



ANZSN

Australian and New Zealand Society of Nephrology

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1. **PRESIDENT'S REPORT**

Paul Snelling

Welcome to the final news letter for 2005. The year has been one of steady progress on a number of fronts. Firstly, the new item number for supervision of home haemodialysis is now available from the 5th November. This would allow physicians to charge a monthly fee, rebatable from Medicare, for supervision of home haemodialysis and peritoneal dialysis. Whilst the rebate is not large (\$128/mth) it is an acknowledgement of the non face-to-face work that is required maintaining dialysis patients at home. Additionally, it aids to some degree in increasing remuneration to all members. Remuneration has been highlighted as one of the factors affecting the attractiveness of nephrology as a specialty. They are all aware of the need to attract more physicians to nephrology training and this is the focus of our workforce task group. This group met earlier in the year and has devised a four part strategy to address the problem. One part of this will be the commissioning of a formal workforce survey and subsequent lobbying of government. We hope that this will occur next year.

The financial support of younger members entering research has been an ongoing focus of the society. The major funding source over the last decade or more has been the Jacquot Fellowships. In association with the RACP we have recently renegotiated the funding of these fellowships and have also made changes to the structure and duration of the fellowships. The Research Entry Scholarships will remain tied to the NHMRC stipend but eligibility will be increased to include those doing part time PhDs. The Jacquot Fellowships will be increased to \$90,000 for those undertaken in Australia and New Zealand and \$100,000 for those overseas. The duration will be longer, between 2-5 years depending on appropriate activity. Finally we have proposed that the Research Establishment Awards be broadened to include those who have performed their post doctoral studies in Australia and New Zealand as well as and that the award be guaranteed for 2 years conditional on evidence of ongoing activity. These proposals will be confirmed at the meeting of the RACP Research and Education Committee in December of this year.

The society in conjunction KHA continues to be active in attempting to increase the profile and understanding of chronic kidney disease at governmental, professional and community levels. As outlined by Tim Matthew's KHA report the Chronic Kidney Disease Strategy is in draft form and all members should take time to peruse the document. In there you will have also noted the routine reporting of eGFR by many laboratories. This will undoubtedly increase the awareness of chronic kidney disease we will undoubtedly have a better idea of its affect upon our everyday referrals and practice over the next year.

Finally I would like to thank the organisers of the recent Annual Scientific meeting in Wellington for an enjoyable and scientifically stimulating meeting. Undoubtedly the highlight, as planned by Grant and his crew, was the retention of the Bledisloe Cup in emphatic fashion by the All Blacks at Eden Park. I expect Dr Langham and her Melbourne team to ensure a similar scenario for the Melbourne meeting next year.

My best wishes to all for a merry Christmas and a happy New Year.

2. **SAC & TRAINEE ISSUES**
Paul Snelling

The SAC meet last week for its annual face-to-face meeting. There are a couple of points of note. Firstly to all trainees I would remind you that should you present your projects at one of the local TSANZ or ANZSN meetings they will be accepted as projects. You do however need to provide copies of the to the SAC so we can accredit you. Other points of note for all members are that from next year supervisors of Advanced Trainees must be accredited by the RACP by having completed a Supervisors Course. If you are not accredited yet these courses will still be available next year. If you still wish to have trainees in your unit and they are not accredited you will need to find an accredited supervisor to co-supervise with. So, from next year ALL unit supervising trainees in the country will be reaccredited by official site visits. This brings the SAC and Nephrology into line with most other SAC. These accreditation visits should not be seen as anything else but a way to ensure that trainees are given the best possible training. Timetables for visits will be drawn up and circulated to appropriate units early next year.

3. **PHARMACEUTICAL'S REPORT**
Ashley Irish

The society has actively lobbied the PBAC and TGA regarding several issues relating to the process of listing Sevelamer and Cincacalcet. Both these agents have TGA approval and are being evaluated for listing on the PBS. We have adopted a proactive system of writing to the PBAC expressing our clinical opinion as to the utility and desirability of these agents in order to facilitate their acceptance, and have attempted to gain invitations to PBAC meetings to assist with their deliberations. In addition we have sought clarification for the use of the S100 listed agents erythropoietin and darbepoietin from the Highly Specialised Drugs Working Party. Clarification of the ability of non-Nephrologists to prescribe these agents under the supervision on Nephrologists for regional and remote patients has been acknowledged by the HIC. Practitioners should note that for GPs or other physicians to supply these agents the first private prescription should be via the Nephrologist using a private hospital provider number (i.e a private hospital pharmacy provider number). Following this the designated practitioner can continue to prescribe but will need access to the private hospital pharmacy provider number. Unfortunately the HIC rejected our request for S85 listing for these agents (similar to immunosuppressants) due to their concern over inappropriate use and "leakage" of product.

4. NEWS FROM KIDNEY HEALTH AUSTRALIA **Timothy Mathew**

Chronic Kidney Disease Strategy

The CKD strategy is nearing completion. All the working groups have met and the final document is going to the CKD Steering Committee at the end of October. It will then be submitted to a public consultation round with a view to finalization in late January. The strategy process is designed to identify issues and problems in the spectrum of kidney disease from beginning to end and to identify opportunities where improvements in health service delivery may be made. The second stage of the strategy will look at implementation of recommendations arising from the first part. Thank you to all members of the working groups and others who have had significant input into the process – a first for Australia in the area of kidney disease and one that is basically designed to promote community and Government awareness and involvement in CKD.

Bootle Award

The second major Bootle Award (\$1 million dollars over 5 years) was announced on September 29 2005 and was awarded to Associate Professor Merlin Thomas from the Baker Heart Research Institute.

The competition for this award was intense with eleven high quality applications reduced to a shortlist of four. Merlin Thomas's area of interest is diabetic nephropathy and centres on the role of AGEs in linking high sugar levels to kidney damage. This is the final major Bootle Award – in addition to this new project, Bootle is currently supporting the AKTN, AusDiab followup study and the Renal Regeneration Project at Monash and Queensland Universities.

eGFR Reporting

Automatic reporting of eGFR is rolling out through Australia at the present time. The Australian Government gave Kidney Health Australia a grant to facilitate the education of general practitioners about eGFR. The KCAT Committee through a special group, working collaboratively with biochemists and pathologists produced a series of action plans and messages around this topic, which were then circulated to all practitioners (both general and specialist) in Australia. The forward impact of automatic reporting of eGFR is not yet clear, but the aim of improving early detection and recognition of CKD, and facilitating its management at primary care is the target.

KCAT

The KCAT GP education program continues with a workshop being held about once a week through 2005. The three modules (Mavis - early detection, Colin – diabetes, and Henry - hypertension) are currently about equally popular and a new module has been developed on the measurement of kidney function (eGFR). In addition, KCAT has gone to online learning with the first parts of the messages from Mavis and eGFR, the subject of a four-part module. This is the first online learning program with kidney disease content ever in Australia. We chose PrimeMeD who have proved most efficient in getting the first module up and running. For those interested the website is www.kidney.primed.com.au

The workshops aimed at Practice Nurses have been gathering momentum, with excellent feedback coming from workshops held in Sydney and Perth and a new one scheduled for Melbourne in November. KCAT is evolving to be the GP education arm of nephrology - we are in the process of establishing means of evaluating the impact (if any) that it has had on GP practice.

Medical Research

The Medical and Scientific Advisory Committee of Kidney Health Australia will be allocating about \$500,000 to medical research at its meeting in November - we have received

24 applications for Biomedical Scholarships, 6 Summer Vacation Scholarships, and 28 applications for Seeding Grant support.

Government Submission

For the first time Kidney Health Australia has put together a submission to Government for funds to support work in the kidney area. The application focuses on four areas, GP education, implementation of our CKD strategy, a drink water campaign and consumer research.

5. 2006 ANNUAL SCIENTIFIC MEETING Robyn Langham

The 42nd Annual Scientific Meeting of the Society will be held at the Melbourne Exhibition and Convention Centre, a couple of weeks earlier than normal, with the Postgraduate Meeting on August 14th-15th, and the ASM August 16th – 18th. Next year's meeting is a once in a decade co-joint meeting with the RSA, including two concurrent sessions and a joint social program. Expect an announcement soon when the website will be activated.

With SPEC, we have enticed three excellent international speakers to attend the Meeting, namely Matthias Kretzler from Ann Arbour, Jan Bargman from Toronto, and Julian Savulescu, the Oehiro Professor of Ethics from Oxford University. This is in addition to the other regular components of the program, which is rumoured to include a CPC where David Power exercises (?exorcises) his revenge on Rob Walker. Everyone else can take a number.

Needless to say, the Local Organising Committee is hoping everyone can come to Melbourne for this exciting meeting. Dress standards for the dinner will require a degree of careful examination by some members of the Society, but for those completely bereft of fashion sense (and I don't need to name names, you know who you are) there is always Friday night footy at the Phone Dome.

6. DNT WORKSHOP 2007 Helen Pilmore

The 2007 DNT meeting will be held in Queenstown, New Zealand from 4 - 7 March. The DNT Subcommittee are organising an educational, stimulating and entertaining programme while you will also have the opportunity to enjoy the fabulous sights of Queenstown and sample some of New Zealand's food and wine. Invitations will be sent in the third quarter of 2006. Looking forward to seeing you there.

7. BOOK REVIEWS

(a) Pocket Companion to Brenner & Rector's The Kidney (Seventh Edition)

By Michael R. Clarkson and Barry M. Brenner

Published 2005

ISBN: 0721605591

RRP: \$82.50 (Inc GST)

Elsevier Saunders

The pocket companion to the 7th edition of the iconic Brenner & Rector nephrology textbook, 'The Kidney', is a masterfully condensed and distinctly clinical version of the parent publication. The eminent authors, Clarkson & Brenner have created a practical ready-

reference on a comprehensive list of topics in renal medicine including dialysis and transplantation. It is presented in a 10 x 17.5 cm soft cover book of 818 pages making it 2.8 cm thick and giving it a weight of 515 grams. It fits quite comfortably into a white coat pocket but does not sit well with pockets on other items of clothing. I carried the book in my doctor's bag as part of a three-month road test. The book can be easily navigated by the two and a half page contents section where topics are divided logically into nine chapters. There is also a fifty-three-page fine print index at the end of the book to find a topic of interest but this is rarely needed. Importantly, the turn around time for accessing information was on most occasions faster than my resident medical officer's hand held computer. The first three chapters of the book are devoted to clinical, laboratory and radiological assessment respectively and are excellent for physician trainees. The rest of the book is a powerful aid in the clinic or by the bedside because of the focus on diagnosis, management and prognosis. It contains useful calculations, tables and tools to assist with patient assessment and clinical decisions. However, the book is much more than a collection of facts and algorithms. For each topic or condition discussed, the authors provide excellent clinical perspective on the issues at hand, their relative importance to one another, and the rational approach to diagnosis and management. It is this fact that sets the book apart from other renal textbooks. My only criticism is the soft cardboard cover that has not fared well with the rougher handling of a constantly used pocket handbook. It should have been made of durable soft plastic but the problem could be overcome by plastic covering. I would thoroughly recommend the book to advanced nephrology trainees, physicians practicing in general nephrology and any doctors with an interest in renal medicine. The book is available from Elsevier Australia (Ph 02 9517 8999 or 1800 263 951, website www.elsevier.com.au) or your medical bookshop.
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(b) Primer on Kidney Diseases, 4th edition

By the National Kidney Foundation 2005

Editor Arthur Greenberg

Associate editors: Alfred Cheung, Ronald Falk, Tomas Coffman, Charles Jennette.

This is the 4th edition of this book which was originally published in 1994. It is a large, beautifully set out soft cover book of 608 glossy pages. The chapters are well set out, with excellent titles and headings making the book both easy to skim through or to study in more detail. Each of the 70 plus chapters utilises numerous tables and high quality colour illustrations to convey its message. I was particularly impressed by the series of stylized graphics depicting the ultrastructural changes in various glomerular diseases by Charles Jennette.

As a primer, its' chapters are short and concise, yet provide a current view of all aspects of renal medicine, including; normal structure and function, genetics, pathophysiology, and the diagnosis and management of kidney disorders. I was pleased to find chapters on pregnancy and the kidney, the kidney in ageing, as well as a small chapter on the kidney in infants and children.

Not surprisingly, as it is an NKF publication, there is a noticeable emphasis on, and references to DOQI guidelines and targets, with widespread reference to eGFR, and the staging of chronic kidney disease published 2-3 years ago, particularly in regard to management/treatment. Despite this NKF flavour, over 70 international experts have contributed, providing a global perspective, controversies are discussed, and the existence of other international guidelines and targets is often alluded to.

I was surprised to find myself actually enjoying reading a textbook, and would recommend it not only to students/junior medical staff, but also to trainees and physicians. It certainly

deserves a place in any renal unit library. Perhaps the only drawback is the lack of a digital version or CD of the book as the tables and illustrations are excellent.

Jeffrey Wong

8. REPORTS FROM JACQUOT RECIPIENTS

Dr Toby Coates, awarded the Don and Lorraine Jacquot Research Establishment Award, 2004

Plasmacytoid Dendritic Cells and Transplantation Tolerance

After returning from Pittsburgh in July 2003, I was awarded the Don and Lorraine Jacquot Research Establishment Award for 2004. These funds have been used to further advance my research into the potential therapeutic use of these rare antigen presenting cells for the induction of transplantation tolerance. Plasmacytoid dendritic cells (DC) have the ability to dampen immune responses mediated by expression of inhibitory molecular signals.

The first problem encountering me on my return was a familiar problem, the lack of laboratory space. For the small sum of \$1400 we converted office space, adjacent to the current renal and haematology laboratories into brand new laboratory space for the Dendritic Cell Laboratory in the Basil Hetzel Institute at The Queen Elizabeth Hospital, Woodville, South Australia. This laboratory space now houses a small group of scientists and clinicians focusing on DC biology in transplantation and renal failure.

In the DC Laboratory during the first 12 months, Dr Wai Lim FRACP, working under my supervision for his PhD, has isolated plasmacytoid DC from dialysis and transplant patients identifying defects in effector function of both myeloid plasmacytoid DC subsets. To perform these studies, Dr Lim used immunomagnetic bead technology employing a magnetic cell separator, with funds from the award contributing to the cost of reagent purchase and performance of cell isolations. Dr Shilpa Prasad FRACP joined the DC laboratory in 2004 for her PhD studies and has worked to develop polymerase chain reaction based MHC class II genotyping techniques. These novel studies allow the rapid identification of genetic similarity between individuals, which has added a new level of sophistication to our transplantation experimental models. Mr Austin Milton has worked to identify novel DC subsets in a variety of tissues using laser confocal microscopy. My research assistant Mrs Svjetlana Kireta, in collaboration with Dr Lisa Jeffs FRACP, developed urine based PCR technologies to identify dendritic cells in the urine of rejecting transplant patients.

The award funded preliminary studies that were subsequently supported by an external peer-reviewed grant. The research direction of the laboratory is to understand DC biology in transplantation and then to use this knowledge to improve the care of transplant patients. Novel tolerance strategies, incorporating DC with the aim of elimination of conventional drug therapy will be the focus of the next few years.

Without the Don and Lorraine Jacquot Research Establishment Award virtually none of this would have been achieved. The award was the major source of grant funding for my small laboratory (2 PhD students, 1 full-time research assistant and 1 part-time medical scientist). The award has allowed us to establish new research initiatives, develop collaborations and develop independently. I am extremely grateful for all of the support that the college and the Jacquot family have provided to me over the past 4 years.

Dr Amanda Mather, awarded the Jacquot Research Entry Scholarship 2004

Abnormal Prenylation of Ras GTPases in High Glucose Vascular Pathology

Institution: Renal Research Laboratory, Kolling Institute, Royal North Shore Hospital

Diabetes mellitus is increasing in prevalence across the Western World. Many of the problems caused by diabetes in the long term can be attributed to its effects on blood vessels, causing both microvascular (retinopathy, neuropathy and nephropathy) and macrovascular disease (cardiovascular, cerebrovascular and peripheral vascular disease).

Abnormally high glucose levels in patients with diabetes have been linked to the development of these abnormalities and clinical trials have shown that better control of blood glucose levels is associated with a reduction in the incidence of such complications. However, perfect blood glucose control is difficult to attain and there is subsequently mounting interest in determining the molecular basis by which high glucose causes such abnormalities with the aim to be able to circumvent them and thus more effectively prevent complications from occurring.

It has long been known that abnormalities in cell growth and proliferation occur in the two main cell types found in blood vessels, endothelial and vascular smooth muscle cells, when exposed to diabetic conditions. In particular, exposure of human endothelial cells to high glucose leads to a reduction in endothelial cell proliferation and a concomitant increase in apoptosis, while vascular smooth muscle cells under similar exposure undergo a proliferative response.

A group of proteins known as the small GTPase proteins have been known for some time to be involved in the regulation of various growth parameters. These proteins require a process called prenylation for activation. During this first year of my PhD I have been exploring a possible relationship between abnormalities seen in cell growth parameters in diabetic vascular disease and abnormalities in the process of prenylation.

To date, the chief finding has been that prenylation is upregulated in endothelial cells that have been exposed to diabetic-like conditions, for two of the main small GTPase proteins, Ras and Rho. I have now begun to explore the different isoforms of these proteins to delineate exact functions in endothelial cells and to expand the studies into vascular smooth muscle cells.

This year has involved an extremely steep learning curve with virtually no laboratory experience prior to commencement. However, I have thoroughly enjoyed working in this environment and appreciate greatly the assistance both from everyone in the lab and financially from the Jacquot Foundation.

Dr Usha Panchapakesan, awarded the Jacquot Research Entry Scholarship, 2003

The role of peroxisome proliferator activated receptor γ (PPAR γ) in progressive diabetic nephropathy.

Institution: The Kolling Institute of Medical Research, Royal North Shore Hospital, NSW.

I commenced a PhD in February 2003 after 2 years of core clinical training in Nephrology. I was fortunate enough to receive The Jacquot Research Entry Scholarship for 2003 and am grateful for this. In brief, I am studying the role of peroxisome proliferator-activated receptor gamma in progressive diabetic nephropathy.

The specific aims of the project are to determine:

1. The expression and activity of PPAR γ under conditions known to be associated with diabetes mellitus.
2. The role of PPAR γ in mediating a downstream inflammatory response (nuclear transcription factors and inflammatory proteins).
3. The role of PPAR γ in mediating downstream signalling pathways
4. The role of PPAR γ in mediating the dysregulated matrix production.
5. The novel gene expressed in the above conditions that are dependent on intact PPAR γ expression.

Diabetes mellitus, or impaired glucose tolerance affects up to 25% of the older population in Australia. Up to 30% of patients with diabetes mellitus are expected to suffer end stage renal disease, representing a significant burden on the health system. Tubulointerstitial fibrosis is a critical component of renal injury in diabetic nephropathy leading ultimately loss of renal function. Thus therapeutic strategies to delay or arrest the onset of and progression of tubulointerstitial fibrosis are essential to the treatment of patients with diabetes mellitus.

Peroxisome proliferator-activated receptors (PPARs) are members of the nuclear receptor superfamily of ligand-activated transcription factors that have central roles in inflammatory and metabolic functions. One of the three isoforms, PPAR γ , is a target of the thiazolidinedione family of compounds that are now commonly used in the improvement of glucose utilisation in diabetes mellitus. However, little is known about PPAR γ in the kidney and what effect long-term PPAR γ activation has on kidney function or the progression of diabetic nephropathy. Studies in animal models and in vitro cell culture have been promising, showing that PPAR gamma agonists reduce scarring and proteinuria. Using immortalized human proximal tubular cell line (HK2 cells), I have shown that high glucose exposure for 24 hours upregulates PPAR γ . Application of PPAR γ agonists further induces its expression. Induction of PPAR γ led to anti-inflammatory effects (reduction of activator protein -1 and monocyte chemoattractant protein 1). Intense upregulation of PPAR gamma led to an antiproliferative effect as evidenced by a reduction in viability and DNA synthesis. Flow cytometry studies were in keeping with this observation and demonstrated G1 phase arrest of the cell cycle and apoptosis.

There has been significant progress with the help of Professor Carol Pollock and Dr Xin Ming Chen culminating in an oral presentation in the 39th Annual Scientific Meeting of the ANZSN held in Perth in September 2003. A manuscript summarizing the progress of this project in 2003 has been submitted to The American Journal of Physiology – Renal, and a revised version has been requested with view to acceptance.

My current work involves the development of a stable cell line with the PPAR γ gene silenced. The aim of this is to serve as a dominant negative strategy to delineate whether the above findings are PPAR γ dependent or independent.

If we can find out some of the factors that regulate the cell responses to glucose conditions we will be in a far better position to ultimately alter the course of progressive kidney impairment in diabetic renal disease.

I am very grateful to the Jacquot Family for providing me with this opportunity.

Dr Merlin C Thomas, awarded the Don and Lorraine Jacquot Fellowship for 2004

The role of advanced glycation end products in the development and progression of diabetic nephropathy

The Don and Lorraine Jacquot Fellowship is the most important postdoctoral award from the College of Physicians. For many of my colleagues this award represents far more, being the

stepping stone to independent research and academic nephrology. In 2004, I was lucky enough to be chosen as its recipient. I used this generous award to travel to South Carolina, USA and work in the laboratory of John Baynes and Suzanne Thorpe, world leaders in the field of AGE biochemistry.

Advanced glycation end products (AGEs) are mediators of receptor-dependent pathogenic pathways that promote tissue injury in diabetes, progressive nephropathy and ageing. AGEs are formed via the non-enzymatic Maillard or 'browning' reaction between reducing sugars and amine residues on proteins, lipids or nucleic acids. This reaction is both concentration and time dependent, the meaning that AGE-modification increases with increasing levels of hyperglycemia and predominantly affects long-lived molecules such as matrix proteins. In addition, chronological age and AGEs have more than just a verbal similarity. Over a person's lifespan the amount and variety of AGE-modified tissue progressively increases, due in part to the time-dependence of the Maillard reaction but also reduced molecular turnover associated with chronological ageing and the resistance of AGE-modified proteins to proteolytic digestion.

Although a variety of AGEs may be chemically distinguished, and many have been shown to have pathogenic activities *in vitro*, the molecular identity of the AGEs that contribute predominantly to the development of diabetic vascular complications has not been clearly determined. In addition, the factors that determine the levels and type of AGE-modification remain to be fully established. The pattern of AGE-products formed in any reaction is critically dependent on the precise conditions in which the reaction is occurring. For example, it may be influenced not just by the reaction on a single amine and sugar, but also by interactions between Amadori products, protein and sugar fragmentation pools. Other factors present during the reaction may also influence the type and quantity of AGEs formed. For instance, time, temperature, pH, the presence of metal ions, oxygen concentration and endogenous Maillard inhibitors (such as spermine) may all result in changes to the observed product ratios. The resulting complex chemistry elaborates a hugely diverse range of heterocycles, polymers and advanced Maillard products.

Some of the best-characterised AGEs, such as pentosidine, MOLD (methylglyoxal lysine dimer) and GOLD (glyoxal lysine dimer), represent 'cross-links' between and within modified proteins. These cross-links can result in important changes to protein structure and function. For example, the glycation of collagen results in altered packing density and surface charge, and is manifested by increased stiffness and resistance to digestion by metalloproteinases. An increased number of cross-links in diabetic collagen are also reflected in the accumulation of acid-insoluble collagen in diabetic tissue, including the heart and vasculature, leading to cardiac and vascular stiffening in the context of diabetes.

Many of these AGE cross-link moieties have intrinsic fluorescence. This means that vascular fluorescence can be used as a surrogate marker for the presence of these AGE-modifications. For example, tissue fluorescence at various sites has been shown to increase with ageing. With the development of diabetes, there is a marked increase in fluorescence within the blood vessels and at other sites of diabetic vascular disease. My work has previously shown that circulating levels of fluorescence also correlate with vascular complications in patients with type 2 diabetes.

A key focus of my Don and Lorraine Jacquot Fellowship was to identify and characterize the major compounds that contribute to the total AGE fluorescence in the plasma and urine. In studies using plasma from uremic and diabetic patients, I was able to identify 6 major compounds that form the bulk of AGE fluorescence signal. Of these, most of the difference in total fluorescence between patients with and without uremia, and with and without diabetes is attributable to the compound we have named fluorescent AGE-1 (FAGE-1). This small molecule is normally tightly bound to anion binding sites on serum albumin, though it can be displaced following protein denaturation using 0.15M trichloroacetic acid. Consequently, it behaves as a middle molecule toxin and is incompletely cleared by normal dialysis. In addition, it gives serum albumin over 2/3rds of its natural fluorescence.

Other AGEs are neither cross-links nor fluorescent. For example, ϵ N-carboxymethyllysine (CML) is a commonly recognized AGE derived predominantly from the carbonyl modification of lysine. CML also constitutes the main epitope for recognition by most commercially available antibodies used for the detection and quantification of AGEs. Like AGE-fluorescence, tissue CML concentrations are increased in ageing and in diabetes. Non-fluorescent CML-AGE levels are also associated with the presence of vascular complications in patients with diabetes. Other non-fluorescent AGEs may involve modification of arginine residues. In particular, the hydroimidazolone AGEs, derived from glyoxal, methylglyoxal and 3-deoxyglucosone, appear to be quantitatively the most common detectable AGEs in diabetic tissue and in the circulation. Some data suggest that hydroimidazolone may be selectively increased in diabetic tissues over and above other AGEs, including CML, argpyrimidine and pentosidine. Moreover, there is evidence that proteins modified only by hydroimidazolone adducts are able to induce the production of the cytokines interleukin 1b and tumour necrosis factor- α in human monocytes and macrophages. My other work in South Carolina was to develop new ways to measure these imidazole AGEs in patients with diabetes and uremia. Although no preliminary data can be presented at this time, some important steps have been taken towards fulfilling this aim.

AGEs have a wide range of chemical, cellular, and tissue effects implicated in the development and progression of diabetic end-organ pathology. AGE-modification of proteins may produce changes in charge, solubility, and conformation leading to molecular dysfunction as well as disrupting interactions with other proteins. AGEs also interact with specific receptors and binding proteins to influence the renal expression of growth factors and cytokines, implicated in the progression of renal disease. The effects of AGEs appear to be synergistic with other pathogenic pathways in diabetes including oxidative stress, hypertension and activation of the renin-angiotensin system in a vicious cycle associated with progressive renal damage. In my most recent work supported by this award, I have demonstrated that an infusion of AGE-modified albumin significantly up-regulates the activity of the intra-renal RAS, in the absence of hyperglycemia. Changes include activation of vasoconstrictor pathways with increased ACE and AT1 receptor expression and reduced ACE2 and AT2 expression, the antagonistic vasodilatory mediators. In addition, an infusion of angiotensin II also elevates circulating AGEs accompanied by AGE-deposition in the kidney and at other sites of microvascular injury. Moreover, the AGE-inhibitor pyridoxamine is able to inhibit changes associated with angiotensin II including renal hypertrophy emphasizing the synergism between AGEs and the RAS. This potential synergism is also demonstrated by our studies showing that ACE inhibition in combination with inhibitors of AGE formation are more potent than either therapy alone in preventing nephropathy. It is probable that therapies that inhibit the formation of AGE or remove established AGE-modifications will form an important component part of future therapy in patients with diabetes, acting in concert with conventional approaches to prevent renal injury.

The formation of intracellular AGEs from reactive intermediates such as methylglyoxal occurs at a much faster rate than glucose-derived AGEs. Indeed, intracellular AGEs are increased after a few days of hyperglycaemia, well before similar changes can be demonstrated *in vitro* from the incubation of protein and glucose. Unless removed or repaired, the intracellular accumulation of AGE-modified proteins threatens cell viability. Most damaged proteins undergo selective degradation. Proteasomal processing is normally efficient, leading to the release of amino acids and oligo-peptides. However, AGE-modification renders a protein resistant to proteolytic digestion. As a result, incomplete degradation of AGE-modified protein results in the release of low molecular-weight degradation products (LMW-AGEs) incorporating AGE-modifications. Consequently, LMW-AGEs may be used as a quantitative and qualitative marker for the tissue AGE burden. Moreover, as some of the effects of AGEs are mediated via interactions with specific AGE-receptors, AGEs 'trapped' in long-lived tissue have little potential for direct interaction with distant receptors, as these proteins are fixed and insoluble. By comparison, mobile LMW-AGEs are free to interact with AGE-receptors implicated in the development and progression of diabetic complications.

The final component of my Fellowship studies has been to examine the role of LMW-AGEs in the development and progression of diabetic kidney disease. In my studies I have previously found that LMW-AGEs are a good predictor of micro and macrovascular complications in patients with both type 1 and type 2 diabetes. In AGE infusion models, these LMW degradation products also directly mediate injury, as intact AGE albumin is not seen in this model. A variety of LMW-AGEs are observed in sera from patients with diabetes or renal impairment including free pentosidine, *CML*, *CEL* and imidazole-AGEs. However, these known adducts constitute <1% of all free AGEs. My characterisation of FAGE-1 and other novel imidazole AGEs as part of this Fellowship has the potential to enhance understanding in this field. I hope that the definition of pathogenic LMW-AGEs and their pathways of activity will greatly facilitate future clinical studies into diabetic complications.

Finally as part of this Fellowship I was invited to assist in the organisation and running of the 8th International symposium on the Maillard Reaction, at which I was invited to speak on the role of LMW-AGEs in diabetes. Despite the fact the conference was struck by a hurricane on the first night, it was a huge success. I am indebted to the RACP and the Jacquot bequest for providing me this opportunity to interact with the leaders in my field, and discuss my research with luminaries like Samuel Rahbar, the discoverer of HbA1c, Vincent Monnier and Helen Vlassara.

The Don and Lorraine Jacquot Fellowship has been the formative experience of my career, and hopefully the stepping stone to future discoveries. I would sincerely thank the RACP and Jacquot family for their ongoing support of young nephrologists from Australia and New Zealand.

9. TRAVEL GRANT REPORTS

Leigh Haysom

Many thanks to the ANZSN for sponsoring my trip to the World Congress of Nephrology post-congress meeting 2005 in Singapore. This meeting looked at the renal disease issues affecting minority groups and developing nations. My research is finding associations for early renal disease in Australian Aborigines, and I found the talks interesting and alarming. Rapid urbanisation of developing nations paradoxically means an explosion of chronic and end-stage renal disease from type 2 diabetes and cardiovascular disease that will overwhelm the capabilities of these countries. The only way this epidemic can be addressed is as a global responsibility, with an emphasis on prevention by reducing poverty and improving standards of living in a responsible way - ie, capacity and infrastructure building, rather than allowing the worst aspects of modern living to exploit vulnerable populations. These issues need the urgent attention of all governments, policy-makers and nephrologists.

Amanda Mather

I would like to thank the ANZSN for their generous support in awarding me a travel grant to attend the 2005 World Congress of Nephrology held in Singapore. This allowed me to attend my first international conference and provided me with the opportunity of presenting my poster entitled "Abnormal Prenylation of Ras in High Glucose Vascular Pathology".

The plenary speakers at the meeting were world class and included several Nobel prize winners. Their talks covered a wide range of medicine and science and the speakers were inspirational in their dedication to their particular area of interest.

The meeting focused on clinical nephrology more than basic science research but it still provided me with a fantastic opportunity to meet researchers working in a similar field and discuss my own work with them. These discussions have generated ideas and new approaches for future studies.

Singapore provided an outstanding culinary back-drop to the meeting and allowed for several excellent functions, well attended by Australian delegates and Singaporean mud-crabs alike.

Once again, I thank the society for providing the support that enabled me to attend this meeting, which was a fabulous social and professional experience.

10. OTHER MATTERS OF INTEREST

Retirement of John Mahony

John Mahony is retiring from Nephrological practice in early 2006. To mark the enormous contribution he has made to Australian, and indeed international Nephrology, a meeting and dinner will be held in Sydney on February 17th 2006.

For further information contact Professor Carol Pollock (02) 9926 7126 or fax (02) 9436 3719

Kidney Health Australia Blog

Anne Wilson, Chief Executive Officer, Kidney Health Australia

Kidney Health Australia Blog has been created specifically for raising awareness of the issues faced by those with kidney and urinary disease, their families and carers. The Kidney Health Australia Blog provides you and members of the public with the opportunity to share your views, experiences, and concerns about the critical issues relating to kidney disease with members of parliament.

By visiting the Kidney Health Australia website at: www.kidney.org.au you are able to view first hand comments already posted as well as ask questions or correspond with others in similar situation. Please help us by passing this information on to others who you believe may be interested and/or share your views with us

New Global Bone and Mineral Metabolism Guidelines for Chronic Kidney Disease

Brussels, Belgium - Kidney Disease: Improving Global Outcomes (KDIGO, www.kdigo.org), an international organization focused on clinical practice guidelines and related quality improvement activities, has announced plans to develop and implement the first global guideline on bone and mineral metabolism in chronic kidney disease (CKD). The guideline development process will follow a Controversies Conference in Madrid, Spain this September.

KDIGO's co-chairs, Dr. Norbert Lameire of Ghent, Belgium and Dr. Garabed Eknoyan of Houston, Texas stated that the worldwide need for better integration of the latest scientific studies into clinical management of bone disease and CKD requires that a new global guideline be developed. Previous guidelines have been published in the United States and elsewhere, however bone disease is a complex and critical problem for patients and requires the most up to date knowledge to improve patient outcomes. No previous guideline has comprehensively covered the spectrum of tests and treatments now available.

"KDIGO is the organization to do this Controversies Conference and subsequent clinical practice guidelines because its global focus will allow us to build on all previous work, recruit the world's leading experts and maintain a scientifically rigorous independent process to publish and implement recommendations for physicians and patients," said Dr. Eknoyan.

"We have learned from 10 years of experience with the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) guideline process that implementation is vital. Implementation of guidelines throughout the world is a major part of the mission of KDIGO.

As KDOQI continues to improve outcomes in the United States, KDIGO will use guidelines and implementation to improve outcomes on a global basis," he said.

This guideline on bone and mineral metabolism in CKD will be KDIGO's second original global guideline. It follows an effort initiated earlier this year to develop the world's first guidelines on hepatitis C and kidney disease. KDIGO will utilize an independent expert work group, professional methodologists and broad community review and input. The guideline development will take 18 months. This new bone and mineral metabolism guideline will provide the world's nephrology community with up to date information and new recommendations that will replace and update previous guidelines published by KDOQI and others. KDIGO guidelines will be published and supported by implementation tools and materials that will be distributed worldwide.

"We are beginning with a major Controversies Conference which will bring 70 to 90 international experts together to identify key clinical questions for the guideline. It will also help us decide what we know and can do now with it, as well as determine what we need to know," said Dr. Lameire.

"This will lead to a consensus on current practice recommendations and the issues for our evidence based guideline. We have asked Dr. Sharon Moe of Indianapolis, Indiana and Dr. Tilman Drueke of Paris to chair the conference. Taking into account what we learn at the Controversies Conference, KDIGO will appoint a work group this fall to develop the guidelines," he said.

KDIGO is a non-profit Belgian foundation in the public interest with its fiduciary responsibility vested in a forty member international Board of Directors and managed by the National Kidney Foundation, a United States non-profit organization with ten years experience in guideline development and implementation. More information is available at www.kdigo.org.

Medicare Australia Replaces HIC

On 1 October 2005 the Health Insurance Commission (HIC) became Medicare Australia.

Medicare Australia will perform all the functions and continue to deliver all the services that were the responsibility of HIC.

It is important to note that the way Medicare Australia works with health care providers won't change. There will be no changes to claiming, payment or provider registration systems other than to incorporate the new name. Medicare Australia will honour any cheques issued by HIC, and any agreements entered into with HIC will continue to apply. Providers need make no changes to their billing or claiming arrangements, and Medicare Australia will continue to build a strong, open and responsive relationship with Australia's health care providers.

The move to Medicare Australia is part of the Minister for Human Services Joe Hockey's vision for the future of the six agencies that operate under his department. In an address at the National Press Club in April 2005, the Minister said his department would focus on "making people's lives easier through simpler access to government services and benefits". To facilitate this, Medicare Australia will maintain and extend the current strong commitment to online claiming services.

To reach Medicare Australia via the Internet, simply replace "hic" with "medicareaustralia" to give:

Website: www.medicareaustralia.gov.au

E-mail: firstname.surname@medicareaustralia.gov.au

Note that for a period of time, the www.hic.gov.au web address will be automatically redirected to www.medicareaustralia.gov.au. However, if you have any bookmarks or favourites stored in your web browser (e.g. Internet Explorer), you might like to update them to the new web address. If you have any queries, please contact your regular HIC liaison person.

11. POSITIONS VACANT

Visit the ANZSN website www.nephrology.edu.au for more details about the following opportunities:-

- Clinical Epidemiology Training Scholarships in Renal Medicine
 - Consultant Nephrologist, Mildura, Victoria
 - Locum Consultant Nephrologist, Leicester, UK
 - Locum Physician in Wollongong
 - Nephrology Trainee, Royal Brisbane & Women's Hospital Qld
 - One Year Job Swap Opportunity in England
 - PhD opportunity based at Brisbane Hospital
 - PhD Positions in Clinical and Experimental Nephrology, Westmead Millennium Institute
 - PhD Scholarships in Renal Medicine
 - Research Fellows - PhD / MD students, St Vincent's Health, Melbourne
 - Research/Senior Research Fellow (Renal), The George Institute for International Health
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12. MEETINGS

Visit the ANZSN website www.nephrology.edu.au under Clinical & Scientific Meetings for details about forthcoming meetings.

13. JACQUOT RECIPIENTS 2006

Don & Lorraine Jacquot Fellowship
Dr Usha Panchapakesan

Jacquot Research Entry Scholarships
Dr Adam Hedley
Dr Jane Holt
Dr Suetonia Palmer

Jacquot Research Establishment Awards
Dr Alan Cass
Dr Fiona Chow
Dr Hilton Gock
A/Professor Robyn Langham

14. RACP Research and Education Foundation Fellowships and Scholarships for 2006
– closing date 31 May

For further information about the following awards, please contact Mrs Chris Ernst at the College, by email (chris.ernst@racp.edu.au) or phone 61 2 9256 5434.

-NEW R E ROSS TRUST TRAVELLING SCHOLARSHIP IN PAEDIATRICS & CHILD HEALTH

Re-advertised awards:

-J P COGLAN VISITING FELLOWSHIP

-GEOFFREY T EY TRAVELLING FELLOWSHIP FOR ISOLATED RURAL PHYSICIANS (\$5000)

-MURRAY-WILL FELLOWSHIP FOR RURAL PHYSICIANS (\$10,000)

-MAYNARD RENNIE FELLOWSHIP FOR ISOLATED RURAL PHYSICIANS (\$5,000)

-JUVENILE DIABETES RESEARCH FOUNDATION FELLOWSHIP

-RACP-CONROD FELLOWSHIP

-TRASH & TREASURE
