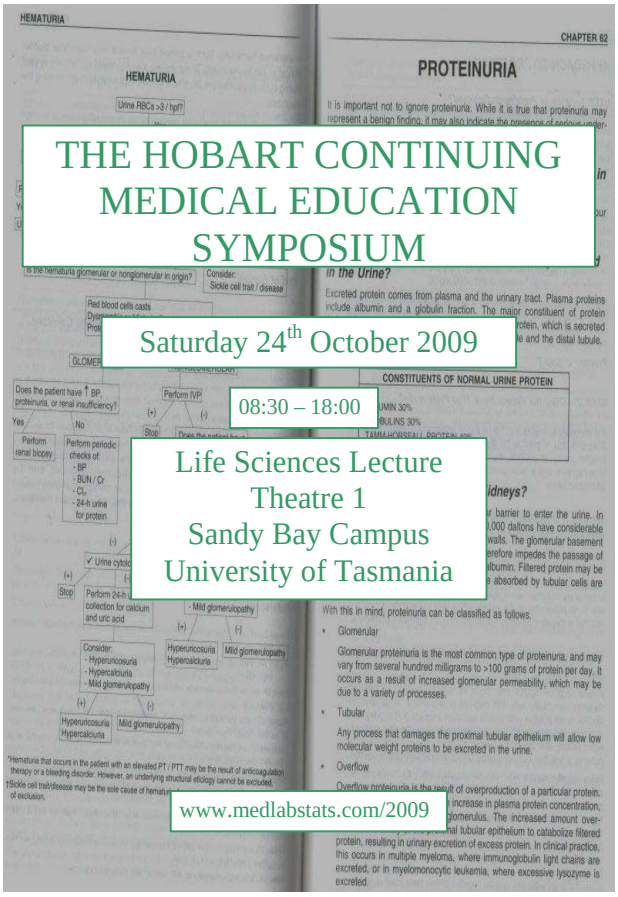
HOBART CME SYMPOSIUM 2009



INTRODUCTION

This year we have departed from our usual practice of giving the symposium a theme title. Instead we have just coined the term ‘continuing medical education’ – something that we are all going to have to participate in throughout our professional careers given that the pace of progress of in medical science shows no signs of slowing down. Keeping up to date as well as keeping up with our workload is a continual challenge and we hope that this year’s symposium is going to prove to be an effective and efficient educational activity for all registrants. Certainly within the space of a day we are going to hear a wealth of new information on a broad spectrum of topics from a talented group of professionals who have been very generous with their time. As always meetings such as these provide us not only new information but also new networking opportunities which in combination will enrich the professional satisfaction and skills of all concerned.

SPEAKER PROFILES

KEYNOTE SPEAKERS

Glenn McConell, joined the Department of Physiology at The University of Melbourne in 2003 after spending 8 years in the Department of Physiology at Monash University. His research interests include the regulation of glucose uptake into skeletal muscle during exercise and the factors contributing to the increase in skeletal muscle mitochondrial volume following exercise training.

His research focuses on examination of the regulation of skeletal muscle glucose uptake during exercise in humans using tracer methodologies, femoral artery-vein measurements as well as skeletal muscle biopsies. We also utilize human and mouse cell culture, isolated contraction muscle preparations and running rat and mouse models. These studies are conducted in collaboration with Professor Bruce Kemp (St Vincent's Institute/CSIRO), Assoc Prof Gordon Lynch and Prof Mark Hargreaves (University of Melbourne), Assoc Prof Stephen Rattigan and Prof Michael Clark (University of Tasmania) and Dr Bronwyn Kingwell (Baker Heart Institute).

Recently he has begun investigation of the factors regulating the increase in muscle mitochondria with exercise training. These studies involve exercising humans, muscle cells (human and rat) and exercising rats and mice. These studies are conducted in collaboration with Assoc Prof David Cameron-Smith (Deakin University), Assoc Prof Mary Wlodek (University of Melbourne) and Dr Lance Macaulay (CSIRO).

These research areas have implications for increasing the understanding of Diabetes

Merlin Thomas. The growing epidemic of diabetes already affects over 1.3 million Australians and twice that number again is at risk of developing diabetes in the next 5–10 years. Despite the clear and present danger of diabetes, the role of high sugars in causing blindness, kidney failure and heart disease is poorly understood. Merlin is working on breaking the links between sugar and the damage it causes.

Merlin's team's research has concentrated on Advanced Glycation End-products (AGEs), formed when sugars bind to protein, making it sticky, sweet and brown. In food like chocolate and caramel, this reaction is appetizing. But when sugar accumulates in diabetes, this same process contributes to blindness, kidney failure and heart disease. Merlin's research has shown that this reaction leads to changes in the shape and function of AGE modified proteins. In the same way that lamb is more tender than mutton, AGE-modified proteins tend to be inelastic. This means that AGEs gradually build up in tissues, making them in turn more stiff; literally 'hardening' the arteries. Where the sugar concentration is high, AGEs accumulate much more quickly. This is one reason why strong sugar control is so important in diabetes. For Merlin and his team, the best way of reducing the impact of diabetes is to break the link between high sugar levels and the damage they cause because even with the best treatment, patients can suffer from kidney failure, amputations and blindness from their diabetes.

AGEs are one of those links. For the millions with diabetes who struggle to control their sugars every day, an understanding of this pathway will provide an important advance to their care.

Another key focus of the Biochemistry of Diabetic Complications lab is the renin angiotensin system (RAS), a pivotal element of vascular function in both health and disease. Many patients with diabetes are already taking drugs that block the RAS, in an attempt to prevent some of the complications of diabetes. However, these agents are only partly effective. Merlin and his team are working to define novel regulators of the RAS, using unique methods to disrupt the RAS, with the aim of making current interventions for diabetes even more effective.

This group is also coordinating the NEFRON study, the largest study of patients with type 2 diabetes across Australia. NEFRON is a collaborative effort of Baker IDI, Kidney Health Australia and Servier Australia, that aims to define the prevalence and severity of complications of diabetes in Australian general practice. Already this study has been able to show that every second individual with type 2 diabetes in Australian currently has chronic kidney disease, with clear potential to influence their health and wellbeing, as well as contribute to premature mortality.

GUEST SPEAKERS

Dr Jerome Staal is a Masonic Research Fellow at the Menzies Research Institute and a member of the The Neurorepair Group. This group has research programs focussed on the major human neurodegenerative diseases (Alzheimer's, Parkinson's and motor neurone disease) as well as traumatic brain/spine injury. These studies seek to determine the principal brain changes and cellular alterations that lead to pathology in these conditions. In addition, they have established cell culture and animal models that replicate these diseases and conditions and are using these to identify new therapeutic approaches. Team members are involved in a range of associated projects such as neuron-glia interactions, the olfactory system, cortical organisation, neural development and the neuronal cytoskeleton.. The title of his thesis was ‘Traumatic brain trauma: The neuronal response to diffuse axonal injury’

Presentation: *Neurological diseases associated with aging, trauma and other disorders are commonly reliant on characterized by their specific pathological features. However, the neuropathological mechanisms and consequences of these features remain unclear. This presentation will report on the various experimental models implemented at the Menzies Research Institute to explore the significant pathways associated with Traumatic brain injury, Alzheimer’s disease, Parkinson’s disease, and Motor Neuron disease.*

Dr Venkat Parameswaran is the Scientist in Charge of the Endocrinology Laboratory, RHH Pathology Services.

Presentation: *Obesity is a leading cause of morbidity and mortality and is associated with a spectrum of diseases like diabetes, cardiovascular disease, cancer, osteoarthritis and breathing disorders. The factors that predispose this condition include genetic, physiological, “obesogenic” lifestyle, stress and environmental factors. Management approaches commonly recommended include dietary programmes, exercise regimes and lifestyle modifications. Newer drug therapies are being trialled for use and also surgical options have been resorted to in those that remain refractory to obesity*

management. Reducing the incidence of obesity will require greater commitment, extensive support and additional health resources.

Dr Udayan Ray is the Director of Clinical Chemistry at the Royal Hobart Hospital, also a Clinical Associate Professor of Pathology at the University of Tasmania, practised in the fields of O&G, General Practice, Industrial Medicine &Toxicology and Pathology in India, Papua New Guinea. He did his MD on 'Toxaemia of Pregnancy' in 1986 under the University of Calcutta. His did Fellowship of the Australasian Association of Clinical Chemistry in 1995 and the Fellowship of the Royal Australasian College of Pathologists in 1996. He was awarded the Fellowship of the National Academy of Clinical Biochemistry of USA in 2005. He completed PhD on 'The Role of Insulin and Nitric Oxide in Acute Ischemic Heart Disease' in 2007 under the University of Calcutta. His major interests are medical education and ischemic heart disease markers.

Presentation:

In Acute Ischaemic Heart Disease (AIHD) or Acute Coronary Syndrome (ACS), atheromatous plaque rupture invites platelets aggregation. ADP, thromboxane A2 released by initially aggregated platelets, adrenaline and collagen (circulation and tissue) accelerate platelets aggregation further which eventually form clot/thrombus in the coronary circulation. Inhibition of thromboxane formation is thus paramount in the prevention and management of ACS. Acetyl salicylic acid or aspirin does this job by inhibiting cyclooxygenase which is a key enzyme in the prostaglandins biosynthesis. In addition, aspirin takes part in the thrombolysis.
On the other hand, insulin, a hypoglycaemic hormone plays a very crucial role in the thrombogenesis (formation of thrombus). Insulin resistance or lack of insulin plays a significant role in this clinical scenario. That is why there is 3 fold increases in acute ischaemic episode in diabetes mellitus.
There is diminution of nitric oxide synthesis in acute ischaemic heart disease
Insulin takes a cardinal part in the nitric oxide synthesis and so does aspirin.
Thus insulin and aspirin should be regarded as synergistic role players in the salvage pathway in the management of Acute Ischaemic Hearty Disease or Acute Coronary Syndrome.

Clinical Assoc. Prof. George Razay, School of Medicine, University of Tasmania and Director of the Memory Disorders Clinic at the Launceston General Hospital. As well as his work as a general physician, Assoc. Prof. Razay has extensive research experience in Australia and the UK in the field of Alzheimer's disease, especially in the role of vascular risk factors. His early research explored menopause and Alzheimer's disease. Findings have been presented at national and international meetings and have been published in international journals. He is the Tasmanian representative on the Clinical Reference Group of the Australian Health Minister's Advisory Council, Care of Older Australians Working Group. He has recently returned from sabbatical leave as a Visiting Professor, Clinical School of Medicine, John Radcliffe Infirmary, University of Oxford, Oxford.

Presentation:

George Razay[1], Anthea Vreugdenhil[1], John Liddell[2]
[1]Launceston General Hospital, University of Tasmania, Launceston, Tasmania, Australia
[2]***Royal Hobart Hospital, University of Tasmania, Hobart, Tasmania, Australia***

Introduction: Idiopathic normal pressure hydrocephalus (INPH) is one of the few potentially treatable forms of dementia, but our understanding of the condition remains poor. The clinical and radiological diagnosis of INPH is notoriously difficult and the reported effectiveness of shunting remains variable.

Aims: This study investigated the clinical outcomes of ventriculo-peritoneal shunting for patients with INPH in a nonrandomised, open labelled, controlled trial.

Methods: Thirty-three consecutive memory clinic patients diagnosed with probable INPH were enrolled in the study over a 4 year period. Nineteen patients underwent shunt surgery. Fourteen patients did not undergo surgery and were included as controls. Clinical outcomes were measured at baseline and 3-4 months follow-up by independent assessors. The primary efficacy measure was the Clinician's Interview Based Impression of Change with Carer Input (CIBIC-plus) rating scale. Secondary efficacy measures included the Mini Mental State Examination for assessment of cognitive functioning and the Timed Up and Go test for assessment of mobility. Urinary disturbance was recorded if patients reported urinary incontinence or frequency.

Results: There were 21 men and 12 women. All were living at home, their mean age was 77.2 years (range 58 to 92 years) and duration of symptoms was 4.6 years (3 months to 14 years). There were no significant differences between the shunted and control groups in age, duration of symptoms, cognition, balance and gait or urinary functioning, or the prevalence of vascular diseases. At 3-4 months follow-up, patients who were shunted, compared with controls: had significantly better global change ratings (median CIBIC-plus rating of 'moderately improved' versus 'moderately worsened' respectively, $P < 0.001$); had increased Mini Mental State Examination scores by 5 points ($P<0.001$); and were 6.3 seconds faster on Timed Up and Go ($P=0.008$).

Conclusion: We conclude that ventriculo-peritoneal shunting is associated with improved clinical outcomes for patients with INPH.

Dr Deborah Speden is a Staff Specialist Rheumatologist at the RHH.

Presentation: *Advances in the Treatment of Inflammatory Arthritis. The role of biologic therapies in changing the management of inflammatory arthritis will be discussed. These target therapies have not only created much needed new treatment options, but have been instrumental in driving the development of clinical assessment strategies. This presentation will provide an overview to the changes in the management of inflammatory arthritis that have occurred over the last 10 years.*

Dr Phil Roberts-Thompson is the Director of Cardiology, Royal Hobart Hospital. Phil is a Tasmanian Medical Graduate who trained in Cardiology at Flinders Medical Centre and at the Royal Adelaide Hospital. He was awarded his PhD by Flinders University. He worked for two years at the University of Iowa before returning to Hobart in 1999 where he has been Director of Cardiology since 2003.

Dr Warwick Bishop is a Consultant Cardiologist with the RHH and Calvary Hospital and a clinical academic of UTas. He qualified with Bachelor of Medical Sciences in 1985, MBBS in 1988 from UTas and a Fellow of the Royal Australian College of Physician in 1997. He is also trained in cardiac imaging techniques.

His main research interests are:

- Research project established in conjunction with the Echocardiography Unit at the Royal Hobart Hospital studying the TEI index and its utility and anthracycline therapy.
- Carbohydrate regulation in cardiac health

Richard Y Yu, MMed (Clin Epi) FRACP is a clinical Nephrologist and General Physician at the Royal Hobart Hospital. His previous Research interests include the epidemiology of Proteinuria in the Australian population as captured by the Ausdiab study. He also has a research interest in the epidemiology and mechanisms of Post Transplant Diabetes.

Presentation: *In the mid 1940's, conventional medical wisdom held that elevated BP did not require treatment; and that higher perfusion pressures (reflected in a natural increase in BP) was needed as we aged. Within 24 years, that paradigm would be turned on its head. Today, health systems throughout the world spend billions annually on anti-hypertensives making it the single biggest pharmacological class marketed globally. How did we get to this point? What is the evidence based for the widespread medical management of an asymptomatic condition? What are the future directions in the epidemiology of hypertension? What are the challenges and barriers to changing health outcomes through the management of hypertension in the 21st century?*

Dr Tom Hartley is the Quality Manager and a senior Clinical Biochemist at the RHH Pathology Services and also a Senior Research Fellow in the School of Human Life Sciences, UTas. He has a longstanding interests in instrumental methods of analysis, quality control, laboratory testing relevant to Nutritional Biochemistry and the statistical analysis of clinical laboratory data.

Presentation: *As part of the Summing Up he will highlight the advantages of carefully and prospectively recording your observations so that they are amenable to formal statistical analysis later on. He will focus on the power of simple non-parametric statistics to provide useful analysis of the typically small datasets that are collected during one's clinical practice.*

FULL ABSTRACTS OF THE CLINICAL SCHOOL PRESENTATIONS

Siddarth Trivedi, Clinical School, University of Tasmania.

Clinical Evaluation of a New Technique to Monitor Skin Temperature at the Return Electrode During Radiofrequency Ablation

Presentation: *Return electrode burns occur occasionally in cardiac radiofrequency ablation, and more frequently in tumour radiofrequency ablation. A return electrode incorporating a thermochromic liquid crystal (TLC) layer, which changes colour with temperature, has been shown in sheep studies to accurately indicate underlying skin temperature. This study aimed to validate the accuracy of TLC-coated return electrodes in indicating skin temperature in the clinical setting of cardiac radiofrequency ablation.*

Methods and Results: *The top layer of a standard return electrode was replaced with TLC. Fluoro-optic thermometer (FOT) probes were laid on the skin side of the return electrode, which was then placed on the left lateral mid-thigh of 18 patients (mean age = 61 ± 12 years, 12 males) undergoing cardiac radiofrequency ablation. Return electrode photographs were taken when FOT temperature exceeded 35 ºC. TLC colour changes, observed in 11 patients, were converted to temperature and compared with FOT temperature. TLC temperature correlated well with FOT temperature (Pearson's coefficient = 0.97 ± 0.03). Bland-Altman analysis showed good agreement (mean temperature difference = -0.04 ± 0.08 ºC, upper limit of agreement = 0.11 ± 0.005 ºC, lower limit of agreement = -0.19 ± 0.005 ºC). The maximum FOT temperature recorded was 39.6 °C. There was no thermal injury at the return electrode site on any patients, when assessed immediately after and the day following the procedure.*

Conclusion: *TLC-coated return electrodes accurately indicate underlying skin temperature in cardiac radiofrequency ablation, and may help prevent burns. This technology might be essential in tumour radiofrequency ablation.*

David Russell, Clinical School, University of Tasmania.

Venting Your Spleen

Presentation: *Splenic rupture in Waldenstrom's Macroglobulinaemia (WM) is a previously unreported phenomenon. We report a case of WM complicated by spontaneous splenic rupture.*

Case Presentation: *A 49 year old Spanish woman presented after being referred by her general practitioner, with a three week history of malaise, night sweats, 6kg of weight loss, intermittent nausea and vomiting, progressive upper abdominal pain, and easy bruising. The blood film revealed a leukocytosis of predominantly small atypical lymphocytes and plasmacytoid cells. Flow cytometry confirmed this to be a Clonal B-cello population. Serum electrophoresis demonstrated markedly elevated IgM protein and immunofixation highlighted a monoclonal IgM kappa band, consistent with a diagnosis of WM. On the fourth day post admission the patient had a rapid clinical deterioration; she was found profoundly hypotensive and complaining of generalised abdominal pain. An ensuing CT scan exposed an extensive haemoperitoneum with active bleeding from a ruptured spleen. An emergency splenectomy was performed with subsequent histology demonstrating widespread splenic parachymal infiltration consistent with that of WM.*

Conclusion: *Spontaneous splenic rupture is a complication of rapid disease progression, and therefore is not an expected complication of low-grade lymphoplasmacytic lymphomas (LPL's) such as WM. This case highlights that despite the typical disease course of low-grade haematological malignancies, signs and symptoms of imminent splenic rupture should be considered when formulating a clinical assessment.*

Robert Anderson, Clinical School, University of Tasmania.

The Effect of Cyanide on Neutrophil Function in Cystic Fibrosis

Objective: *To investigate the effect o cyanide on neutrophils function in Cystic Fibrosis (CF).*
Background: The u7nderlyinig genetic defect in CF leads to failure of airway mucous clearance, creating anidus for bacterial infection, particularly with Pseudomonas aeruginosa. With an extensive virulence profile and biofilm forming ability, P. aeruginosa is persistent and most CF patients succumb to chronic infection with this bacterium. P. aeruginosa virulence factors can cause functional defects and modulate the activation state of CF polymorphonuclear leukocytes (PMNLs). Cyanide is a well known toxin produced by environmental P. aeruginosa isolates and is known to impair components of PMNL function. However, the entire cyanogenesis story in CF is not clear. Whether cyanide reduces the immunological clearance of P. aeruginosa by impairing CF peripheral PMNL function was the focus of this study.

Hypotheses and methods: *This study hypothesised that cyanide impairs PMNL fu7nction in CF and contributes to the failure of the host immune response to eradicate this organism. The first objective was to confirm earlier findings from the CF Reseqarch Group at UTAS with respect to increased cyanide in sputum samples from patients chronically infected with P. aeruginosa and to determine whether systemic cyanide toxicity may be a contributory factor in chronic ill health in this disease. The second objective assessed the effect of cyanide on peripheral blood PMNL function ex vivo to determine if cyanide is an important factor employed by P. aeruginosa to avoid the host immune responde in the CF lung. Sputum and peripheral blood samples were collected from healthy controls, stable, acute, post-acute CF patients and protocols were developed to isolate PMNLs from whole sputum and peripheral blood mediums. Established assays assessed components of peripheral PMNL function including chemotaxis, phagocytosis, oxidative metabolism and cell viability.*

Results: *Elevated cyanide levels in whole sputum were confirmed from P. aeruginosa-infected CF patients during both stable and acute phase of disease. These data also demonstrated for the first time that cyanide can be detected in peripheral blood CF samples during times of acute respiratory exacerbation. Covering the range of cyanide concentrations previously detected in CF sputum, cyanide did not affect PMNL migratory potential but did significantly impair P. aeruginosa phagocytosis and enhance the oxidative burst in PMNLs.*

Conclusion: *Cyanogenesis is an important virulence mechanism in P. aeruginosa's pathogenicity and has implications in terms of exacerbating lung damage, promoting disease progression and reducing the effectiveness of the host response.*

Significance and impact of study: *The findings from this study suggest an important disease modifying role for cyanide produced by P. aeruginosa in CF that warrants further investigation and development of targeted therapies to reduce potential toxicity.*

Michael Thompson, Clinical School, University of Tasmania.

Lipids and the Kidney

Background : *The prevalence of chronic kidney disease (CKD) is increasing in Australia and worldwide. Prevalence of cardiovascular disease (CVD) in CKD is grossly increased. Risk of CVD rises proportionally to the degree of kidney impairment and is dramatically reduced following restoration of kidney function by kidney transplantation, indicating a high degree of reversibility to CVD risk. Dyslipidemia frequently occurs in CKD. Dyslipidemia is a well known modifiable risk factor for CVD and may be the single largest contributor to CVD in CKD. Whether dyslipidemia is antecedent to, or a result of, kidney impairment is uncertain.*

Hypotheses and methods: *We hypothesised that restoration of kidney function by kidney transplantation improved subject lipoprotein profile, which may contribute to the reduction in CVD risk associated with kidney transplantation.*

We conducted a retrospective before-after cohort analysis of sixty patients cared for at the Royal Hobart Hospital who received a transplanted kidney in the last ten years. Our primary, secondary and tertiary outcome measures were high density lipoprotein (HDL), total cholesterol/HDL ratio and triglyceride concentration.

Results: *HDL was inversely associated with kidney function before and after kidney transplantation. This relationship was apparent even in the earliest stages of kidney impairment. Triglycerides, low density lipoprotein (LDL) and total cholesterol were positively correlated with kidney function following, but not prior to kidney transplantation. Kidney transplantation resulted in a significant increase in HDL and reduction in triglycerides. Reductions in LDL and total cholesterol were not significant. The change in HDL concentration following kidney transplantation occurred in a temporal period that suggested the restoration of kidney function itself may be an important determinant of HDL concentration. Total cholesterol/HDL ratio was correlated with kidney function prior to and following kidney transplantation, reflecting the relationship between kidney function and HDL and triglyceride concentrations. Total cholesterol/HDL ratio decreased significantly following kidney transplantation, suggesting a reduction in atherogenicity of the plasma lipoprotein profile.*

Conclusion: *In conclusion kidney impairment was associated with proatherogenic changes in plasma lipoprotein profile, particularly triglycerides and HDL, which were significantly ameliorated following restoration of kidney function by kidney transplantation. The relationship between kidney function and plasma lipoproteins may contribute to the increase in CVD risk in patients with CKD and its' subsequent reduction following kidney transplantation.*

Convenors

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