchie Centre and would highly recommend it to anyone considering undertaking a project in either O&G or paediatrics. I was fortunate enough to incorporate some clinical experience into my year, spending a number of days in the antenatal clinic at MMC. As I am interested in pursuing a career in obstetrics I considered this a great opportunity to improve my clinical skills. I am more than happy to answer any questions if you are considering undertaking a project in this area. Feel free to contact me via e-mail at srhoy1@ student.monash.edu.

Background: Rates of caesarean section (CS) are increasing at an unprecedented rate in most middle- and high-income countries globally, despite no evidence of a concurrent decrease in neonatal or maternal morbidity or mortality. Nulliparous women undergoing induction of labour (IOL) offer an important opportunity to reduce rates of primary CS, with rates 2-3 times higher than women entering labour spontaneously. The American College of Obstetrics and Gynecology (ACOG) have introduced new guidelines which specify longer durations of latent phase (<6cm cervical dilation) and active phase arrest before decision for CS for failure to progress (FTP) in an attempt to reduce rates of medically unnecessary CS.

Method: 457 nulliparous women with a live singleton pregnancy undergoing IOL at ≥37 weeks gestation over the 12-month period 1st July 2015 - 30thJune 2016 and delivered via CS were included in this study. Manual chart review was performed to determine the indication for IOL and the duration of labour. Neonatal and maternal morbidity measures were exported from the birthing outcomes system.

Results: 57% of CS for FTP were performed at <6cm (latent phase of labour) and 97% of these did not meet revised ACOG guidelines (≥24 hours). 28% of CS for FTP were performed at 6-9cm and 55% of these did not meet the revised ACOG guidelines (≥4 hours). 15% of CS for FTP were performed in the second stage of labour and none of these met the revised ACOG guidelines (≥3 hours of pushing). There were no statistically significant differences in neonatal or maternal morbidity measures with longer durations of latent phase (18-24 hours), active phase arrest (≥6 hours) or active pushing in the second stage of labour (2-3 hours).

Conclusions: There may be opportunities to reduce rates of CS in nulliparous women undergoing IOL at Monash Health by allowing longer durations of latent phase (18-24 hours), labour arrest (≥6 hours) and active pushing in the second stage (2-3 hours), with no apparent increase in neonatal or maternal morbidity. However, larger sample sizes are needed to accurately describe the incidence of rare but potentially important neonatal and maternal outcomes.

TALIA IGEL

Impact of gout flare prophylaxis and urate-lowering therapy on endothelial function, smooth muscle responsiveness and markers of inflammation

Prof Eric Morand, School of Clinical Sciences, Monash University
Prof Michael Pillinger, NYU Langone Medical Center, Department of Medicine, Division of Rheumatology
Dr Svetlana Krasnokutsky-Samuels, NYU Langone Medical Center, Department of Medicine, Division of Rheumatology

I chose to complete a BMedSci(Hons) after fourth year to venture into the world of research. With a keen interest in rheumatology and a love of overseas travel, I emailed every rheumatologist in the northern hemisphere in the hope one would accept an enthusiastic medical student from Australia. I was fortunate enough to spend the year working alongside a fantastic team at NYU in Manhattan. Not only was I exposed to the unparalleled research expertise of my supervisors, but I was also given the opportunity to enhance my clinical experience by participating in the NYU rheumatology fellowship educational programs, practicing joint aspirations, and chatting with patients at paeds rheum clinics.

Living in New York was an absolute dream. With evenings spent at the theatre or shopping and weekends spent visiting a new site, state or sometimes even country, I truly was in heaven. I couldn't recommend going abroad enough!

Background: Gout patients have increased cardiovascular morbidity. To date most studies of gout and cardiovascular disease have been cross-sectional and retrospective, and have addressed the issues of atherosclerosis and coronary arterial disease. Much less is known regarding basic arterial health including endothelial function and smooth muscle responsiveness, and little about clinical gout as compared to hyperuricaemia. I assessed whether initiating gout treatment with colchicine and urate-lowering therapy (ULT) as recommended by American College of Rheumatology guidelines, was associated with reduced C-reactive protein (CRP, a marker of inflammation), and improvements in arterial endothelial function and smooth muscle responsiveness as measured by brachial artery flow-mediated dilation (FMD) and nitroglycerin- mediated dilation (NMD) respectively.

Method: Demographics and cardiovascular risk factors were collected, and CRP, FMD and NMD were measured at baseline. Baseline FMD and NMD values were compared with healthy controls. CRP, FMD and NMD were reassessed after 6 weeks of colchicine (0.6mgs daily), and again 14-16 weeks later after addition of ULT, titrated to target urate (<0.33 mmol/L, 6.0 mg/dL or <0.28 mmol/L, 5.0 mg/dL for patients without or with tophi respectively).

Results: 34 untreated male gout patients were enrolled. 64 healthy male patients were used as controls at baseline. Gout subjects had significantly worse FMD (2.20±3.12 vs. 3.56±2.50, p=0.021) and NMD (16.69±9.01 vs. 24.51±7.18, p=0.00002) when compared to healthy controls. Gout subjects had significantly worse FMD and NMD even after adjustment for individual cardiovascular risk factors. 32 and 26 gout subjects completed the post-colchicine and post-ULT phases respectively. Both CRP and FMD improved post-colchicine and post-ULT, however this was not significant (p=0.302, p=0.324 respectively). There was no overall improvement in NMD (p=0.055). Subjects who had CRP decreases were more likely to have FMD improvements than CRP non-responders after ULT (p=0.026). Similarly, subjects who had NMD improvements were more likely to have FMD improvements than NMD non-responders after colchicine treatment (p=0.030). In the post-ULT phase subjects with lower BMI were more likely to have an FMD response (p=0.021) or CRP response (p=0.047). The overall cohort was stratified based on smoking status. Non-significant post-colchicine and post-ULT trends were observed towards improvement in both FMD (p=0.693, p=0.685) and CRP (p=0.407, p=0.451) in non- smokers, but not smokers. Co-morbid disease and chronic tophaceous gout did not impact on the likelihood of FMD, NMD or CRP improvement at either stage of the study.

Conclusions: Gout patients have reduced arterial function when compared to healthy controls, even after adjustment for co-morbidities. There were trends to improvement in FMD and CRP after therapy, however these were not significant. There was no overall improvement in NMD. Response in FMD was associated with response in CRP post-ULT, response in NMD post-colchicine and lower BMI post-ULT. Response in CRP was associated with lower BMI post-ULT. Smoking appears to adversely affect responsiveness to colchicine and urate-lowering therapy, with larger studies needed to confirm this association. Co-morbid disease and chronic tophaceous gout were not associated with response in FMD, NMD and CRP.

EMILE JASEK

Epidemiology of Sexually Transmitted Infections in Melbourne, Australia, 1918 to 2016: the longest record

Supervisors: Professor Christopher Fairley and Dr Eric Chow
Melbourne Sexual Health Centre, Alfred Health, Monash University

I finished 4th year in 2015, and chose to do a BMedSci in 2016 to gain experience in research. My BMedSci was done at Melbourne Sexual Health Centre in Carlton under the excellent supervision of both Prof Christopher Fairley and Dr Eric Chow. I believe I gained an invaluable understanding of sexual health medicine, epidemiology and, more broadly, of research and the scientific method. I would highly recommend any student contemplating doing a BMedSci to seriously consider looking into research at MSHC as it is such a supportive environment with excellent supervisors (and is also fantastically located). Feel free to contact me at emilejasek@gmail.com

Background: Changes in the rates of sexually transmitted infections (STI) in the developed world have been attributed to large changes in society including world war, the advent of antibiotics and the Acquired Immune Deficiency Syndrome (AIDS) pandemic. An understanding of such factors is helpful in evaluating current and future healthcare policy. With increasing notifications of STI in Australia in the last 25 years, the emergence of multi-drug resistant Neisseria gonorrhoeae strains and predicted decreasing rates of condom use amongst high-risk men who have sex with men using pre-exposure prophylaxis for the human immunodeficiency virus it is thus important for Australian STI research to address this area.

Method: This study was a retrospective analysis of the numbers, proportions and rates of STI diagnoses in all clinic attendees at MSHC and all six previous government sexual health clinics in Melbourne over a 98-year period, between 28 June 1918 and 1 June 2016. Client records from five discrete sources from different time periods have been digitised, collated, and analysed. Variables examined include the diagnoses of the clients, and some demographic characteristics including age, sex, country of birth, and sexual practice information.

Results: This study showed large changes in numbers, proportions and rates of STI diagnoses attributable to changes in Australian society over a 98-year period. Notable changes seen in this study in the number of STI diagnoses include increases seen with World War II and the Sexual Revolution, and decreases seen with the advent of antibiotics, the introduction of Medicare and the beginning of the AIDS pandemic.

Conclusions: My thesis demonstrated a number of changes in the number of STI diagnoses, the proportion of attendees diagnosed with STI, and the rates of STI spanning nearly a century's worth of data. We may learn from these past trends in STI rates and the changes in public health and society in general to combat future increases in STI rates. Indeed, now, in a period of significantly, rapidly increasing numbers of STI diagnoses it is imperative to look to the past to both fight current trends and see into the future.

SADUNEE JAYASURIYA

Decision regret in families being offered Fertility Preservation at the Royal Children's Hospital

Dr. Yasmin Jayasinghe[1,2], Dr. Peter Downie[3,4,5], Dr. Matthew Kemertzis[1], Dr. Michelle Peate[1], Dr. Lynn Gillam[6,7]
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I decided to complete a BMedSci after finishing my fourth year of medicine to gain an insight into the world of research. I am passionate about Women's and Children's health and my area of research allows me to combine both by delving into the burgeoning field of paediatric oncofertility.

My project was undertaken at the Royal Children's Hospital (in collaboration with researchers from the Royal Women's Hospital) which is home to the first established paediatric fertility preservation program in Australia. This year has given me a much greater appreciation for evidence-based practice and the importance of research in improving all fields of medicine. I am extremely grateful to my incredibly passionate, supportive and knowledgeable team of supervisors, and I would like to thank Dr. Yasmin Jayasinghe in particular, for offering me this wonderful opportunity and providing me with guidance throughout what was a difficult but equally rewarding year.

Background: Regret around healthcare decisions negatively impacts long-term quality of life for patients. Decisions regarding fertility preservation (FP), that is, procedures undertaken to help protect fertility prior to cancer therapy, may result in high levels of decision regret (DR), due to limited time available to make the decision and distress at the time of a cancer diagnosis. In the paediatric and adolescent population, techniques are largely considered experimental, therefore decision-making is not a straight-forward process. Little is known about DR in this population where not only the patients as cancer survivors could regret the decision that was made for them, but also their parents when acting as surrogate decision-makers. Paediatric oncofertility is a burgeoning field. With over 80% of young cancer patients aged 0-19 surviving to adulthood, DR in parents and patients may become a greater issue in the future. To date, there have been no studies performed evaluating DR over the decision regarding FP in the paediatric and adolescent cancer setting. We aimed to examine DR around FP decisions in patients and their parents who have attended the Royal Children's Hospital (RCH) since 1987, and to explore factors that contribute to it.

Method: This was a single-centre study conducted at an established paediatric oncofertility centre, the RCH, Melbourne. The program aims to provide fertility discussions to all cancer patients with curative intent. Parents of children receiving gonadotoxic treatment that were enrolled in the FP research program and had consented to be contacted for research were invited to participate. Patients were invited if they were ≥15 years. Participants were asked to complete the DR survey which consists of 10-items including a validated decision regret scale to obtain qualitative and quantitative data regarding satisfaction with the decision to pursue or forego FP. A score ≥30 indicates high regret.

Results: Of the 144 eligible families, 74.3% completed our study, including 104 parents and 25 patients. Most participants (83.5%) reported low regret (mean score 13.7, SD 18.8; range 0-95). Referral to an oncofertility specialist and pre-treatment discussions were significantly associated with low regret on univariate analysis (p<0.05), with having an FP procedure being the independent predictor of low regret on multivariate analysis.

Most participants believed that FP offers hope for future fertility, however those that are still satisfied with their decision still raise issues regarding the process of decision-making which highlights dissatisfaction with current clinical pathways. Namely, that consultation felt "rushed," and that they had to initiate the discussion on FP. Reasons for regretting the decision made related to a lack of adequate information provision, and inadequate time for consultation. Furthermore, many participants that had samples preserved before the introduction of the program, requested contact to enquire about storage and sample quality.

Conclusions: Overall levels of regret in the study population were low, with having a procedure and quality discussion influencing regret, similar to what is known regarding the adult FP population. However, dissatisfaction with the decision-making process itself reveals that refinements to the program are required to meet families' information needs.

KATE JOHNSON

The Perceptions of Interns With Regards to their preparedness for their roles in clinical pharmacology/prescribing

A/Prof Shane Bullock and Ms Anne Leversha (School of Rural Health – Monash University)

My name is Kate Johnson. After fourth year I needed to do something a bit different to my medical degree for a year. This project allowed me that chance and provided me with a chance to learn more about completing research and working towards getting a paper published. My project was looking at the perceptions of interns with regards to their preparedness for clinical pharmacology/ prescribing after they finished medical school. Hopefully, our results will be translated into improved teaching of pharmacology teaching in medical schools!

Enjoy your BMedSci year future students! It's a great opportunity. I'm happy to be contacted if anyone has any questions.

Background: Medicine is the most common intervention used to treat patients. Within Australia 750,000 patients experience adverse events from medications that are believed to be preventable. Medication charts average 4 to 5 errors per patient and almost a quarter of medication orders have been deemed unclear in terms of medicine name, route, dose or frequency.

Interns are known to make the most prescription errors with an error rate 1.5 times that of their seniors. Several studies have demonstrated medical interns do not feel prepared for various aspects of their role upon completion of medical school.

In an attempt to improve patient safety through revision of education during medical school the following study was undertaken.

Aims and Hypothesis:

The aims of this study were:

To examine whether medical interns, with the perspective gained from their first few months of practice, believe they were adequately prepared for their roles in clinical pharmacology/prescribing

And to discover which aspects of clinical pharmacology/prescribing require more attention in medical school and what methods would be best to address those identified.

Method: This was a mixed methods study consisting of an anonymous online survey and focus group interviews. The online survey was distributed to the 2016 cohort of 808 medical interns within Victoria via flyers, Medical Education Officers (MEOs), and e-mails from the Postgraduate Medical Council of Victoria (PMCV). It consisted of questions regarding participant demographics, specific aspects of therapeutics/prescribing teaching, educational resources, and comparisons between prescribing skills and other clinical skills. 100 interns attempted the survey. The focus group interviews contributed the majority of the qualitative data and consisted of two 45minute interviews, via Skype, with a total of 5 participants.

Quantitative data analysis was undertaken using SPSS. Measures of central tendency, chi squared and Wilcoxon signed paired rank tests were used.

Constant comparative qualitative analysis was undertaken with the assistance of NVivo software.

Results: The participants identified several aspects of clinical pharmacology/ prescribing for which they felt they were underprepared. Timing of teaching and lack of clinical correlation was consistently shown to be problematic across the 6 defined domains.

Conclusions: Methods to address the problems identified include shifting pharmacology teaching towards the final years of medical school, introducing pharmacology/prescribing specific assessments and mandatory inclusion of the NPS medicine wise learning modules.

AIDAN KASHYAP

Antenatal sildenafil to prevent pulmonary hypertension in congenital diaphragmatic hernia

Dr Ryan Hodges, Department of Obstetrics & Gynaecology, Monash University; Dr Kelly Crossley, The Ritchie Centre, Hudson Institute of Medical Research, Monash University; Dr Philip DeKoninck, Department of Obstetrics & Gynaecology, Monash University.

I completed my project at The Ritchie Centre after completing my 4th year of medicine, and particularly enjoyed the self-direction and challenges that came with entering the world of medical research. I was very grateful to have both clinician-scientists and pure scientists within my supervising team and wider lab group, and appreciated the different perspectives that they have impressed upon me.

Whilst it is not without its challenges, and I'm looking forward to returning to a patient-base that can (usually) communicate verbally, animal work has been incredibly rewarding. The practical (both surgical and clinical) and collaborative skills I developed this year, by working with the large team responsible for our animals, may not have been as easily obtainable in a clinical (data-based) or laboratory project.

A BMedSc is a great opportunity to gain a taste of medical research, develop your skills in scientific writing, method and presentation, and to gain a deeper understanding of the science that underpins clinical practice – I'd be more than happy to answer any questions at aidankashyap@gmail.com.

Background: In congenital diaphragmatic hernia (CDH), herniation of abdominal viscera into the thoracic cavity during fetal development leads to pulmonary hypoplasia and neonatal pulmonary hypertension. Severe pulmonary hypertension is associated with over 50% mortality, and occurs due to abnormal pulmonary vascular remodelling in utero. Antenatal administration of the phosphodiesterase-5 inhibitor sildenafil appears to attenuate abnormal pulmonary vascular remodelling in small animal models of CDH. To determine if this structural change translates into a functional effect, we aimed to (i) characterise an ovine model of CDH, then (ii) examine the effect of antenatal sildenafil on the neonatal transition, to determine if this novel medical therapy may offer a new treatment modality in the care of pregnancies with severe CDH.

Methods: At ≈84 days of gestational age (GA), diaphragmatic hernia was surgically induced in the CDH group, and sham surgery performed in the sham group. CDH and sham were compared to investigate the effect of CDH. From ≈GA105 – 138, a subset of CDH lambs were administered intravenous maternal sildenafil at a dose of 0.66 mg/kg/day (CDH + sildenafil). CDH and CDH + sildenafil were compared to investigate the effect of antenatal sildenafil. At ≈GA138, all groups were delivered via caesarean section. During a 2-hour neonatal ventilation, physiological (pulmonary and carotid blood flow and pressure) and ventilatory (tidal volume and airway pressure) parameters were continuously monitored.

Results: In comparison to sham, CDH lambs demonstrated decreased lung:body weight ratio (pulmonary hypoplasia), decreased pulmonary blood flow due to increased pulmonary vascular resistance (pulmonary hypertension), and an oxygenation index consistently above the clinical indication for invasive extracorporeal membrane oxygenation (inadequate gas exchange). Antenatal sildenafil significantly increased lung:body weight ratio as compared to CDH, however did not attenuate pulmonary hypertension or improve oxygenation. Interpretation of these results was limited by the low fetal plasma

sildenafil concentrations (2.017 ng/mL, range: 0 ng/ml [non-quantifiable] – 6.165 ng/mL) achieved. Promisingly, animals that received quantifiable sildenafil levels (n=2) demonstrated decreased pulmonary vascular resistance, increased pulmonary blood flow and an oxygenation index consistently below the clinical indication for extracorporeal membrane oxygenation.

Conclusion: We have successfully characterised an ovine model of CDH that demonstrates severe pulmonary hypoplasia and pulmonary hypertension. Our ovine model reflects the clinical phenotype of CDH: reduced lung size, increased pulmonary vascular resistance and decreased pulmonary blood flow, and evidence of impaired gas exchange. Interpretation of results associated with our second aim, to investigate the physiological effect of antenatal sildenafil in CDH, is severely limited by experimental issues related to inconsistent dose delivery. However, subgroup analysis of fetuses with quantifiable plasma levels of sildenafil shows promise and has informed the study design of our future research. We remain encouraged that after further investigation antenatal administration of sildenafil may one day help CDH neonates, and their parents, breathe a little easier.

SOPHIE KINNEAR

Uterine SOX17: a potential target for a novel, non-hormonal contraceptive

Dr. Jemma Evans and Professor Lois Salamonsen, Centre for Reproductive Health, The Hudson Institute of Medical Research

I decided to undertake a BMedSc (Honours) year after finishing Year 4 MBBS in 2015. During the course of fourth year, I discovered a passion for women's health, and decided to further pursue this interest by undertaking research with the Centre for Reproductive Health at the Hudson Institute of Medical Research. This was a lab-based project, characterising the role of a transcription factor protein, SOX17, in the human endometrium, and the part that it plays in embryo implantation. This research was undertaken with an aim to exploring the possibility of blocking SOX17 as a potential novel, non-hormonal contraceptive. This year has been a wonderful experience and although going from a clinical to a laboratory environment was very challenging, learning those skills played a large role in what made this year so enjoyable. I can't express enough gratitude to my wonderful supervisors; Dr. Jemma Evans and Professor Lois Salamonsen, for all of their help and encouragement along the way. I would encourage anyone considering a lab-based BMedSc to give it a go and I'm happy to be contacted if future students have any questions at sckin5@student.monash.edu.

Background: Despite significant advances in the development and availability of contraceptive options over the past century, unmet contraceptive need is still a significant issue that, globally, results in 84 million unintended pregnancies each year. Current hormonal contraceptives do not suit all women, due to side effects, contraindications, pharmaceutical interactions and poor accessibility. Thus, there is a clear requirement for contraceptive development, to reduce maternal morbidity and mortality, increase choice and empower women worldwide. Sox17, a transcription factor belonging to the SOX-F family of proteins, is upregulated at the site of embryo implantation in mice. Additionally, Sox17 heterozygous mice are sub-fertile; blastocysts do not implant due to a uterine defect. However the role of SOX17 in the human uterus has yet to be characterised. Thus, the aims of this study were to examine the hormonal regulation of endometrial SOX17, assess SOX17 expression at the point of embryo implantation, and determine the impact of endometrial SOX17 inhibition/knockdown on embryo adhesion.

Method: To examine hormonal regulation of SOX17 expression, endometrial epithelial (ECC-1) cells were cultured in two ways, 1) grown on Transwell® inserts, allowing the cells to become polarised as in vivo, or 2) grown on cell-culture plastic. Cells were then treated with hormones; estrogen (E2), progesterone (P4), human chorionic gonadotropin to mimic the proliferative and secretory phases of the menstrual cycle and conception cycles. To examine localisation of SOX17 at the 'embryo-endometrial' interface, a 3-dimensional co-culture model, using a monolayer of ECC-1 cells and a 'blastocyst mimic' spheroid of trophectoderm (L2-TSC) cells was used. ECC-1 cells were grown on sectionable coverslips and hormonally treated, with spheroids subsequently placed onto monolayers for 6 hours to adhere. This structure was then fixed in agar, processed, embedded and sectioned for immunohistochemistry. 'Implantation sites' (spheroid-monolayer adhesion sites) were identified and immunohistochemistry performed to examine SOX17 expression.

The co-culture model was also used to examine the impact of inhibition/knockdown of SOX17 on spheroid adhesion. Stable ECC-1 cell lines with SOX17 knockdown were made using a CRISPR/Cas9, double nickase knockdown plasmid. These knockdown cells and an inhibitor of the SOX-F family were used to determine the role of SOX17 in endometrial-embryo adhesion/implantation.

Results: SOX17 was expressed in ECC-1 cells, with expression significantly ($P<0.05$) upregulated by estrogen and progesterone treatment in cells grown on inserts. Immunohistochemistry confirmed the presence of SOX17 in ECC-1 cells and identified localization/up-regulation of SOX17 at the 'embryo-endometrium' interface. Treatment of ECC-1 cells with 20µM and 50µM of the SOX-F inhibitor (MCC177) significantly inhibited E2/P4 mediated spheroid adhesion (50% in E2/P4 treated cells, 4.6% in 20µM and 0% in 50µM SOX-F inhibitor treated cells, $P<0.0001$). Similarly, E2/P4 treated SOX17 knockdown cells exhibited a significant reduction in spheroid adhesion, with the degree of adhesion correlating with level of knockdown. A reduction of >90% ($P<0.0001$) was seen in all knockdown cells when compared to E2/P4 treated control cells.

Conclusions: These results confirm a likely role for SOX17 in human embryo implantation and suggest that targeting SOX17 in the human endometrium is a viable target for contraceptive development.

TEJAS KUMAR

Oxygen Induced Retinopathy – A New Model in Sight

Principal Supervisor: Professor Paul McMenamin –Department of Anatomy and Developmental Biology, Monash University (Clayton), Melbourne, Australia
Associate Supervisor: Doctor Marcus Fruttiger –Faculty of Brain Sciences, Institute of Ophthalmology, University College London, London, United Kingdom

Hi I'm Tejas. Since I was little (1st year MBBS) I've always wanted to do a BMedSc. After finishing 4th year, I was fortunate enough to be given the opportunity to travel to UCL Institute of Ophthalmology (London) for research on an exciting project. Here, I built on skills I'd learnt during the summer in Melbourne such as dissecting mice eyeballs and immunostaining.

Having never lived out of home, living in London was a fantastic learning experience both intellectually and in making me a more independent person. I was able to immerse myself completely when in the laboratory, and elsewhere was able to explore all that the UK and Europe had to offer (I mention them separately because Brexit). Some of the friendships I forged while away were truly special and will remain with me for years to come.

I am extremely grateful to my supervisors Prof Paul McMenamin and Dr Marcus Fruttiger who helped ease my transition into a challenging and exciting research year; and my family who made it all possible.

I can confidently say that doing a BMedSc and travelling to London was one of the best decisions I've made.

Background: Retinopathy of Prematurity (ROP) is a vitreoretinopathy characterised by abnormal vascular development in premature infants.

A commonly used model of ROP whereby mice are exposed to 75% hyperoxia from post-natal day (P) 7 to P12 to produce an oxygen induced retinopathy (OIR) has been helpful in elucidating the oxygen dependent role of low VEGF in vaso-obliteration, and elevated VEGF in neovascularisation; and the oxygen independent role of low insulin-like growth factor 1 (IGF-1) in delayed vascular growth. However, this model produces a transient pathology and does not replicate the severe stages of disease.

A recent OIR model by McMenamin et al. whereby mice are exposed to 65% hyperoxia from P0-P7 shows a lasting pathology up to 40 weeks of age. Analysis prior to P21 is incomplete in the new OIR model.

We hypothesised that early exposure to hyperoxia would inhibit vascular growth and compensatory upregulation of VEGF would occur after return to normoxia. The hyaloid vasculature was thought to play a hypoxia-relieving role in the early development of OIR.

Method: Three groups of mice were tested:

Normoxia (room air only) at P7, P14 and P21

75% O_2 P0-P7 (New model) at P7, P14, P21

75% O_2 P7-P12 (Traditional model) at P12, P17 and P21

Retinal blood vessels were visualised using Isolectin B4 and avascularity was calculated using Image J software. Relative expression of retinal VEGF and IGF-1 mRNA was quantified using real time RT-PCR.

Results: Upon dissection thick hyaloid vasculature was noted posterior to the lens at P14 and P21, but not at P7.

In the new model, P7 retinas exhibited marked avascularity with only sparsely located peripheral vessels of hyaloid origin. At P14, there was evidence of vascularisation from the optic nerve head and periphery; but no distinct vessels were observed. There was a two-fold increase in VEGF expression ($p<0.0001$), relative to controls (normalised to 1.00). At P21, disorganised but distinct vessels were present. The central retina stained weakly, surrounded by a prominent ring of vascularisation. The peripheral retina was largely avascular, with only few vessels.

Across all time-points the new model exhibited significantly higher avascularity than the traditional model and controls.

Conclusions: Findings from this study can be used to divide the early stages of OIR in the new model into 3 phases:

Hyperoxia exposure at birth more severely inhibits retinal vascular growth relative to the traditional model.

Upon removal from hyperoxia, upregulation of VEGF drives proliferation of vascular endothelial cells.

Normalisation of total retinal VEGF at P21 despite obvious pathology can be explained by VEGF downregulation in the face of damage to metabolically active tissue in the weakly staining central and largely avascular peripheral retina. Findings of attenuated retinal function beyond 5 weeks by McMenamin et al. support this claim.

Results from this study are promising and provide avenues for future research on the mechanisms underlying the phenotype of this novel OIR model in that hope that these findings edge us closer to the development of treatments for severe ROP.

ROSIE LATIMER

Pelvic Inflammatory Disease caused by Mycoplasma Genitalium: Symptoms, Signs & Treatment

Associate Professor Catriona Bradshaw, Dr. Timothy Read, Dr. Lenka Vodstrcil, Melbourne Sexual Health Centre, Alfred Health, Monash University

I undertook my BMedSci at the Melbourne Sexual Health Centre. I chose this project as I have an interest in public health and womens health, and the sexual health centre seemed like the perfect place to combine these interests. My supervisor was so supportive throughout the year and I couldn't have asked for a better place to do my BMedSci. And being located just off Lygon Street meant easy access to incredible coffee and cake.

Background: Mycoplasma genitalium (MG) is a recently established cause of pelvic inflammatory disease (PID). The clinical features of MG-associated PID (MG-PID) are poorly documented.

Current first line therapy for MG is azithromycin, however there is increasing macrolide resistance, particularly in the Asia-Pacific, with current efficacy of azithromycin in Melbourne estimated at 60%. There is increasing need for evidence for a highly effective antibiotic agent to manage MG.

Aims:

1) To describe the clinical characteristics of MG-PID and to determine how they differ from those associated with Chlamydial trachomatis (CT)-PID.

2) To determine the proportion of women

i) microbiologically cured of MG-PID following moxifloxacin (i.e. MG not detected by nucleic acid amplification assay at test of cure).

ii) clinically cured of MG-PID following 14 days of moxifloxacin (i.e. asymptomatic following treatment).

Method: We performed a retrospective case series of 82 women who were diagnosed with MG-PID between 2006-2016, with an equivalent number of controls with CT-PID. MG-PID was defined as women fulfilling the key clinical criteria for PID in whom MG was the only STI was detected i.e. chlamydia and gonorrhoea tests were both negative. Health records were extracted from Melbourne Sexual Health Centre databases. Both MG and CT cases had their demographic information, behavioural data, clinical features at presentation, and laboratory findings recorded. The MG cases were followed documenting their treatment regimen, risk of reinfection, test of cure and clinical outcomes. Data were entered and stored in an Excel database and analysed using Excel functions and online statistical calculators. Ninety-five percent confidence intervals (CIs) were calculated for all proportions. P-values were calculated for comparing the characteristics of MG-PID to CT-PID, using a chi-square or Fischer exact test where appropriate.

Results: MG-PID had a milder clinical syndrome than CT-PID. Although many symptoms and signs were similar, there was more vaginal discharge amongst the chlamydial group (p=0.04). There were much higher levels of high vaginal (p<0.01) and cervical (p=0.03) PMNLs in the CT-PID group compared to the MG group, indicating worse inflammation in the chlamydial group. Although cervical symptoms of post-coital bleeding (p=0.07) and sign of mucopurulent cervicitis (p=0.08) were not statistically significant, there is biological plausibility that there is more cervical inflammation with CT-PID. Moxifloxacin, given after presumptive therapy, was found to have microbiological cure rates of 95% (84-99) and clinical cure rates of 77% (64-88). Side effects were experienced by 24% of the patients.

Conclusions: This study showed that MG-PID are similar CT-PID, however MG-PID has a milder clinical syndrome with significantly less vaginal discharge and lower levels of inflammation.

This study has provided the first evidence for treatment of MG-PID with moxifloxacin. Although side effects are of concern, PID is serious and warrants this agent. Moxifloxacin should be used in patients with established MG-PID, with monitoring due to side effects.

CAIUS MARTIN

Perioperative changes in ventilation inhomogeneity and respiratory mechanics

University Hospitals of Geneva:
Prof Walid Habre
Prof Sam Bayat
The Alfred Hospital:
Prof Paul Myles

I undertook a BMedSci year after finishing my fourth year of MBBS. I conducted a project overseas in Geneva - it was a unique opportunity to combine research work with living abroad in a (mostly) French-speaking environment. I worked with the department of anaesthesiological investigations in Geneva, which was a unique experience in a very specialised area of medicine. The BMedSci is a great way to gain experience in research prior to graduation, which I would recommend to anyone considering combining research and clinical practice in their future careers.

My original research project had some unfortunate issues related to ethics approval in Switzerland, so my advice for future students would be to carefully select your project based upon timeframe and the advice of others more experienced in research.

Background: The physiological effects of general anaesthesia (GA) on supine, mechanically-ventilated patients are well-documented. Negative respiratory consequences result from a combination of changes in posture, respiratory muscle activity and ultimately lung collapse and gas redistribution. Factors which influence the extent and duration of respiratory compromise are numerous and include: the type, depth and approach to anaesthesia; patient demographics and baseline characteristics; prior cardiorespiratory disease or illness; and the type of surgery being performed. Importantly, anaesthetic care does not cease immediately after an operation – patients are prone to postoperative persistence of anaesthesia and may require up to several days to fully recover. This study is therefore aimed at characterising the perioperative evolution of respiratory function, specifically: ventilation inhomogeneity described by lung clearance index (LCI), functional residual capacity (FRC), and respiratory mechanics described by parameters of airway resistance (Raw) and tissue compliance properties.

Method: Recruitment occurred from pre-anaesthesia consultations at the University Hospitals of Geneva in Switzerland. A total of 22 children included for data analysis were drawn from a larger overall study conducted at the same institution. Children eligible for the study were healthy adolescents aged between 4 and 16 years planned for simple peripheral surgery with endotracheal intubation. We conducted tests of respiratory function in our paediatric population on 3 separate occasions: a preoperative baseline, during immediate postoperative recovery and 24 hours after anaesthesia. The nitrogen multiple-breath washout (N2MBW) technique was performed using Exhalyser D equipment with ICU insert (Eco Medics, Duernten, Switzerland) for evaluation of lung volumes and ventilation distribution, whilst the forced oscillation technique (FOT) was performed with the tremoFlo device (Thorasys, Montreal, Canada) for assessment of respiratory mechanics. All measurements were taken in a manner consistent with European Respiratory Society (ERS) guidelines. Patients were also monitored for respiratory complications and subclinical hypoxaemia throughout the study period.

Results: Ventilation inhomogeneity (as measured by LCI) was increased significantly in the immediate postoperative period (p<0.05) but returned to near-baseline after 24 hours. Significant reductions in FRC were also detected postoperatively that persisted to the final measurement. There were no significant changes in respiratory mechanics compared to baseline levels.

Clinically, there were no significant respiratory complications or any clinical or subclinical manifestations of hypoxaemia detected in our study population. Overall, the children evaluated in this study demonstrated a rapid return to normal physiology without significant clinical or subclinical manifestations of respiratory compromise.

Conclusions: This study has further characterised the perioperative and perianaesthetic changes in respiratory function, providing normative LCI data for patients undergoing GA which is currently limited. The recovery of relative ventilation homogeneity after only 1 day correlates with the infrequency of clinical complications of GA for minor surgeries, despite the persistence of lung volume abnormalities. Therefore in healthy patients without prior cardiopulmonary disease or anaesthetic risk, there is minimal risk of complications resulting from GA. Our research improves on the existing understanding of respiratory physiology surrounding anaesthesia, also highlighting the utility of the N2MBW and FOT techniques and the potential for their future application.

VALENCIA JANE MARTIN

The Health and Productivity Burden of Diabetes Mellitus in Australia

Prof Danny Liew (CCRET)
Co Supervisor:
Dr Alice Owen (CCRET)
A/Prof Dianna Magliano (Baker IDI)

I'm really glad I could have my Honours year in Monash University. This year has given me tons of amazing experience and a new understanding about research skills. My project about diabetes and its effect on productivity has given me new insights on the burden of diabetes and the results could possibly be applied in my home country, where diabetes prevalence is high.

I am extremely grateful for the supervision from Prof Danny Liew (CCRET-SPHPM), and my co-supervisors Dr Alice Owen (CCRET-SPHPM) and A/Prof Dianna Magliano (Baker IDI) who all have patiently guide me throughout this year. After this year, I will be going back to Indonesia to finish my medical school in University of Indonesia. Thanks for all the great memories, Australia.

So long and thanks for all the fish!

Feel free to contact me at valenciajane@hotmail.com

Background: Diabetes mellitus causes a significant burden of disease. The course of the disease can lead to disability, which in turn causes loss of productivity in terms of lost labour participation. The increasing prevalence of diabetes in the working population will result in a significant economic burden to a country, in terms of lost income earnings, lost tax revenue and lost GDP. Understanding the burden of diabetes in these terms is a novel concept and potentially useful notion. This project estimates impact of diabetes on quality-adjusted life years (QALY) lived and reduction in productive years in diabetes patients by generating a novel concept, the 'productivity-adjusted life years' (PALYs) lived attributable to diabetes.

Method: Life table modelling is used as a tool to quantify the impact of diabetes on health and productivity. Data implemented in the life table are taken from National Diabetes Services Scheme (prevalence), Australian Diabetes, Obesity and Lifestyle Study (RR) and General Record of Incidence of Mortality books (mortality risk). Through literature searching, we found a productivity index attributable to type 2 diabetes (akin to the quality of life index). Using this index, we estimated 'productivity-adjusted life years' (PALYs) to quantify productivity loss among those living with diabetes. The model was run for every 10-year age group and gender to find years lived, mortality, quality adjusted life year, and productivity adjusted life year lived in populations with and without diabetes. Sensitivity and uncertainty analysis (Monte Carlo simulation) were done to account for uncertainties.

Results: Compared to population without diabetes, the excess mortality due to diabetes reached 69.1% (56.7% in men, 92.9% in women). Excess mortality is the extra number of death attributable to diabetes compared to population without diabetes. Overall reduction in life years reduction due to diabetes was 12.2% or 1,653,682 years. The impact of diabetes on life years lived and QALY lived was most notable in those aged 15-54 years old. Total QALY lost was 38.3% (40.4% in men, 36.1% in women) and average QALY lost per person if they develop diabetes is 4.6 years. Diabetes causes reduction in productive years by as much as 25.8% in men and 17.8% in women. The impact of diabetes is most severe in people of the working age. Elimination of diabetes could increase productive years as much as 21.8%.

Conclusions: Elimination of diabetes can prolong life years lived by the whole population and increase both quality-adjusted life year lived as well as productive years. Employers, government and policy makers should not overlook burden of diabetes towards work capacity and implement prevention programs to reduce the development of the disease to maintain productive workforce capacity.

VIVEKA NAINANI

Clinical implications of adverse events following immunisation with the capsular group B meningococcal vaccine

Dr Jim Buttery: Department of Paediatrics, Monash University, Infection and Immunity, Monash Childrens Hospital, Clayton, Victoria, Australia. SAFEVIC, Murdoch Childrens Research Institute, Melbourne, Australia, Monash Immunisation, Monash Health, Clayton, Victoria, Australia. Dr Matthew Snape: NHR Oxford Biomedical Research Centre, Oxford University Hospitals NHS trust, Oxford, Oxford Vaccine Group, University of Oxford, Department of Paediatrics

I conducted my research at the Accident and Emergency department at the John Radcliffe Hospital in Oxford. This year has been an incredible mix of research and travel – it was amazing having the ability to travel to another country after a 2 hour long flight! Living at college was also incredible, as was having the opportunity to join the Oxford Union and see speakers like George Foreman, John Kerry and IBM Watson. I'll really miss Oxford!

Background: The capsular group B meningococcal vaccine (4CMenB) was introduced into the routine infant immunisation schedule of the United Kingdom at 2, 4 and 12 months of age in September 2015. The vaccine is known to be relatively reactogenic, with fever rates in clinical trial of approximately 61%. The aim of this study was to determine whether the introduction of routine infant 4CMenB immunisation could be associated with an increase in infants presenting to Accident and Emergency departments with vaccine reactions, and the clinical management of these infants.

Method: A retrospective review of electronic hospital records identified all infants aged 1-6 months presenting to Accident and Emergency at the John Radcliffe and Horton Hospitals in Oxfordshire, between 1 September 2015 and 31 August 2016, and records from this time period in the two previous years were used as a comparison. Discharge diagnoses were reviewed, and a more detailed assessment of the record of the clinical presentation and immunisation history undertaken if the discharge diagnosis recorded a vaccine reaction, was non-specific (e.g. fever, sepsis, irritability) or mentioned a condition of interest (e.g. meningitis, seizure, rash). Presentations were classified as: 'probable vaccine reaction' (i.e. fever/rash/irritability/seizure within 48 hours of immunisation if no alternative cause was found); 'possible vaccine reaction' (as for probable, but with a possible alternative cause) or 'not related' (clear alternative diagnosis or not immunised within previous 48 hours).

Results: During the 'pre' 4CMenB era (2013-15), an average of 12 infants aged 1-6 months presented to Accident and Emergency per year with probable or possible AEFIs (15 in 2013-14, 9 in 2014-15). In the 'post' 4CMenB era (2015-16), the number of presentations was 42. Of these, 37 were considered as having a 'probable' vaccine reaction and 5 a 'possible' vaccine reaction. Amongst the 42 'probable' or 'possible' vaccine reactions in 2015-16, 25 occurred following immunisations at 2 months, 11 at 3 months (4 with 4CMenB in a 'catch up' campaign,

6 without 4CMenB) and seven at 4 months. This represents an increase from 1.01 AEFIs per 1000 immunisation episodes for 2 month olds in the pre-4CMenB era to 3.40 per 1000 in the post-4CMenB era (p = 0.0008). For 4 month olds, these data were 0.07 and 0.82 per 1000 immunisation episodes respectively (p = 0.003). Blood tests were performed in 14 children and lumbar punctures in 10. Only 14 children were discharged directly from Accident and Emergency, 12 were monitored in a 24-hour observation unit and 16 were admitted to the ward. 10 children received intravenous antibiotic therapy.

Conclusions: There has been a significant increase in the number of infants presenting to Accident and Emergency departments with possible or probable vaccine reactions since the introduction of the 4CMenB vaccine. There has also been an associated increase in admissions to the ward and observation unit, blood and urine cultures performed, lumbar punctures performed and IV antibiotics given, increasing healthcare consumption. The clinical implications of this project highlight the need to determine a specific protocol for these infants when they present to Accident and Emergency.

SHAGUN NARULA

The Role of TROP2 in trophoblast Invasion

Dr Megan Wallace - Department of Obstetrics and Gynaecology, Monash University, and The Ritchie Centre
A/Prof Eva Dimitriadis, Centre of Reproductive Health, Hudson Institute of Medical Research

I chose to do a BMedSci with Dr. Megan Wallace after my fourth year of medicine. I'm interested in Obstetrics & Gynaecology and I thought a year of lab-based research was a unique opportunity to learn new skills and gain a basic science understanding that will be vital for future work in research. I'm very lucky to have had the chance to explore the molecular mechanisms behind altered placentation under the guidance of a fantastic supervisor, and I'm glad that I joined the many students of the Ritchie Centre, who formed a little family throughout the year.

Background: Extravillous trophoblast (EVT) invasion into maternal decidua is a critical process in the development of the placenta during pregnancy. Disorders of invasion are associated with numerous prevalent obstetric complications, from pre-eclampsia to intra-uterine growth restriction and adherent placenta. Trophoblast antigen-2 (TROP2) is a transmembrane protein that has been shown to regulate cell proliferation, migration and invasion in tumour cells. It was first identified in normal and malignant trophoblast cells, though its function in these cells has not yet been explored.

Method & Results: We hypothesized that TROP2 regulates trophoblast invasion. Our aim was to firstly determine the localization and mRNA levels of TROP2 in first trimester human placenta, to secondly alter TROP2 levels in trophoblast cell lines to assess effects on cell invasion, migration and proliferation.

TROP2 expression in decidua and villous tissue was measured using real-time PCR and protein localisation was assessed qualitatively using immunohistochemistry. TROP2 mRNA levels were ~5 fold higher in decidual than villous tissue ($p<0.05$) and the TROP2 protein was localized to EVT cells in the decidua basalis and by what is likely to be syncytiotrophoblasts in villous tissue. The invasive first trimester trophoblast cell line, HTR8, was then transfected with either a TROP2 overexpression vector or control vector, and the cells cultured under selection pressure to achieve a stable transfection. Functional real-time cell analysis (xCELLigence) then assessed cell adhesion, proliferation and invasion over time. TROP2 overexpression was confirmed by real-time PCR and immunohistochemistry relative to the control transfected cells. xCELLigence assays suggest that TROP2 overexpressing cells had an increased rate of adhesion, cell proliferation and invasion compared to control cells, though more numbers are needed to determine if these changes are statistically significant. Small interfering RNA was also used to knockdown TROP2 in the JEG3 cell line, with successful knockdown (93% reduction in Trop2 mRNA levels, $p <0.05$) achieved. However, difficulties culturing and accurately counting these cells prevented further analysis by xCELLigence, as the technique requires very accurate determination of starting cell number.

Conclusions: The data generated in this thesis suggests that TROP2 is an important regulator of trophoblast adhesion, proliferation and invasion and as such, may play a role in placental formation and in clinical disorders associated with abnormal trophoblast invasion.

STEPHANIE NESBIT

Exploring Factors Associated with Response to Rituximab in Systemic Lupus Erythematosus

Prof Eric Morand, School of Clinical Sciences, Monash University, Melbourne Australia
Prof Ian Bruce, University of Manchester, Manchester UK

I decided to undertake a BMedSc after 4th year, and with the help of Prof Eric Morand, I was able to organise a collaborative project with him at Monash Health and Prof Ian Bruce at the University of Manchester. I moved to the UK and lived in rainy Manchester for 8 months where I worked at the university, met some incredible people and got to explore Britain and Europe in my time off. Organising such a project overseas isn't easy and requires a significant amount of time and initiative and countless emails. However it was a wonderful academic and life experience and I'm extremely grateful to have had this opportunity. I am happy to be contacted if anyone has any questions about doing something similar - slnes1@student.monash.edu.

Background: Response to the anti-CD20 agent rituximab in Systemic Lupus Erythematosus (SLE) is variable but it is used widely for refractory disease. Observational studies have suggested its efficacy, but two randomised controlled trials did not demonstrate any advantage over standard of care and placebo. Several serological and clinical factors have been suggested as predictors of response.

Aims and hypotheses: The primary aim of this study was to explore factors predicting response to rituximab in the British Isles Lupus Assessment Group Biologics Register (BILAG-BR). We anticipated that there would be quantifiable clinical, serological and demographic factors that would be associated with response to rituximab at 6 months. Secondary aims were to describe efficacy and safety in this cohort.

Methods: We analysed data from the BILAG-BR, a nationwide registry of patients with SLE. We included patients who received rituximab before November 2015, had active disease at baseline according to the national rituximab prescribing guidelines (≥1 BILAG A or ≥2 BILAG B scores or SLEDAI-2K >6 or oral steroids ≥20mg daily) and who had BILAG 2004 and SLEDAI-2K disease activity indices at baseline and 6 months.

The primary endpoint was a modified BILAG-Based Composite Lupus Assessment (BICLA) endpoint defined as: improvement of active systems on BILAG 2004 with no worsening in other systems (all BILAG As at entry to B/C/D, all Bs to C/D, no new As, <2 new B); no worsening of SLEDAI-2K; no increase in oral steroid dose at 6 months. Secondary endpoints included change in global BILAG 2004 score; change in SLEDAI-2K score; change in steroid dose from baseline.

Univariate and multivariable logistic regression was used to explore relationships between baseline variables, and modified BICLA response. Multiple imputation by chained equations was used to account for missing data.

Results: 197 patients were analysed. The rate of response according to the modified BICLA criteria at 6 months was 50.76%. In univariate regression, only the use of concomitant IV cyclophosphamide was associated with response to rituximab, adjusted imputed OR 3.75 (1.56, 9.05). In an imputed multivariable model, the following factors were associated with response: concomitant cyclophosphamide, OR 4.50 (1.77, 10.97), baseline global BILAG, OR 0.96 (0.93, 0.99), increasing oral steroid dose at baseline, OR 1.03 (1.00, 1.06). No other baseline factors, including ethnicity, smoking status, or autoantibody status, were predictive of response.

Conclusion: In a UK-wide cohort of SLE patients receiving rituximab, concomitant cyclophosphamide was associated with response, and 50% achieved a response at 6 months. No baseline autoantibodies or other clinical factors were predictive of response. Rituximab is an important drug in the treatment of refractory SLE, and concomitant cyclophosphamide may have an augmentative effect. Further work will inform how best to stratify patients to receive this drug.

BEN NOWOTNY

Developing a tool to predict medicolegal risk in obstetrics.

Professor Erwin Loh (Monash Health, Monash University)
Professor Euan Wallace AM (The Ritchie Centre, Monash Health, Monash University Department of Obstetrics and Gynaecology)

I chose to defer final year and undertake a BMedSci to explore another side to medicine – research. Knowing nothing about research initially, I met with my supervisors to discuss fields I may be interested in. Having a strong interest in obstetrics, I decided on an obstetric quality improvement project.

There were several challenges that I faced over the course of this project. The first was acquiring and formatting an enormous database of 41,443 patients. Excel cooked it on multiple occasions due to the sheer volume of data. The second was analysing the data in order to create any meaningful predictive model. This proved a major obstacle as I discovered that I had no idea how to statistic. Fortunately, my lab group saved me from statistical torment with several SPSS tutorials (my new favourite program).

Overall, the project was a success (a surprise to everyone myself included) and I discovered that I actually really enjoy research. I would encourage anyone thinking about adding a research element to their medical degree to go for it. I have thoroughly enjoyed the honours year.

Background: Medicolegal claims and complaints are an inevitable part of modern health care, resulting from either perceived or actual deficiencies in care provided. Perhaps surprisingly, there has been only limited research into approaches to predict the likelihood of either medicolegal claims or complaints. Previous work developed forecasting models based on doctor attributes. Whether patient factors are predictive of medicolegal claims or complaints has as yet not been explored.

Aims: To identify factors that contribute to the initiation of a medicolegal claim or complaint in obstetrics. Subsequently, to develop and pilot a tool that enables reliable prediction of the likelihood of a medicolegal event occurring.

Methods: All complaints and medicolegal claims relating to obstetric care at Monash Health from 1 April 2011 to 30 April 2016 were analysed and compared to all births at Monash Health over the same period. Univariate binary logistic regression was performed to identify variables that contributed to medicolegal events. Subsequently, backwards stepwise logistic regression was conducted to develop each model. The receiver operating characteristic curve was then assessed for each model to give a measure of performance, and the sensitivity, specificity, positive and negative predictive values of each model were analysed at varying probability threshold values.

Results: A total of 199 complaints and 19 claims against Monash Health were identified. Over the same time period, there were 41,443 births at Monash Health sites. Complaints relating to communication issues were the most common while complaints relating to medical care and adverse outcomes were the most severe. I developed two predictive models, one for complaints and one for claims. The complaints predictive model included maternal age, spoken language, hospital of birth, gestation, anaesthesia, labour complications and 5 minute APGAR in the final model. The model had only a fair predictive capacity with the area under the ROC curve totaling 0.718 (p<0.001). The medicolegal claims model included gestation, mode of delivery, accoucheur, labour complications, estimated blood loss and 5 minute APGAR in the final predictive model. The predictive capacity was better than 5 the complaints model, with the area under the ROC curve totaling 0.871 (p<0.001).

Conclusions: I have shown that it is possible to predict both patient complaints and medicolegal claims using patient demographics and outcome data, at least at Monash Health in the field of obstetrics. The insights afforded by my findings, if confirmed prospectively, could be used by a health service to proactively identify high-risk situations and to develop approaches to proactively mitigate risk. This represents a new quality improvement opportunity for health services to improve the care and follow up provided to patients who may otherwise feel dissatisfied with their care.

ANTONIA CHRISTA PARAMITHA

Targeting platelet thrombin receptor as a novel anti-thrombotic approach: Can we develop a mouse with the same thrombin receptor profile as human platelets?

Dr Justin R. Hamilton, Australian Centre of Blood Diseases
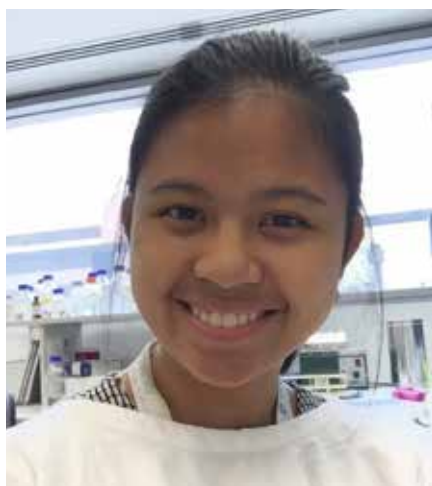
I am an Honours student conducted a research project under Dr Justin Hamilton in Australian Centre of Blood Diseases, Melbourne. I started my project on August 2015. I chose this project because I am interested in a research focusing on thrombosis, especially in a novel pharmacological aspect. I had a very pleasant experience working in Hamilton Lab Group from which I learned a lot about research and Melbourne. During my research year in Hamilton Lab, I did characterisation of the mouse model that has been made previously. It was my first time working with mouse but finally I can get through it well with a continuous help from my lab team. I am delighted to have the chance working with an amazing lab as Hamilton Lab group. Knowing what you want to learn and finding a perfect place to learn it would be my suggestions for the future Honours students of Monash University. If there is any enquiry, I am happy to be contacted on my email antoniaparamitha@gmail.com.

Background: Cardiovascular disease is the leading cause of death globally, contributing to more than 30% of all deaths. The two major causes of cardiovascular disease are myocardial infarction and ischaemic stroke – both of which are caused by platelet-rich arterial thrombi. Thrombin is the most potent platelet activator, which it achieves via protease activated receptor (PARs). Therefore, PARs are leading drug targets for improved anti-thrombotic therapy. There are two PARs on human platelets, namely PAR1 and PAR4. Recently, vorapaxar was approved as the PAR1 antagonist to prevent arterial thrombosis in a clinical setting. However, vorapaxar lacks some safety and has limited clinical utility. As a result, PAR4 has become of interest as an anti-thrombotic drug target. In order to investigate the relative effects of targeting these two platelet PARs during thrombosis, preclinical pharmacology studies would generally be performed in an appropriate animal model. However, only primates share the human platelet PAR profile of PAR1 and PAR4. For example, mouse platelets express PAR4, but express PAR3 in place of PAR1. To address this limitation, a genetically modified mouse model was developed in which mouse PAR3 was replaced with human PAR1 specifically in platelets (hPAR1-KI mouse).

Method: The expression and function of PAR1 in the platelets from these hPAR1-KI mice was assessed. PAR1 function was examined by two independent assays (platelet aggregometry and P-selectin expression) and PAR1 expression was examined by flow cytometry.

Results: Platelets from hPAR1-KI mice failed to respond to a PAR1-specific agonist in both activation assays, but responded similarly to littermate control mice in response to other agonists. In addition, no PAR1 expression was detected in platelets from hPAR1-KI mice. However, thrombin-induced responses in platelets from hPAR1-KI mice were diminished to a level similar to that observed in PAR3-/- mouse platelets. Together these findings suggest that correct targeting of PAR3 has occurred in these mice, but that PAR1 is not expressed in their platelets and therefore does not function.

Conclusions: Although the reasons for this lack of expression remain unknown, this study suggests that genetic targeting of human PAR1 to mouse platelets is unsuitable for the generation of a small animal model for the study of PARs in thrombosis.

PUTRA RIZA PRATAMA

The role of intrarenal nerves in diabetic and hypertensive kidney

Dr. Anna Watson and Dr. Stephen Gray, Diabetic Complications, Baker IDI Heart and Diabetes Institute

I completed my BMedSci year doing research at the Baker IDI of the Central Clinical School. I took a year off from med school at Universitas Indonesia to be exposed to the backbone of medicine that is research. My research was about the intrarenal nerves and how it relates with diabetes and hypertension. I was always interested in studying diabetes, since I'm afraid it might run in the family.

My honours year was a blast! I've learned so much and it has given me a great insight into the world of research. I am grateful for everyone from the Diabetic Complications lab, especially my supervisors Dr. Anna Watson and Dr. Stephen Gray, for giving me the opportunity to join this project and providing me with all the necessary resources and guidance throughout the year.

Background: Diabetes has increased in global prevalence and a range of complications may develop with diabetes with the most prevalent being nephropathy. Epidemiological data shows that most diabetic patient develop hypertension, which further worsens nephropathy. Diabetes when concomitant with hypertension gives greater risk of developing end stage renal disease in patients. Many hypertensive patients cannot achieve controlled BP through lifestyle modifications and antihypertensive drugs. Thus new approaches are needed.

Recent therapies targeting hypertension aim to reduce sympathetic neural activity, which is vital in the pathogenesis of hypertension. It is known that the main neural signalling molecules are the catecholamines (CA). Reactive oxygen species (ROS) is also known to mediate sympathetic activation, particularly if due to renal disease.

Method: Schlager mice were obtained between 6 to 8 weeks of age. They were allocated to 4 different groups, which are control normotensive, control hypertensive, diabetic normotensive, and diabetic hypertensive.

CA contents were assessed through high performance liquid chromatography. CA-producing enzymes in the cortex (proximal and distal tubules) and medulla (loop of Henle) were quantified through DAB-stained immunohistochemistry studies.

To assess the oxidative stress, hydrogen peroxide (AmplexRed) and catalase activity were measured as per kit's instructions. Gene expression of NADPH oxidase isoforms and antioxidants were also measured through real-time PCR.

Statistical analyses were done with post-hoc test and ANOVA by SPSS, with $p < 0.05$ considered as significant.

Results: *In hypertension only*

Upregulation of cortical TH staining with hypertension confirms a previous study with these mice. The increase of this rate limiting enzyme could be linked to a rise in the CA levels (dopamine and noradrenaline). The main contributor of ROS in the kidney, Nox4, is high with hypertension. This result was mirrored by hydrogen peroxide, and also activity of catalase, which breaks down hydrogen peroxide.

In diabetes only

Diabetes leads to an increase in ROS and decrease in renal antioxidants. There were no significant differences in the cortical TH levels. However, dopamine and noradrenaline were lower with diabetes. Our diabetic model showed no significant changes in the level of either hydrogen peroxide nor antioxidant activity, represented by hydrogen peroxide and SOD gene expression along with catalase activity, respectively.

In hypertension and diabetes

TH staining in diabetic BPH is lower than control BPH. This difference in TH may cause the CA level to be reduced, as shown by the results of dopamine and noradrenaline. Nox4 gene expression shows a trend to be higher ($p=0.078$) in diabetic hypertensive group compared to diabetic normotensive group. Hydrogen peroxide is also increased, however catalase activity did not follow this increase. This indicates that there are hydrogen peroxide, and probably ROS excess, which may lead to more damage and a worse nephropathy.

Conclusions: The results show that diabetes and hypertension alter the CA and their enzymes inside the kidney of this experimental model. Not only that, but changes in CA also affects the oxidative stress state in the kidney. We have found that hypertension up-regulates both catecholamines and oxidative stress, however this was attenuated in diabetes. When hypertension is concomitant with diabetes, ROS excess was found. Targeting CA enzymes, especially TH, may be a potential approach to reduce oxidative stress in the future.

DAVID PRIEST

Understanding the pattern of gonorrhoea by anatomical site and by age amongst men who have sex with men.

Melbourne Sexual Health Centre. Prof Christopher Fairley and Dr Eric Chow.

This year I have had an incredible time doing my bmedsci at Melbourne Sexual Health Centre. I have always been interested in sexual health medicine, and this year has enabled me to have significant exposure to the field. Although I did not originally see myself as someone who would be interested in research, this year has changed my mind completely; this change of opinion certainly influenced by the extremely supportive environment at MSHC, and the incredibly knowledgeable supervisors at the centre. I was fortunate enough to be involved in a number of projects this year, including some with clinical contact, however my main project involved understanding which groups are at greatest risk for gonorrhoea infection, in an attempt to understand why gonorrhoea rates are rising in the population. This year has provided a number of amazing opportunities and I would highly recommend a bmedsci at MSHC. Feel free to contact me on davidpriest@live.com.au!

Background: Gonorrhoea rates have been increasing rapidly, particularly amongst men who have sex with men (MSM), worldwide, and in Australia. Although some studies have suggested the pharynx is the key site responsible for gonorrhoea transmission amongst MSM, and that kissing is a risk factor for pharyngeal gonorrhoea, it is unclear how gonorrhoea positivity is associated with different age groups, anatomical sites, detection methods, and kissing practices.

Aims and hypotheses: This thesis includes two separate studies. The aim of the first study (study A) was to determine the gonorrhoea positivity amongst MSM by site and different age group. We hypothesised that younger men would be disproportionately infected by gonorrhoea, particularly at the pharynx, compared to older men.

The aim of the second study (study B) was to determine the kissing practices of MSM, and to see if they differ by age. We hypothesised that younger men would have more kissing partners than older men – especially non-sex kissing partners.

Methods: Study A was a retrospective data analysis of MSM attending Melbourne Sexual Health Centre (MSHC) between 2007 and 2016. Demographic characteristics, sexual behaviour data and laboratory results for gonorrhoea and chlamydia were collected as part of routine care at MSHC. Analyses were performed to determine gonorrhoea and chlamydia positivity by year and age group. Univariate and multivariate logistic regression analyses were performed on risk factors that were associated with gonorrhoea and chlamydia (age, condom use and number of partners).

Study B was a cross-sectional survey amongst all MSM at MSHC in 2016. Men were asked about the number of partners they kissed; with and without sex. Survey answers were matched with electronic records of demographic characteristics and laboratory results for pharyngeal gonorrhoea. Analyses were performed to determine the relationship between age and the number of kissing partners, and

pharyngeal gonorrhoea positivity was calculated by age group and the number of kissing partners.

Results: Study A analysed 128,671 consultations. Even after adjustment for sexual risk behaviour, such as the number of sexual partners and condom use, men <25 were 4.8 and 7.8 times more likely to be positive for pharyngeal gonorrhoea than men ≥55 by NAAT and culture respectively, and 5.4 and 4.3 times more likely to be positive for anal gonorrhoea than the men ≥55 by NAAT and culture respectively. This increased risk amongst younger age groups did not occur with chlamydia, with men under 25 only 1.4 times more likely to be positive for anal chlamydia than the oldest age group, and no association between age and urethral chlamydia positivity.

Study B had 1148 respondents included in the analysis. Younger men reported more kissing only partners than older men, and there was a significant association between the number of kissing without sex partners and pharyngeal gonorrhoea positivity; however there was no association between the number of sex without kissing partners and pharyngeal gonorrhoea positivity.

Conclusion: Younger men are at a greater risk of gonorrhoea infection than older men, and this increased risk does not occur with chlamydia. Younger men reported more kissing only partners than older men, and a greater number of kissing partners was associated with higher pharyngeal gonorrhoea positivity. These findings suggest public health campaigns targeting young MSM, and potentially even focusing on the kissing practices of young MSM, are essential for gonorrhoea prevention and control.

MITCHELL PRYCE

3D Printing of Wrist Pathologies – An Educational Tool for Patients

A/ Prof David J. Hunter-Smith[1,2], A/Prof Warren M. Rozen[1,2]
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I completed my Bachelor of Medical Science (Honours) after finishing my fourth year of medicine. The decision to work with the Department of Surgery at Peninsula Health was a simple one. I had previously spent time fabricating 3D printed models of the first carpometacarpal joint at Peninsula Health a year earlier. This transformed under the guidance of my supervisors A/Prof David Hunter-Smith and A/Prof Warren Rozen, and local 3D printing guru Dr Michael Chae, into an honours project focussing on patient education and clinical communication.

Highlights of this year include the immersion with novel imaging technologies that may be widespread in future surgical practice and introducing the world of 3D printing to patients. The research experience has been a challenging one, but it has also been rewarding; and working with the Plastics team at Peninsula Health was truly an unforgettable experience.

Introduction: Patient understanding of pathology is essential for building rapport and obtaining informed consent for surgical interventions. The wrist is a region of complex anatomy that is difficult to explain without visual aids. Thus three-dimensional (3D) printing, fabricating a life-like representation of patient-specific anatomy, has the potential to redefine how patients understand their own anatomy. Although 3D printing has been validated as a useful adjunct in medical and surgical training, its application in patient education has not been well established. Thus the primary aim of this study was to validate the educational benefit of using 3D printed models as visual aids in the patient population. Secondary objectives include measuring the intuitive nature of 3D models and comparing results between two separate pathologies of the same anatomical region.

Methods: This was a prospective, randomised study that used the general public as surrogates for patients with complex wrist pathologies – a hamate fracture and basal joint arthritis. Two sets of 3D printed models were fabricated from patients' computerised tomography (CT) scans. Participants were randomised between four groups (fracture 3D + CT, fracture CT, arthritis 3D + CT, arthritis CT) and asked to complete a questionnaire pre and post a video tutorial on the pathology. Outcomes were measured using a health literacy assessment, true/ false questions and a survey.

Results: Data collection is ongoing. Sixty-one participants were included. There was no benefit of 3D printing in questionnaire scores for the fracture (71.3% vs 71.0%, $P=0.93$) or arthritis (73.0% vs 68.0%, $P=0.51$) groups. Survey results showed participants believed 3D models and CT scans to be equal for discussing the anatomy (79.3% vs 88.0%, $P=0.24$), the pathology (79.3% vs 86.7%, $P=0.3$) and for ease of use (78.8% vs 87.3%, $P=0.29$) in the fracture group. Survey results favoured 3D printing for discussing pathology (93.0% vs 77.6%, $P=0.019$) and ease of use (92.3% vs 72.3%, $P=0.004$), but not anatomy (91.0% vs 83.0%, $P=0.14$) in the arthritis group. Overall, 93.4% of verbal feedback reported a preference in visualising the pathology on a 3D model (26.3%) or on both a 3D model and the CT scans in combination (67.2%).

Conclusion: Though there was no objective educational benefit in the clinical setting, it was revealed that 3D printed models are useful for discussing complex wrist pathologies. Results also suggest that for explaining difficult spatial pathologies, 3D models have an advantage over CT scans; when explaining spatially simpler pathologies, this may not be the case. Considering this, the study has paved the way for future research regarding the implementation of 3D printing in discussing a patient's own complex spatial pathology. Further, the results show that 3D printed models would be widely appreciated by patients, and thus have a strong foundation for use in clinical communication

ASTARI RIDHANYA PUJI

Fish intake and incidence of type 2 diabetes: The AusDiab study

Dr Alice Owen, A/Prof Dianna Magliano, Prof Danny Liew
School of Public Health and Preventive Medicine

I was fortunate enough to undertake my honours year in Monash University, particularly in School of Public Health and Preventive Medicine. I was so grateful to took an epidemiological research in the field of diabetes under supervision of Dr Alice Owen, A/Prof Dianna Magliano, Prof Danny Liew. All in all, it has been a wonderful year and I gained a lot of new knowledge and experience.

Background: The prevalence of diabetes mellitus s increasing substantially, with the majority of cases being type- 2 diabetes. Type 2 diabetes is related to lifestyle and diet, and these factors play a key role in diabetes management and risk. Fish, the major source of long chain n-3 polyunsaturated fatty acids in the diet, has been linked to diabetes risk. However, current evidence is conflicting as to whether fish intake increases or decreases the risk of diabetes. The reason for this disparity in the results is not clear, but may be due to geographic factors or disparity in other diabetes risk factors between populations. To date, no study has examined the relationship between fish intake and diabetes risk in Australia.

Method: This study used the Australian Diabetes, Obesity, and Lifestyle (AusDiab) cohort study, which is a national population-based cohort study from Australia. Among AusDiab participants of age 25 years and older, those who had diabetes and had missing diabetes status at baseline were excluded leaving a final sample of 10,172 participants at baseline. Participants returned for one or both of the two follow-up assessments of diabetes status. Among these, 434 developed diabetes over follow-up. The outcome of interest was incident diabetes over 12 years measured by oral glucose tolerance test (OGTT), as defined by the World Health Organisation criteria. Fish intake was measured by self-administered validated semi-quantitative food frequency questionnaire (FFQ). Fatty acid intake was estimated by RMIT database of Australian foods. Cox regression was used to examine the relationship between types of fish preparation method (non-fried, tinned, and fried) in frequency of serves and quintiles intake (in grams) and diabetes risk. The relationship between fatty acids and diabetes risk was examined according to types of omega-3 fatty acids (docosahexaenoic acid, docosapentaenoic acid, eicosapentaenoic acid, and total omega-3 fatty acid) in tertiles of intake (in grams). All analyses were performed in STATA version 14.1.

Results: Consuming tinned fish frequently (two or more serves per week) showed a higher risk of diabetes significantly (HR 1.4, 95% CI 1.04-1.88). Fried fish occasional consumption was positively associated with diabetes (HR 1.31, 95% CI 1.02-1.68). Those in the second to the fourth quintiles (Q2, Q3, and Q4) of non-fried fish, tinned fish, and total fish intake showed an inverse relationship with diabetes risk in minimally adjusted models. After full adjustment, only those in the second quintiles of tinned fish remained statistically significant (HR 0.69, 95% CI 0.49-0.96). Those with consumption of EPA in middle tertile (T2) showed a lower risk of diabetes (HR 0.75, 95% CI 0.58-0.99).

Conclusions: Our study provides weak evidence that moderate intake of total fish and non-fried fish intake is protective to diabetes. However, consuming fish frequently ablates the protective effect, and may even be harmful. Moderate intake of EPA also showed a lowered risk of diabetes. Fried fish intake is associated with higher risk of diabetes. This study provides important findings that may be used to support current dietary guidelines for prevention as well as management of diabetes.

JASMINE ARINI PUTRI

Development of Protein-Based Nanoparticles with Stealth and Biocompatible Properties

A/Professor Christoph E. Hagemeyer and Doctor Thomas Bonnard
NanoBiotechnology Laboratory, Australian Center for Blood Diseases, Monash University

I'm a medical student from University of Indonesia taking an honours course in Monash University after finishing my preclinical studies. I looked at BMedSc project booklet to know which project is available at that moment and found the information about Australian Center for Blood Diseases (ACBD) and NanoBiotechnology laboratory there. I really interested in all of their projects, especially the one related to nanoparticles.

This year was just fantastic. Being able to learn about how to fabricate nanoparticles and tested it both in vitro and in vivo were really wonderful experiences to me. Having such supportive, extremely patient supervisors (A/Professor Christoph E. Hagemeyer and Doctor Thomas Bonnard) and very welcoming lab teams makes me sad that my honours year is finally comes to an end and I need to go back to Indonesia.

For the next honours students who are interested in taking a project in NanoBiotechnology lab in ACBD, I am happy to be contacted (ariniputri.jasmine@gmail.com) and share my experiences and also give the information related to the lab.

Background: Engineered nanodevices, such as nanoparticles, produce significant improvements in the therapy and diagnosis of certain disorders. However, nanoparticles made from non-natural building blocks might accumulate in the human body and can cause toxicity after long-term use. New stealth and biocompatible nanoparticle made from more natural building blocks are required to avoid organ accumulations and thus adverse effects.

Method: The protein building blocks were produced using Escherichia coli bacterial systems and highly purified. Particle templates were used for the building blocks to be cross-linked and shaped into spherical nanoparticles. Mass spectrometry was done to analyse the composition of the nanoparticles. Confocal fluorescent microscopy analysis was performed to determine the morphology of the nanoparticles. Phagocytic association to determine the low-fouling properties of nanoparticles was investigated using two cell lines: THP-1 cells (human monocytic cells) and RAW 264.7 cells (murine macrophage cells). The biodegradability of the protein nanoparticles in trypsin was analysed using flow cytometry. Nanoparticles conjugated to infrared dyes were injected in mice and analysed using an Odyssey imaging system to determine their organ distribution. Histology analysis of the mouse spleen was done to determine the possibility of the particle's degradation.

Results: The synthesis of nanoparticles exclusively made from protein was successful and confirmed by mass spectrometry. The protein nanoparticles showed low phagocyte association ($p < 0.001$ with THP-1 and RAW 264.7 cells) and degraded quickly with trypsin ($p < 0.001$). The nanoparticles distributed mainly to the spleen and liver after 30 minutes and 24 hours. The protein nanoparticles showed very low signal in the spleen indicating that they might have been degraded.

Conclusions: Fabrication of nanoparticle solely made from protein is feasible. The nanoparticles have stealth properties and showed possible degradation in the spleen. However, further research is required to improve the effectiveness of this novel nanoparticle platform.

RATU LUCKY NITIBASKARA PUTRI

The Relationship between Stress, Anxiety, Memory, Cortisol, and Telomere Length

Dr. Caroline Gurvich (Monash Alfred Psychiatry research centre), Ms. Elizabeth Thomas (Monash Alfred Psychiatry research centre), Dr. Kiymet Bozaoglu (Baker IDI)

I'm a medical student from University of Indonesia and I'm absolutely delighted to be able to be involved in this exceptional research project for my BMedSc(Hons) degree. Stress and anxiety are very common in modern day society and I was interested to investigate the underlying psychological and biological mechanism, particularly exploring a novel area which is telomere length. In this project, I've been examining 61 people to assess their level of stress and anxiety as well as their cortisol levels and telomere length at Monash Alfred Psychiatry research centre (MAPrc) also with the help from Baker IDI Heart and Diabetes Institute. This project was originally initiated by my main supervisor, Dr. Caroline Gurvich. I'm beyond grateful to have her as my main supervisor, and I'd like to thank my other supervisors who are very helpful and compassionate, Ms. Elizabeth Thomas and Dr. Kiymet Bozaoglu. I have learned a lot and I have gained wonderful and valuable experiences throughout this honours year.

Background: Stress and anxiety are pervasive in daily life and each individual has different mechanism of stress response psychologically and biologically. Stress and anxiety have been strongly associated. Anxiety itself can manifest in two different ways, state anxiety or trait anxiety. Here, we would like to observe the relationship between stress and state or trait anxiety with memory performance as well as the potential biological markers which can be characterized by cortisol levels and telomere length.

Method: This is a cross sectional study which involved 61 participants from a healthy adult population who were assessed at one time. At the day of the testing, the participants were required to collect their own saliva samples in the morning for three times; immediately after awakening, 30 minutes after awakening, and 60 minutes after awakening to measure their cortisol levels. The participants were then required to complete an array of tasks to evaluate their perceived stress with Perceived Stress Scale (PSS), state-trait anxiety with State-Trait Anxiety Inventory (STAI), and verbal memory performance with Rey Auditory Verbal Learning Test (RAVLT). At the end of the testing, the participants were required to donate blood samples for 2mL to analyze their telomere length.

Results: The results among participants showed that higher perceived stress is significantly correlated with higher state-trait anxiety. State-trait anxiety, specifically state anxiety, appears to be significantly correlated with verbal memory performance that was assessed with RAVLT. RAVLT encompasses two different list of words to be memorized and recalled; interestingly, we only found significant correlation between state anxiety and the second list of words in RAVLT. As regards potential biological markers which are cortisol levels and telomere length, there are no significant correlations between the biological markers with perceived stress, state-trait anxiety, and verbal memory.

Conclusions: Perceived stress and state-trait anxiety are significantly correlated, which is consistent with previous literatures. State anxiety appears to be significantly correlated with verbal memory performance, particularly the second list of words in RAVLT; the observed result could be attributed to the information overload that the participants experienced during verbal memory recall which requires encoding different list of words within a short amount of time that may affect their memory processing as well as memory storage accuracy. However, one possible explanation of the insignificant correlations between the biological markers with perceived stress, state-trait anxiety, as well as verbal memory performance might be due to the study limitation that is not able to completely validate the accuracy of the cortisol levels samples that is associated with the participants' compliance.

SHAFIRA ANDRIANI RACHMADI

Molecular Regulation of Platelet Adhesion Receptors

Dr. Elizabeth Gardiner & Assoc Prof Robert K Andrews, Australian Centre for Blood Diseases, Central Clinical School

Hi, I'm Shafira! I was doing my honours project under the supervision of Liz and Rob in system haematology group at ACBD CCS. Throughout the year, platelets have been my main focus. The ultimate aim of my project was to produce mAb that can recognize both cleaved and uncleaved GPIbα receptor which is important to determine platelet quality. This year has been such a roller coaster to me, it's so challenging yet stressful at the same time lol! I never imagined that I could finish it but I'm glad I did it. I never regret doing this because there won't be any opportunities coming anymore!

Background: Glycoprotein Ibα (GPIbα) shedding by metalloproteinase ADAM17 has been linked to increased platelet clearance. Studies using ADAM17 inhibitors have been shown to support this theory. However, these findings are still debatable as ADAM17 has broad specificity. In order to address this issue, development of reagents that specifically inhibit ADAM17-induced GPIbα shedding is necessary. Our lab has previously raised an antibody against the new N-terminal GPIbα after cleavage by ADAM17 called RB3. This project aims to check the platelet reactivity of RB3 subclones and assess whether the subclones specifically recognize the cleaved form of GPIbα receptor.

Methods: There were two RB3 subclones assessed, E6 and C10. Isolated human platelets from healthy donors were mixed with the hybridoma medium of the antibody to check its platelet reactivity by flow cytometry. The bound antibody was stained using secondary antibody FITC-conjugated anti mouse Ig. Additionally, calmodulin (CAM) inhibitor W7 was also used to induce shedding of GPIbα and RB3 subclones were assessed whether they bound to cleaved GPIbα. Screening of the supernatants of E6 and C10 subclones was performed to ensure clonality. Ultimately, affinity purification of the antibody with GPIbα 'uncut' peptide was performed.

Results: E6 bound to human platelets with high affinity even at a 1000-fold dilution while C10 demonstrated only background binding to resting washed platelets. The binding of E6 did not significantly change under GPIbα 'shedding conditions' whereas binding of AK2, an antibody against the extracellular region of GPIbα, was decreased with W7 treatment. Affinity purification of E6 hybridoma medium revealed that E6 did not bind to GPIbα 'uncut' peptide. A second round of subcloning of E6 and C10 produced six subclones of E6 with high platelet reactivity and C10 did not produce any positive clones.

Conclusion: This study revealed that RB3E6 was shown to have strong platelet reactivity by flow cytometry analysis. Future studies will determine binding properties of mAb RB3E6 and assess recognition of both uncleaved and cleaved GPIbα and whether RB3E6 can disrupt ADAM17-mediated GPIbα proteolysis.

RAISA CECILIA SARITA

Do Endothelial and Trophoblast Cells Alter Monocyte Responses to Infected Erythrocytes?

Associate Professor Anthony Jaworowski (Burnet Institute)

Its been a challenging year for me to do a lab-based project during my Bmedsci Honours year. Its such a golden opportunity for me to expose myself to a research field that I've never experience before. There are numerous advantages I got from honours year : I've learned how to build a critical thinking throughout the project, time-management, scientific writing, public speaking, and many more All is worth it! Burnet Institute provide an opportunity for me to focus to the field of infectious disease, which has been a hot topic in the world, and my country as well. It is been one great year to be a part of Burnet institute where I met so many people who really compassionate to achieve a better health for the community. This institute has provided me a positive environment to learn, especially my supervisor Associate Professor Anthony Jaworowski and other team from the lab as well!

Background & Aims: Malaria infection remains a crucial global issue in infectious disease, which manifests a range of conditions from uncomplicated to clinical disease. Pregnant women and children under 5 years old are most likely to suffer from severe malaria (SM) however the host determinants governing why some individuals manifest severe disease are unclear. Severe malaria is caused mainly by a particular species of malaria parasite called Plasmodium falciparum that is able to attach its host erythrocytes to the surface of tissues via its protein antigen Plasmodium falciparum erythrocytes membrane protein-1 (PfEMP1). This avoids clearance of the infected erythrocyte (IE) by macrophages in the spleen. Attachment stimulates an innate immune response mediated by monocyte phagocytosis that triggers a variety of immunological responses including cytokine and chemokine production to coordinate further innate and adaptive immunity. However, the specific effects of tissue attachment of IE to cytokine and chemokine elicitation and monocyte responses are unknown. Therefore, this project examined the effect of IE attachment on the surface of trophoblast and endothelial cells, a feature of severe maternal and childhood malaria respectively, on the production of cytokine and monocyte chemoattractants.

Methods: Monolayers of BeWo and HUVEC, established models of primary human trophoblasts and endothelial cells respectively, were incubated with Immunoglobulin (IgG) opsonised IE that were infected with two different laboratory strains of P. falciparum: CS2 which attaches to chondroitin sulphate A (CSA) expressed on trophoblast cells and E8B which attaches to CD36 and ICAM-1 expressed on activated endothelial cells. Purified human monocytes were added and incubated overnight. Culture supernatants were collected and analysed using a bead array assay to quantify levels of selected cytokines and chemokines: TNF-α, IL-1 , IL-12, IL-18, IFN-γ, IL-16, IL-10, CCL2, CCL5, and CX3CL1. Phagocytosis of IE was confirmed by flow cytometry.

Results: Attachment of CS2-IE to BeWo caused a significant decrease in the production of the pro-inflammatory cytokines TNF-α (162.3 pg/mL c.f. 26.3 pg/mL, n=8, p=0.0078), IL-18 (11.1 pg/mL c.f. 1.2 pg/mL, n=8, p=0.0078) and chemokines CCL5 (78.2 pg/mL c.f. 16.6 pg/mL, n=8, p=0.0078) by monocytes while level of anti- inflammatory cytokines IL-6 (76.2 pg/mL c.f. 74 pg/mL, n=8, p=0.3125), IL-10 (1.9 9 pg/mL c.f. 1.6 pg/mL, n=8, p=0.547) was not changed. In contrast, attachment of E8B-IE to HUVEC significantly increased production of pro-inflammatory cytokines IL-1β (4,320 pg/mL c.f. 494.2 pg/mL, n=8, p=0.0078), IL-12 (85.1 pg/mL c.f. 57 pg/mL, n=8, p=0.0078), IFN-γ (283.6pg/mL c.f. 209.1 pg/mL, n=8, p=0.0078) and IL- 18 (116.1 pg/mL c.f. 80.8 pg/mL, n=8, p=0.0234), the anti-inflammatory cytokine IL- 10 (249.5 pg/mL c.f. 31.4, n=8, p=0.0078) and the chemokine CX3CL1 (13,095 pg/mL c.f. 1,639 pg/mL, n=8, p=0.0078) Transwell experiments confirmed that physical contact between monocytes and BeWo was required for BeWo modulation of TNF-α production by monocytes.

Conclusions: Cytokine elicitation by monocyte in response to IE is modulated by attachment of IE to tissue surfaces. The change in the balance between pro- and anti-inflammatory cytokine production in response to the attachment of IE to BeWo cells suggests that trophoblasts may function to produce an immune suppressive environment jn the placenta to limit harm to the fetus, which may favor parasite survival but also minimizes immunopathology. The significant increase of pro- inflammatory cytokine, anti-inflammatory cytokine, and chemokine altogether in response to IE attached on HUVEC may represent the immunopathology process lead to severe malaria in cerebral or childhood malaria.

FEBY FARISKA SAVIRA

Investigation of Mechanisms Underlying the Contribution of Uremic Toxins to Cardiorenal Syndrome

A/Prof Bing Hui Wang & Dr Andrew Kompa, Centre of Cardiovascular Research and Education in Therapeutics, School of Public Health and Preventive Medicine, Monash University

I worked in Clinical Pharmacology Laboratory of CCRE Therapeutics in The Alfred Centre. Our lab focuses on cardiovascular therapeutics, an area that is relatively stagnant in development yet an urgent unmet need for a more effective therapy is still present due to ever increasing morbidity and mortality rates for patients with cardiac dysfunctions. My study was an in vitro investigation of the effect of uremic toxins on cardiorenal remodelling, as these solutes are inadequately removed in concurrent heart failure and chronic kidney disease patients – even with dialysis. I was guided by A/Prof Bing Wang - the best supervisor I could ever ask for, surrounded by the most loving and kindest lab mates ever. Honours year was hands down the most precious, amazing year of my life. If you're thinking of doing an honours year, then go for it! You will be doing A LOT of work in just a year, but everything will be so worth it. I started the program with the thought research wasn't for me, but came out fully in love with it. Just make sure you are fully interested in the project you are applying for, ask around regarding prospective supervisors, and you are good to go.

Background: Indoxyl sulfate (IS) and p-cresol sulfate (PCS) are undialyzable protein-bound uremic toxins linked to cardiac hypertrophy and cardiorenal fibrosis, the hallmark of cardiorenal syndrome. The Apoptosis Signal-Regulating Kinase 1 (ASK1) cascade is involved in cellular stress responses associated with the dysfunction of the heart and kidneys, and its activation by IS and PCS has yet to be established. The aim of this study was to demonstrate direct effects of IS and PCS on cardiac and renal cells and explore the role of ASK1 pathway in uremic toxin-induced cardiorenal remodelling.

Method: Cultured heart and kidney cells were pre-treated with selective ASK1 inhibitor and stimulated with either IS or PCS. Cardiac myocyte hypertrophy was determined by 3H-leucine incorporation. Collagen synthesis of cardiac fibroblasts, kidney proximal tubular cells and renal mesangial cells was evaluated by 3H-proline incorporation. Western blot analysis was utilized to identify key signalling pathways. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay was used to determine cellular viability.

Results: IS and PCS augmented cardiac myocyte hypertrophy (by 119.4% and 129.1% vs. control, respectively, $p<0.0001$). IS increased collagen synthesis of cardiac fibroblasts, kidney proximal tubular cells and renal mesangial cells (by 115.1%, 115.9% and 122.7% vs. control, respectively, $p<0.0001$) whilst PCS enhanced collagen synthesis of kidney proximal tubular cells and renal mesangial cells (by 123.9% and 133.8% vs. control, respectively, $p<0.0001$). Selective ASK1 inhibitor dose-dependently suppressed these effects. Furthermore, increased activation of ASK1 and mitogen activated protein kinases (MAPKs) (p38 and ERK1/2) was observed in PCS-stimulated cardiac myocytes, in addition to nuclear factor-kappa B (NF-κB) in IS- and PCS-stimulated renal mesangial cells. MTT assay showed that stimulation by IS and PCS and co-treatment with selective ASK1 inhibitor did not affect the viability of these cells.

Conclusions: IS and PCS have pro-hypertrophic and pro-fibrotic properties, advocating the role of these protein-bound uremic toxins in cardiac and renal remodelling. The direct detrimental effects occur, at least in part, via the activation of ASK1 and downstream pathways (p38, ERK1/2 and NF-κB). Inhibition of ASK1 may be a potential therapeutic target in ameliorating cardiorenal syndrome progression caused by IS and PCS in the setting of chronic kidney disease.

STEPHANIE SEE

The Patient Experience with Early Pregnancy Bleeding in the Emergency Department

Gabriel Blecher[1], Simon Craig[1,2], Euan Wallace[3,4], Diana Egerton-Warburton[1]
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After completing my fourth year of medicine, I decided to undertake a BMedSci to explore the world of research. I believe that the "human" aspect of medical care is important but often overlooked, so I decided to conduct a study that would have the potential to improve the patient experience. Under the guidance of my supervisors, I was able to design and conduct a study which explored the patient experience with early pregnancy bleeding in the emergency department. I have particularly enjoyed the opportunity to develop skills in both qualitative and quantitative research methodologies. I would highly recommend a BMedSci to prospective students to get a taste of research and explore areas of interest!

Background: Early pregnancy bleeding is a common presentation to the emergency department (ED). For many women, such bleeding is emotionally traumatic because of the potential for pregnancy loss. Understanding women's expectations and experiences of their care in the ED may help to improve care for women at this distressing time.

Method: We conducted a multi-centre, mixed methods study which aimed to explore the care of women who attended the ED with early pregnancy bleeding.

The quantitative component was a retrospective chart review of consecutive ED presentations of early pregnancy bleeding to three metropolitan EDs over two months to provide the context of what consists of standard practice of care. We collected data on patient and ED service delivery characteristics. Data were analysed using descriptive statistics.

The qualitative component involved the recruitment of participants from three metropolitan EDs presenting with early pregnancy bleeding. We conducted two semi-structured interviews with participants. The initial interview took place in the ED and focussed on expectations of care. A follow up interview was conducted one week after discharge to explore experiences with care. Interviews were audio recorded, transcribed and de-identified. Transcripts were coded and an iterative thematic analysis was used to identify key themes. Interviews were conducted until thematic saturation was reached.

Results: We analysed 413 presentations of early pregnancy bleeding which accounted for 1.6% of all ED presentations in the three study hospitals. 20% of presentations were repeat visits. 66% attended after business hours and 70% were seen within the triage time. The median waiting time was 25 minutes (IQR 14, 48) and median length of stay in the ED was 167 minutes (IQR 103, 220). 84% were discharged home and 10% were admitted as an inpatient. 6% of patients self-discharged at their own risk.

For the qualitative component, 30 participants completed the initial interview and 22 participants completed the follow up interview. We identified five key themes relating to the patient experience which were: 1) women had variable knowledge and expectations about early pregnancy bleeding which affected their perception of their care, 2) staff interactions played a key role in alleviating distress through comprehensive explanations and showing empathy, 3) the physical environment of the ED, particularly the provision of privacy, affected women's perceptions of their care, 4) women's feelings of distress were exacerbated during periods of waiting, particularly if experiencing pain or not receiving updates on progress, and 5) women's expectations of emotional support were not routinely met during their stay.

Conclusions: The care of women experiencing early pregnancy bleeding in the ED should include the acknowledgement and alleviation of women's distress. Recommendations for an alternative model of care include: 1) a separate or fast tracked service which is available 24 hours, 2) discrete waiting spaces and cubicles, 3) routine provision of information including clear instructions about care after discharge and psychological support services, 4) training for staff about acknowledging and validating women's feelings, and 5) a dedicated phone service for women to ask questions or check if attendance to the ED is necessary.

GENEVIEVE SHANDLER

Impact of Obstructive Sleep Apnoea in Overweight/Obese Children on Cardiovascular Health

Professor Rosemary Horne[1,2], Dr Lisa Walter[1,2]

[1] The Ritchie Centre, Hudson Institute of Medical Research and [2] Department of Paediatrics, Monash University, Melbourne, Victoria, Australia

I undertook my BMedSci after completing my final year of Medicine in 2015. I chose to do a paediatric research project at The Ritchie Centre under the supervision of Prof. Rosemary Horne and Dr Lisa Walter. This year has been a steep learning curve but I have really enjoyed participating in research and getting a taste of what its all about. Doing a BMedSci has been a fantastic experience, and while challenging it was also extremely rewarding. I would definitely recommend a BMedSci year to all medical students.

Background: Up to 50% of overweight or obese children have Obstructive Sleep Apnoea (OSA) compared to 6% in normal weight children. Childhood overweight/obesity and OSA have independent adverse cardiovascular effects. Research into the combined effects of overweight/obesity and OSA in children is limited. This study aimed to compare polysomnographically defined sleep quality and architecture, cardiovascular variables and urinary catecholamines between normal weight and overweight/obese children with and without OSA, and controls.

Method: Seventy children (8-18 years) were recruited from children referred to the Melbourne Children's Sleep Centre, and twenty-eight normal weight non-snoring controls recruited from the community underwent overnight polysomnography (PSG). Wake office blood pressure was taken and BMI z-score calculated. PTT, an inverse surrogate measure of continuous blood pressure (BP), was calculated and each participant's PTT was normalised to their wake PTT. BP 'non-dippers' were the quartile exhibiting the least percentage change in PTT from wake to sleep. An overnight urine collection measured urinary catecholamines, as an indicator of overall sympathetic activity. HRV, measuring cardiovascular autonomic control, was analysed using time and spectral domain analyses. Children were grouped according to whether they had OSA (Obstructive Apnoea Hypopnoea Index >1 event/h) and weight status (overweight/obese BMI z-score ≥1.04): (1) non-snoring normal weight control group; (2) normal weight non-OSA group; (3) normal weight OSA group; (4) overweight/ obese non-OSA group, and (5) overweight/obese OSA group.

Results: Sleep quality and architecture were similar between groups except for the normal weight OSA group who spent more time in N1 compared with the control and normal weight non-OSA groups ($P<0.05$). The overweight/obese OSA group had increased office systolic BP compared to the control group, normal weight and overweight/obese non-OSA groups ($P<0.05$). Office systolic BP was moderately correlated with BMI z-score ($P<0.01$). In N3 the overweight/obese non-OSA group had decreased PTT compared to the normal weight non-OSA group ($P<0.05$). The overweight groups had a higher proportion of BP 'non-dippers than the normal weight groups ($P<0.0001$). The overweight/obese OSA group had increased heart rate in N3 and sleep compared to controls. During N3 the overweight/obese OSA group had significantly decreased HRV parameters reflecting sympathetic and parasympathetic activity compared with the normal weight non-OSA group. They also had significantly decreased parasympathetic activity compared to the normal weight OSA and non-OSA groups during N3. There were no differences in overall sympathetic activity as assessed by urinary catecholamines between groups.

Conclusions: This study suggests that although overweight/obese children with OSA do not have altered sleep quality or altered sympathetic activity indicated by their urinary catecholamines, they did have impaired parasympathetic control. This was indicated by their increased wake systolic BP and heart rate during sleep, and decreased HRV. The overweight groups also had a higher proportion of BP 'non-dippers' than the normal weight groups. This impaired cardiac autonomic control is important as elevated blood pressure during childhood is a strong predictor of hypertension in adulthood. Adult hypertension is a risk factor for many serious health complications. This study reinforces the notion that it is crucial to treat overweight/obese children who have OSA prior to the development of these long-term consequences.

ROHIT SHARMA

Superficial Siderosis and Cerebral Microbleeds in Cerebral Amyloid Angiopathy

Professor Richard Gerraty (Monash University, Epworth HealthCare)
Dr Bernard Infeld (Monash University, Epworth HealthCare)

I undertook the BMedSc(Hons) after my fourth year of medicine. Having developed an interest in neurology and radiology during my clinical years, I was fortunate to be able to find an exciting project in the field of neuroradiology at Epworth Hospital Richmond. Having the opportunity to complete this project under the watchful eyes of my supervisors and mentors – neurologists Professor Richard Gerraty and Dr Bernard Infeld – has been a privilege and an incredibly educational and enjoyable experience.

Throughout the year I was also fortunate to have the opportunity to get involved with Epworth Hospital Richmond in many other ways. I attended weekly stroke and neuroradiology meetings, participated in weekly clinical neurology bedside tutorials, taught the third year Monash and second year Melbourne medical students in weekly tutorials, and contributed an abstract and scientific poster to Epworth Research Week. Having these opportunities allowed me to strike a healthy and interesting balance between my project and my other academic interests.

This year has been a rewarding experience and I would strongly encourage the BMedSc(Hons) year to any student who wants to challenge themselves and get a taste for medical research.

Background: Cerebral amyloid angiopathy (CAA), an important cause of lobar intracerebral haemorrhage (ICH) in the elderly, has other radiological manifestations. Certain magnetic resonance imaging (MRI) sequences, gradient-recalled echo (GRE) imaging or the newer and more sensitive susceptibility-weighted imaging (SWI), can detect other lesions characteristic of CAA. These lesions, cerebral microbleeds (CMBs) and cortical superficial siderosis (cSS), are utilised by the Modified Boston Criteria to make a radiological diagnosis of CAA. CMBs and cSS are known markers of CAA affecting cortical and leptomeningeal vessels respectively, but not much is known regarding their relationship to each other or their patterns of distribution or temporal progression. Most studies so far reported have utilised GRE and not SWI.

This study aimed to use SWI MRI, in patients with 'probable CAA' as per the Modified Boston Criteria, to quantify and compare the burden of CMBs and cSS, compare the left and right cerebral hemispheres for their burden, and record their temporal progression. The hypotheses were that extent of cSS will be independent of CMB count, that these lesions will be distributed asymmetrically, and that patients with multiple scans will show temporal progression of these lesions.

Method: Retrospective brain MRI data was analysed from a five-year period at Epworth Hospital Richmond in patients who had a diagnosis of either CAA, a haemorrhage potentially caused by CAA, or a presentation with clinical features mimicking CAA. Patients were excluded who did not have a SWI MRI, or did not meet the Modified Boston Criteria, or had a history that suggested an alternative cause for their radiological findings. From the remaining patients, demographical, clinical, and radiological data was collected and analysed.

Results: After excluding 575 patients, 59 patients were available for analysis, including six patients with two SWI MRIs. Analysis of scatterplots of CMB and cSS counts revealed R2 values that were very low, with the implication being that there was no relation between CMBs and cSS. Asymmetry was highly prevalent in the study population, with 67.8% of patients with lobar CMBs and 66.7% of patients with cSS having two-thirds or more of these lesions in one hemisphere. Moreover, 32.2% of patients with lobar CMBs and 48.1% of patients with cSS had lesions in only one hemisphere. In the six patients with two SWI MRIs, all patients demonstrated an increase in CMB and cSS counts between scans. There were also multiple instances of new lesions appearing in close anatomical proximity to older lesions, in these patients.

Conclusions: These results suggest that CAA may not progress uniformly or symmetrically through the brain, and that there may be differences between cortical and leptomeningeal CAA. The findings are consistent with the notion of amyloid proteins 'seeding' and 'spreading' along vessels, analogous to the progression of prion diseases and Alzheimer disease. These results also have potential diagnostic significance in differentiating CMBs due to CAA from their many radiological mimics. This research can hopefully be used as a platform for further investigations into the radiological characteristics and pathophysiology of CAA.

SASHA SKINNER

Partial Amniotic Carbon Dioxide Insufflation for Fetoscopic Spina Bifida Repair

Dr Ryan Hodges[1,2], Dr Kelly Crossley[1]
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[2] Perinatal Services Monash Health, Monash Medical Centre, Victoria, Australia

I deferred my internship year to do a Bachelor of Medical Science (Honours) after completing 5th year of MBBS. I have had a fantastic year and thoroughly enjoyed working with such passionate and dedicated people. I have learnt so much, not just about science and the laboratory, but also an unexpectedly large amount about my personal ambitions and capabilities. This year has sparked a passion in me and research will undoubtedly be something I remain involved in for many years to come. For anyone considering doing a research year, finding a supportive and passionate supervisor is really worthwhile, as much as finding a project that interests you. There are many projects out there, so choose one that you are happy to dedicate a year of your life to. I chose my project based on my clinical interest in obstetrics, and by the variety that this project offered, with experience in animal surgeries and laboratory work. My supervisors, the Hooper lab-group, and all the other honours students were amazing people to work with and I have made many invaluable long-term friendships.

Background: Prenatal repair of spina bifida improves neurological outcomes and prevents intracranial complications at birth. To reduce significant maternal morbidity and high rates of preterm birth associated with open fetal surgery, fetoscopic spina bifida repair is proposed as a minimally invasive alternative. Partial amniotic carbon dioxide insufflation (PACI) is one method to overcome the technical challenges of operating endoscopically in amniotic fluid. PACI involves partially draining amniotic fluid and insufflating the uterus with carbon dioxide. PACI increases space, improves visualisation and allows the use of surgical glues. However, evidence of fetal safety during PACI is not well established. In sheep models, PACI causes fetal hypercapnia and acidosis, yet the effects on fetal-placental circulation or the developing fetal brain are unknown. Furthermore, insufflation pressures used clinically far exceed what has been tested in animal models.

We aimed to assess the effect of PACI, at clinically used insufflation pressures, on the fetal-placental circulation, fetal and maternal acid base status and on the developing fetal brain in a sheep model.

Method: Pregnant ewes at 105 days gestation, underwent surgery to instrument the fetal, placental and maternal circulation. Following fetal surgery, amniotic fluid was drained and the experimental group underwent an 80 minute period of PACI. Insufflation pressures were altered every 20 minutes from 5mmHg to 15mmHg to 25mmHg and back to 15mmHg and monitoring continued for 20 minutes post desufflation. Control animals were monitored for 100 minutes without PACI. Throughout the experimental, fetal-placental blood flow and fetal and maternal blood pressure and heart rate were continuously recorded and blood gas samples collected intermittently. At the conclusion of the experiment, ewes and fetuses were euthanized and fetal brains were collected for histology.

Results: PACI decreased uterine artery flow by up to 79%. PACI caused severe fetal hypercapnia ($PaCO_2$ 143mmHg), acidosis (pH 6.8) and hypoxia (fetal SaO_2 31%), with a significant rise in fetal lactate (8.4mmol/L). Fetal carotid artery pressure and heart rate increased during PACI. There were comparatively small changes in maternal $PaCO_2$ (51mmHg) and pH (7.35). As insufflation pressures increased, the discrepancy between maternal $etCO_2$ and $PaCO_2$ increased, maternal oxygen saturation decreased and there was a significant rise in maternal carotid artery pressure. On histological analysis, large dilated and congested blood vessels were present in fetal brains exposed to PACI.

Conclusion: PACI has detrimental implications for fetal physiology including large reductions in uterine blood flow, severe fetal hypercapnia, acidosis, hypoxia and lactic acidosis, increased fetal heart rate and blood pressure. Small changes in maternal acid base status do not correlate with severe changes in fetal physiology and therefore cannot be used to monitor fetal wellbeing. PACI leads to cerebrovascular changes on fetal brain histology. PACI should not be performed in human fetuses until further studies have addressed these safety concerns in animal models.

RAELENE TAN

Borderline Personality Disorder (BPD) and Polycystic Ovary Syndrome (PCOS): A cross-sectional study

Dr Jasmin Grigg[1], Professor Jayashri Kulkarni[1,2]
[1]Monash Alfred Psychiatry research centre (MAPrc), [2]Department of Medicine, Monash University

I decided to do a BMedSci(Hons) year because I wanted experience in research, and thought that after 4th year was the best time to do it. I was very lucky to have been offered the opportunity to work on my project at the Monash Alfred Psychiatry research centre (MAPrc), and to be a part of the Women's Mental Health team there. I have learnt so much this year, and am so grateful to my supervisors and the team at MAPrc for their support and for making my experience a tremendous one.

Background: Borderline personality disorder (BPD) is a common and severe psychiatric illness, whilst polycystic ovary syndrome (PCOS) is a complex endocrine disorder that commonly affects women of reproductive age. Both of these disorders can have a profound effect on the well-being and outcomes of the individual. Recent studies have shown a higher prevalence of PCOS in women with BPD. However, no studies exist yet that have investigated a possible relationship between the two disorders.

Childhood trauma is a major risk factor for BPD. Studies have shown that it can cause hyperactivation of the hypothalamic-pituitary-adrenal (HPA) axis, which can then affect the hypothalamic-pituitary-gonadal (HPG) axis and cause symptoms seen in PCOS such as hyperandrogenism and menstrual dysfunction.

As such, this study aimed to identify if PCOS in women with BPD is associated with a) increased severity of childhood trauma and b) more severe BPD symptoms. Exploratory analyses looking at the relationship between free testosterone levels, childhood trauma, and BPD severity were also conducted. It was hypothesised that the presence of PCOS would be associated with increased severity of childhood trauma and also increased severity of BPD symptoms.

Method: Thirteen women with either a current clinical diagnosis of BPD or who experienced symptoms of BPD aged 19-43 years underwent several quantitative assessments for BPD, PCOS, and childhood trauma respectively. They were then divided into two groups based on their PCOS status. Women were considered to have PCOS if they had a previous diagnosis, or if they met the 1990 National Institutes of Health (NIH) Criteria for PCOS (n=6). Independent t-tests and Mann-Whitney U tests were used to analyse the variables. Exploratory correlational analyses were carried out using the Spearman Rho test.

Results: Childhood trauma scores yielded non-significant mean differences between the "PCOS" and "No PCOS" groups. The presence of PCOS was also not significantly associated with more severe BPD symptoms ($p > 0.05$). However, exploratory analyses looking at the sample as a whole (100% of whom have experienced at least one form of early life trauma) revealed a significant correlation between free testosterone levels and childhood trauma scores.

Conclusions: We were not able to demonstrate childhood trauma or BPD symptoms to be associated with the presence of PCOS in women with BPD in this small research study. However, we were able to show that in the entire BPD cohort, severity of trauma was significantly associated with higher levels of the specific blood marker of PCOS, free testosterone. Our results partially support the strong theoretical rationale for childhood trauma causing endocrine dysregulation and therefore increasing one's risk of developing PCOS. Given the harmful collective effects and burden of BPD and PCOS comorbidity on the individual and society, this should be tested further in future larger studies.

ANGUS TAYLOR

Distribution of Transition Metals within the adult Marmoset Amygdala

Dr. David Reser (School of Biomedical Sciences, Physiology Department, Monash University), Prof. Marcello Rosa (School of Biomedical Sciences, Physiology Department, Monash University)

After completing my preclinical years, I decided to try something different and undertake my BMedSc (Hons), rather than moving straight into clinical years. After discussing project opportunities with a number of supervisors, I decided to work with Dr. David Reser on campus at Monash Clayton, examining the distribution of transition metals in the healthy primate brain.

It was a challenging experience, learning to producing academic quality scientific work, and I found (perhaps not unsurprisingly) it was remarkably unlike the rushed last-minute assignments of years 1 and 2. Despite feeling slightly out of my element and in over my head for most of the year, with the support of my supervisors I produced a piece of work that I am very proud of. I'm now to continue working towards the hopeful publication of this work.

I'd recommend this year to all students looking to try something different during their medical schooling. With more freedom than regular study, this year allows you to both further the current state of medical research and also explore your own interests in areas you may not have considered.

Any students considering undertaking a BMedSc, if you have any questions, feel free to email me atay24@student.monash.edu

Background: The normal distribution of transition metals across the primate brain is not well understood. These metals, such as iron, manganese, copper and zinc, when regulated correctly, are involved in many normal brain functions. However, loss of metal homeostasis is associated with neurodegenerative processes, including Alzheimer's disease. These pathologies affect many parts of the brain, including the deep brain structure known as the amygdaloid complex (AC). The AC is a subcortical nuclei made up of 13 different subnuclei, and is thought to play a role in associating internal responses to external stimuli. Current understanding of the normal iron, manganese, copper and zinc distribution within the subnuclei of the AC is limited to qualitative histological studies. This limits our ability to detect any changes in AC metal distribution or homeostasis that occur during pathological processes, as there is no normal baseline with which to compare it.

Aim: This project aimed to quantify and compare the distribution of iron, manganese, copper and zinc within and across the subnuclei of the AC in the Common Marmoset. This is a contribution to the formation of an atlas of non-pathological metal distributions within the whole primate brain.

Methods: Scavenged marmoset brain tissue was collected from previously conducted experiments. After fixation and cryoprotection, the tissue was sectioned in a cryostat into 5 series, at 40um. One of these series was analysed through laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) to quantify the metal levels across the tissue sections. The other series underwent histological staining (myelin, Nissl, cytochrome C oxidase, and calbindin) to allow for identification of the AC subnuclei, as well as other brain structures. After mounting and scanning the stained sections, borders of the AC subnuclei were drawn onto these images and transferred onto the relevant LA-ICP-MS data. Statistical analysis was then performed on the distributions within each of these identified other subnuclei. Due to the limited literature regarding the metal distribution in the AC, our methodology

and results were verified by performing a secondary comparison between iron, manganese copper and zinc distributions in the AC, hippocampus and basal ganglia. These metal distributions have been comparatively more widely reported.

Results: The copper data was not able to be analysed due to possible contamination. Our preliminary findings found no significant difference was detected between the lateral, basolateral and basomedial subnuclei of the AC for the distribution of iron ($H(2, 37)=2.345$, $p=0.31$), manganese ($H(2, 37)=4.521$) or zinc ($H(2, 37) =5.821$, $p=0.05$). Other AC subnuclei were not examined due to difficulties in identification. The secondary analysis detected variation between the AC, hippocampus and basal ganglia for the distribution of iron ($H(2, 67)=48.96$, $p<0.01$), manganese ($H(2, 67)=11.39$, $p<0.01$) and zinc ($H(2, 67)=12.93$, $p<0.01$).

Conclusions: The subnuclei of the basolateral AC appear have uniform iron, manganese and zinc distributions. Whether this is true for the AC as a whole or just this division is unclear. The results of the secondary comparison were consistent with the published literature, suggesting that the methodology and technique used in this project were valid.

JACK TU

Paediatric Acute Non-Traumatic Limp: An evidence-based approach to assessment of the limping child presenting in Emergency Department

A/Prof. Simon Craig; Monash Emergency Research Collaborative, School of Clinical Sciences; Paediatric Emergency Department, Monash Health; Murdoch Children's Research Institute.
Dr. Peter Gowdie; Department of Paediatrics and Department of Rheumatology, Monash Children's Hospital; Department of Paediatrics, Monash University

Jack is a medical student from Monash University. Having completed his fourth year in 2015, he has a taken a year off to undertake a BMedSci(Hons) to understand the role of clinical research and also pursue his interests in paediatrics and emergency medicine.

Supervised by A/Prof. Simon Craig and Dr. Peter Gowdie, he conducted a research project investigating children presenting with acute non-traumatic limp to three Victorian EDs that are a part of the Monash Health network. His experiences from this research year have inspired him to become a clinician scientist in the future.

Jack encourages any student wishing to pursue an interest in clinical research to undertake a BMedSci(Hons) for the valuable learning opportunities it has to offer and may be contacted at jacktu. melb@gmail.com for further information.

Background: Non-traumatic limp is an infrequent paediatric ED presentation. The differential diagnoses range from benign processes such as transient synovitis, to serious pathologies, such as septic arthritis or SUFE. The key 'diagnostic dilemma' centres on safely discriminating benign and serious disorders. Delayed diagnosis can result in long-term complications, whereas over-investigation can result in unnecessary painful procedures.

No single clinical or investigation finding readily distinguishes benign and serious disorders. Clinical decision rules have been developed to better differentiate these groups. There remains a lack of consensus on the optimal evaluation of the limping child given their variable performance. Little is also known about this presentation in the Australian context.

Our study objectives were to:

Describe the clinical presentation, ED workup and management of children with non-traumatic limp in three Victorian hospitals.

Determine differences in clinical presentation, ED workup and management of children with benign and serious disorders.

Method: Two observational cohort studies were conducted.

A retrospective chart review of children presenting with non-traumatic limp to three EDs during 2015 was performed. Data on clinical presentation, management and outcomes was systematically collected on all eligible patients.

From June 1st 2016, a three-month prospective pilot study recruited patients and collected data at time of ED visit via a mandatory form. Follow-up phone calls conducted two to four weeks after their first ED visit determined their final outcome.

Results: *RETROSPECTIVE STUDY*

Of 63,941 ED presentations, 1033 patients were screened and 516 met inclusion criteria. The median (IQR) age of presentation was 5 (2-8) years, with a male predominance (61%).

Blood tests and imaging were performed in 41% and 53% respectively. The most commonly performed tests were FBE, CRP and x-ray. No investigations were performed in 34% of cases.

The most frequent ED diagnoses were transient synovitis (34%) and viral myositis (15%). 82% were discharged home after ED evaluation. Patients presenting to a tertiary centre were less likely to have any investigation performed (OR=0.39, 95% CI:0.26–0.59, p<0.001) and more likely to be managed in the ED (i.e. not admitted or transferred) (OR=3.71, 95% CI:2.34–5.89, p<0.001).

PROSPECTIVE STUDY

57 patients met inclusion criteria. 75% completed follow-up. Of these (n=43), 93% and three were diagnosed with a 'benign' and 'serious' disorder respectively. Clinical presentation and investigation rates were similar to our retrospective cohort.

Improvements were noted in the proportion of patients with recorded data on variables (e.g. range of motion) collected via a mandatory form. Follow-up rates also improved using follow-up phone calls when compared to our retrospective cohort (75% vs. 40%).

Conclusions: Many children with non-traumatic limp undergo ED investigations, but are subsequently discharged with conservative management. Variation in the ED workup and management between tertiary and non-tertiary centres highlights a need for an evidence-based consensus on the optimal evaluation of the limping child.

For future prospective studies looking to identify significant clinical and investigation predictors for serious pathology of non-traumatic limp, the use of mandatory forms and follow-up phone calls are feasible methods to conduct data collection and follow-up.

JOANNA WANG

Neonatal enterococcal infections: epidemiological trends & healthcare risk factors

Dr. Kenneth Tan (Monash University Department of Paediatrics; Monash Newborn, Monash Health)
Dr. Mark Anthony (John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust, UK)
Prof. Paul Heath & Dr. Christina Kortsalioudaki (Institute of Infection and Immunity, St. George's, University of London, UK; neonIN Surveillance Network)
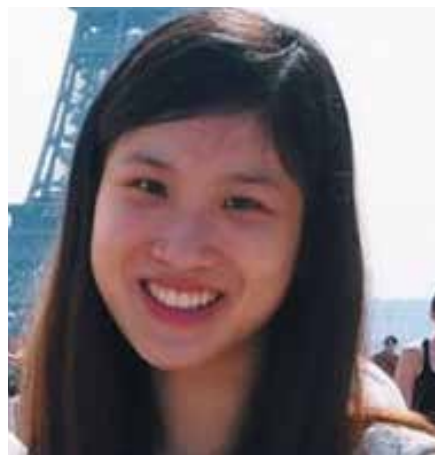
In between the fourth and fifth year of the MBBS, I undertook a BMedSc (Hons) at the John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust, UK. I was incredibly fortunate to work under the fantastic supervision of Dr. Mark Anthony (Oxford University NHS Foundation Trust), Dr. Kenneth Tan (Monash Health), and Prof. Paul Heath & Dr. Christina Kortsalioudaki (St. George's, University of London; neonIN Surveillance Network). The project investigated epidemiological trends, characteristics and healthcare risk factors relating to neonatal enterococcal infections, with the goal of informing prevention efforts. It would not have been possible without the marvellous guidance, support and inspiration of my supervisors and other researchers.

I've loved every moment in Oxford. The year has been an eye-opening experience that has stretched my thinking, enriched my skillset, and strengthened my passion for both medical research and clinical medicine. It's also been amazing living abroad on the other side of the world, making friends from many different countries and learning about different cultures. Would highly recommend the BMedSci to anyone interested.

Background: Enterococcus spp. cause significant morbidity and mortality in neonates worldwide. They are increasingly recognised as ubiquitous pathogens with an expanding antibiotic resistance profile. In critically-ill neonates, enterococcal sepsis is the major concern; this primarily manifests as late-onset sepsis (defined as sepsis with onset after 48 hours of life).

Despite increasing interest in neonatal enterococcal infections, there remain important gaps in knowledge. Specifically, there is a paucity of data regarding recent epidemiological trends and healthcare risk factors for these infections.

Method: To address these key gaps in the literature, we conducted a multi-centre, multi-national retrospective cohort study.

Infection data from 2004-2016 was retrieved from neonIN, while a questionnaire distributed to the neonIN units was used to retrieve six years' worth (2011-2016) of unprecedented data regarding healthcare risk factors specific to neonatal enterococcal infections. Healthcare risk factors were categorised as 'general', 'staffing' or 'policies and clinical practice'.

neonIN, the Neonatal Infection Surveillance Network, is an international platform for national audits and interventional studies. It receives neonatal infection data from 60 neonatal units internationally – from the UK, Greece, Estonia and Australia.

All infection cases reported from 2004 to May 2016 were retrieved, with infection defined as a positive culture from a normally sterile site, including blood and cerebrospinal fluid. Infection data were then synthesised with unit questionnaire results.

Results: The neonIN database indicated that, from 2004-2014, rates of neonatal enterococcal infections did not increase overall. However, there were spikes in the rate of these infections in 2005 and 2012, with a mean of 9.96 and 8.26 cases of enterococcal infections per 1000 admissions during these years respectively.

From 2004-2016, 388 infants experienced 414 enterococcal infections (total of 5,091 infants, 6,055 infections and 6,389 isolates). Enterococcus spp. were the second most common cause of late-onset infection (385/5,377 isolates=7.2%) and the fourth most common cause of all infection (416/6,389 isolates=6.5%). Each week increase in postnatal age and associated necrotising enterocolitis increased the odds of Enterococcus spp. infection by 5% (OR 1.05, 95% CI 1.02-1.07, p<0.001) and 50% (OR 1.50, 95% CI 1.08-2.10, p=0.017) respectively, when compared to other infections.

The healthcare factors questionnaire was completed by twenty-four neonIN units. Twenty-one of these units were Level-3 (British Association of Perinatal Medicine standard), and the mean annual number of live births was around 4500.

Regarding healthcare factors, multivariate analysis found that the number of trainee medical staff was on the cusp of significance (per 1 increase: OR 1.06 95%, CI 1.00-1.12, p=0.050). There were also near-significant associations with number of neonatal admissions (per 100 increase: OR 0.89, 95% CI 0.79-1.00, p=0.059) and infection/infection-control protocols (per 1 increase: OR 1.03, 95% CI 1.00-1.06, p=0.064).

Conclusions: Our study provides novel insights into the epidemiology of and healthcare risk factors for neonatal enterococcal infections. Further, the unique finding of a clear association between enterococcal infection and necrotising enterocolitis could be instrumental in reducing infection rates. Through redirecting infection prevention efforts, we aim to reduce rates of enterococcal and other nosocomial infections alike, thus reducing antimicrobial use and providing newborns with a healthier start to life.

ESHWAR YOGAKANTHI

The Clinical Utility of a Biomarker of Immune Function following Lung Transplantation

Associate Professor Glen Westall, Department of Allergy, Immunology and Respiratory Medicine, Alfred Hospital
Professor Anton Peleg, Department of Infectious Diseases, Alfred Hospital

Having had a long-standing interest in research, I undertook my BMedSci after completing my 4th year of medicine. My honours year was based at the Alfred Hospital, working within the lung transplant and infectious disease departments. Overall, I had a very rewarding year, with the opportunity to work with some amazing clinicians, and come away with a great insight into the world of research.

Background: Lung transplantation is an established treatment for patients with end-stage lung disease. Despite improved short-term outcomes, acute cellular rejection (ACR), chronic lung allograft dysfunction (CLAD) and infection continue to pose barriers to long-term survival. Addressing these is contingent on avoiding both over-immunosuppression (a risk factor for infection) and under-immunosuppression (a risk factor for ACR). At present, there is an unmet need for a biomarker that measures net immunosuppression. Preliminary data suggests the mitogen control, an integral component of the QuantiFERON CMV Assay that assesses T cell reactivity may fulfil this need.

Method: 101 adult lung transplant recipients who had a QuantiFERON CMV assay performed and an 18-month minimum post-transplant period were included in this retrospective cross sectional and longitudinal study. The mitogen response was assessed at 5, 8 and 11 months' post-transplant. Parameters collected for analysis included baseline demographics, immunosuppressant doses, white cell and lymphocyte count, microbiological results, lung function tests, and transbronchial biopsies. Linear mixed effects models were used to compare mean mitogen responses in patients with differing clinical outcomes and to assess associations with time, immunosuppressants and blood parameters.

Results: An increase in mitogen response was seen with time post-transplant, with mean increases of 1.46 IU/mL and 1.75 IU/mL between 5 and 8 (P = 0.0002) and 5 and 11 months respectively (P <0.0001). Univariate analysis of immunosuppression showed inverse relationships for prednisolone (P < 0.001) and tacrolimus (P = 0.028) upon the mitogen response. Of these two agents, prednisolone showed the greater estimated effect upon the mitogen response, and furthermore remained statistically significant in a multivariate model (P < 0.001).

A positive relationship for lymphocyte count with the mitogen response was seen in both a univariate (p = 0.0004), and multivariate model (p = 0.001) incorporating baseline demographics. No associations were seen for white cell count. No differences in mean mitogen response were seen in patients developing acute cellular rejection nor were changes seen in risk of developing CLAD in relation to mitogen response at any of the three time points.

Increased mean mitogen responses were seen in patients developing infection (all sites) (P = 0.04) and CMV replication in the blood or bronchoalveolar lavage (P = 0.003) compared to those unaffected. Differences in the duration of anti-viral prophylaxis prescribed to patients may have affected these results.

Conclusions: Results of this study suggest T cell function, as measured by the mitogen response, increased with time post-transplant, predominantly between 5 & 8 months. Furthermore, the mitogen response was inversely associated with levels of prednisolone dosing, and positively associated with lymphocyte count. The clinical implications of these observations will be most optimally analysed in a future prospective study.

AQILA SAKINA ZHAFIRA

Development of Xeno-Free Conditions for Cultured Epithelial Autografts (CEA)

Shiva Akbarzadeh, Marisa Herson,
Skin Culture Lab, Department of Surgery, Central Clinical School, Monash University, Melbourne, VIC, Australia

I'm a fourth year of medical student from Universitas Indonesia. I had my honours years in Skin Culture Lab, Burns unit, Surgery Department. I focused on developing xeno-free condition for cultured epithelial autograft. My Honours year is very magical, I learned new things, met new people, and achieved so many things. This honours year also help me in deciding what I want to do in the future and what my passion is. For new student, it is important to know what you like before choosing the project, so you won't waste your time in the honours year, Goodluck .

Background: Cultured Epithelial Autografts (CEA) is an in vitro Human Adult Keratinocyte (HAK) culture method that utilize small amount of healthy skin to form epidermal sheets that can be applied onto the injured area. Despite many advantages of CEA, there are several limitations associated. The presence of xeno-derived material is the focus of this study, especially the use of murine fibroblasts or 3T3-J2 as the feeder layer and Bovine Serum (BS) as nutrients, that could be the vectors of zoonosis to human recipients such as agent Bovine Spongioform Antigen or other animal derived antigens. Considerable efforts have been made to find the human derived substitute of feeder cells and serum. This project focus in the use of Primary Human Dermal Adult Fibroblasts (PHADF) and Human Serum (HS) as the alternatives.

Method: Bovine serum is routinely used in PHADF cell isolation and expansion. In order to establish a xeno-free PHADF isolation protocol, human serum (0%, 2%, and 5% HS) was tested against the control (5% BS) during tissue digestion. Cell recovery and cell viability from three different batches of skin samples, in three different conditions (0%, 2%, and 5% HS) and a control (5% BS), were compared. After establishing the isolation protocol, three batches were used to determine the best HS concentration for PHADF expansion. This was done by comparing the proliferation rates of PHADF in four different HS concentrations (5%, 7.5%, 10% and 12.5%) to the control, 10% BS. The proliferation rates were assessed using two methods: for short term – MTT Assay and for long term – Cell growth and (passaging) longevity. As feeder cells, PHADF should be mitotically inactive. To determine the suitable irradiation dosage, three batches of PHADF were treated with three different irradiation dosages (60 Gy, 80 Gy and 150 Gy) and the cellular post irradiation proliferation response was measured. Optimal PHADF seeding density as HAK feeder layers was tested at 8,000, 14,333, 21,666, 28,000/cm2 in a co-culture assay.

Results: 2% HS can effectively replace 5% bovine serum for PHADF isolation and 12.5% HS is a better alternative to 10% BS for the in vitro expansion of PHADF. PHADF isolated and expanded in HS require higher irradiation dosage (i.e. 80 Gy) than 3T3-J2 murine cells (i.e. 60 Gy). Fewer PHADF (i.e. 14,333 cells/cm2) compared to murine cells (28,000 cells/cm2) are required for an effective feeder layer in co-culture with HAK.

Conclusions: PHADF isolated and expanded in human serum can be an effective alternative to murine fibroblasts as a feeder layer and successful co-cultures with HAK can be sustained with HS supplemented media.

MICHAEL ZHU

Towards Prevention of Acute Kidney Injury after Cardiac Surgery

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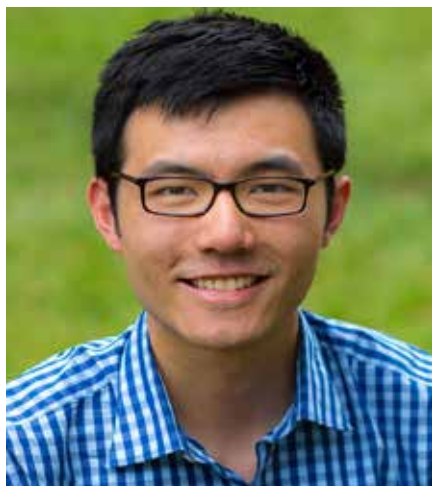
I completed my BMedSc(Hons), with the Department of Cardiothoracic Surgery (Monash Medical Centre) and Department of Physiology (Monash University), under the supervision of three fantastic supervisors. My project was a prospective clinical study looking at a novel method to detect the risk of acute kidney injury in patients undergoing open-heart surgery.

The Honours year allowed me to gain invaluable skills and experience in clinical and translational research, and helped me follow my interest in cardiothoracic surgery. I had the opportunity to undertake both clinical and lab-based research. Throughout the year, I felt very well supported and I am very grateful for the opportunities that I have had. Overall, the BMedSc was an outstanding experience - I learnt so much and I would like to thank everyone who made this year possible.

To anyone who has an interest in research and in surgery, I would highly recommend the BMedSc(Hons) program. If I can help, please feel free to contact me: michael.zhu107@gmail.com.

Background: Acute kidney injury (AKI) complicates recovery from cardiac surgery with cardiopulmonary bypass (CPB) in more than 30% of patients. Thus, early detection and prevention of AKI after CPB remains a topic of major international interest, yet no ideal strategy has been found. Renal medullary hypoxia may be a common pathway in the development of AKI. There are no validated methods to detect medullary hypoxia in patients. However, experimental findings indicate that changes in urinary oxygen tension (PO_2) also reflect changes in renal medullary PO_2. This study aimed to evaluate the relationship between urinary PO_2 and the development of AKI after CPB.

Method: Thirty-five adult patients undergoing cardiac surgery with CPB were prospectively enrolled. Urinary PO_2 was continuously recorded intra-operatively and early post-operatively via a fibre-optic probe advanced to the tip of the urinary catheter. Routine clinical and perfusion parameters, as well as urine flow, were recorded concurrently with urinary PO_2. We also measured serum creatinine and, in a subset of patients, several novel blood and urinary biomarkers of AKI at two intra-operative (during, and after CPB), and five post-operative time-points (0, 3, 6, 24, 48 hours after transfer to the ICU).

Results: Urinary PO_2 fell during surgery, particularly during CPB, and often did not recover to pre-bypass levels after weaning from CPB. The lowest (nadir) value of urinary PO_2 was most frequently observed during the rewarming phase of CPB, or during the post-bypass period (n=25, 71%).

Fourteen patients (40%) developed AKI as defined by an absolute increase in serum creatinine from pre-operative baseline by $\geq$ 27 μmol/L within 48 hours, or $\geq$ 50% within 5 days of surgery. Nadir intra-operative urinary PO_2 was lower in patients who later developed AKI (8.5 ± 5.4 mmHg, mean ± SD) than in those who did not (16.5 ± 12.2 mmHg, p=0.02). Furthermore, for every 60 minutes of surgery, patients who later developed AKI experienced a median of 14.1 minutes where their urinary PO_2 was $\leq$ 15 mmHg compared to just 30 seconds in patients who did not develop AKI (p=0.03). In the ICU, patients with AKI again had a lower nadir urinary PO_2 (6.9 ± 3.4 vs. 12.5 ± 5.2 mmHg, p=0.002), and experienced a median of 5.4 minutes vs. 20 seconds where urinary PO_2 was $\leq$ 15 mmHg for every hour of ICU stay (p=0.001). A lower nadir urinary PO_2 measured during surgery, and in the ICU, was correlated with a greater peak post-operative increase in serum creatinine (Intra-operative, $r2$=0.13, p=0.04; ICU, $r2$=0.23, p=0.005).

Conclusions: Urinary hypoxia, detected both intra- and post-operatively, is associated with the development of AKI after on-pump cardiac surgery. Continuous monitoring of urinary PO_2 thus appears to show promise as a clinically translatable tool to monitor risk of renal injury in a simple and relatively non-invasive manner. Early detection of risk of AKI may in-turn provide a window of opportunity to intervene, and thus avoid development of AKI.

LUIGI ZOLIO

Medical interpreting in an Australian context: an applied linguistic analysis of the interpreted medical consultation.

Prof Paul Komesaroff, Professor of Medicine and Director, Centre for Ethics in Medicine and Society, FMNHS, Monash University)
Dr Riki Lane, Research Fellow, School of Primary Care, FMNHS, Monash University
Dr Helen Tebble, Adjunct Associate Professor, School of Literatures, Languages and Linguistics, Faculty of Arts, Monash University

It's been extraordinarily rewarding to step outside clinical medicine for a year and explore medical research from a humanities perspective. My interest in medical interpreting came about because of my bilingual background, as well as from an ethics and patient safety perspective. In this project I learnt about the principles of qualitative research and also had the opportunity to upskill myself in the discipline applied linguistics. I'm very grateful for the guidance and supervision which Paul, Riki and Helen were able to provide me. As I prepare to go back into my final year of medical school, I genuinely believe that this research project has given me valuable perspectives which will allow me to be a better doctor for my future patients with low English proficiency. If you are interested in a similar project, you can contact me at Luigi.zolio.94@gmail.com.

Background: the CALD population in Australia is rapidly growing and aging. Portuguese-speakers are one of the fastest-growing migrant groups in recent years in Australia. In Australia and internationally, professional interpreters are used in medical settings to ameliorate the language barrier between health professionals and patients with LEP. The role of interpreters in Australia is determined by their professional code of conduct, the AUSIT Code of Ethics. This code of conduct has been reported to place interpreters in difficult ethical situations in medical settings. Telephone interpreting is widely used in medical settings but remains a largely under-researched topic. This project aimed to explore the ways in which professional interpreters influence the doctor-patient communication, within the outpatient specialist medical consultation setting. Key research questions were devised around communicative strategies used by interpreters, interpreter conduct as a reflection of the AUSIT Code of Ethics, ways in which doctors and patients influence the work of the interpreter and how telephone interpreters differ from face-to-face interpreters in enabling doctor-patient communication.

Methodology: outpatient interpreted medical consultations with a Portuguese interpreter were audio-recorded, transcribed and analysed through Discourse Analysis. Participants from those consultations underwent semi-structured follow-up interviews in their preferred language. Doctors utilising telephone interpreting in an outpatient setting were observed and underwent similar semi-structured follow-up interviews. All interviews were transcribed verbatim, translated into English where required and analysed using the inductive qualitative approach of thematic analysis. Once themes were established, analysed excerpts from consultation scripts were grouped with quotes from interviews, and the two data-sets were compared and analysed.

Results: 6 Portuguese-speaking patient participants were invited. 2 declined to participate and 1 participated incompletely. 3 sets of audio-recorded consultations and interviews were obtained after 3 groups of doctors, patients and interpreters participated. 5 additional doctors were invited and interviewed about outpatient consultations using telephone interpreting. 7 main themes were identified: communication strategies; interpersonal dynamics; ethical conduct; stages of the medical consultation; interpreter-specific matters; telephone interpreting; and interference of the researcher.

Conclusion: caution is required by doctors in using rhetorical devices when communicating through interpreters. Healthcare institutions should evaluate their use of telephone interpreting to ensure it is not placing limitations in doctor-patient encounters. Interpreter codes of conduct should reflect the complexity of situations which interpreters face in their professional practice.
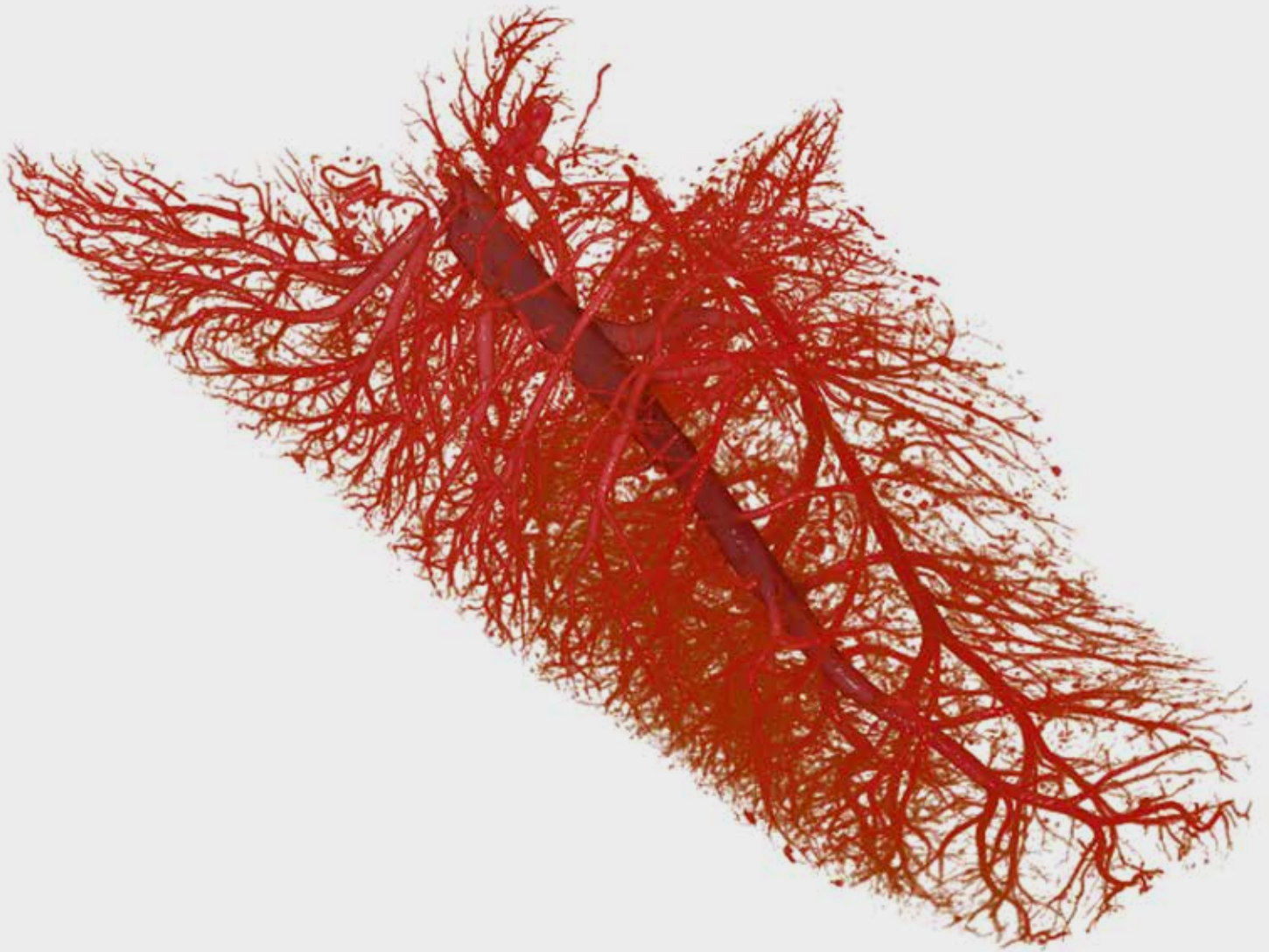
"A Vascular Tree" by Aidan Kashyap

(Image credit: Marcus Kitchen, Genevieve Buckley, Anton Maksimenko.)

A three-dimensional visualisation of the blood vessels within the lung of a newborn lamb, reconstructed from CT images taken at the Australian Synchrotron.

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"Retinal Flower" by Tejas Kumar

Retina from a mouse model of retinopathy of prematurity (ROP).
A 17-day old mouse was exposed to 75% O2 from day 7 to 12 of
life. Collagen IV (green) in blood vessel walls is overproduced when
mice are returned to room air, allowing for easy visualisation and
quantification of pathological neovascularisation.