The abstracts are available online, free of charge, under
www.karger.com/doi/10.1159/000076082

NephroAsia 2004

February 9–12, 2004, Singapore

Abstracts

Contents

Speakers' Abstracts	1–111
Delegates' Abstracts	112–240
Medical	Basic Science 112–120
	Clinical Nephrology 121–158
	Dialysis 159–201
	Transplantation 202–218
Nursing	Advanced Practice Stream 219–226
	Nephrology Practice Stream 227–235
Technology	Technology/Bioengineering 236–240

Author Index

KARGER

Basel · Freiburg · Paris · London · New York ·
Bangalore · Bangkok · Singapore · Tokyo · Sydney

1

Focal and Segmental Glomerulosclerosis

D. Adu

Queen Elizabeth Hospital, Birmingham, UK

Focal and segmental glomerulosclerosis (FSGS) may be secondary to a variety of well defined causes. These may be acquired e.g. following reduced renal mass, HIV infection or scarring in patients with other glomerulonephritides. FSGS may also result from mutations in podocyte associated genes; NPHS1 (encoding Nephrin), NPHS2 (encoding Podocin) and ACTN4 (encoding α -actinin 4). The classification of nephrotic syndrome associated idiopathic FSGS encompasses classical, cellular, glomerular tip and collapsing varieties. There is no consensus on whether these variants influence steroid responsiveness or the prognosis for renal function. Overall approximately 30–50% of patients with FSGS and a nephrotic syndrome develop end stage renal failure within 5–10 years. Treatment is hampered by the lack of randomised controlled trials. Treatment with steroids for 6 months induces remission in 30–40% of cases and those patients who respond have a much improved renal survival. In steroid resistant cases two randomised trials have shown that treatment with cyclosporin and low dose prednisolone increases the proportion of patients going into remission as compared with prednisolone alone and also leads to better preservation of renal function. A retrospective study of 5 UK Renal Units showed that patients treated with relatively long term prednisolone were more likely to go into complete or partial remission of the nephritic syndrome (65%) than untreated patients (23%). Further patients who went into remission were significantly less likely to develop end stage renal failure or to die. Our own studies suggest that patients with the Glomerular tip variant of FSGS are more likely to respond to steroids than patients with multiple segmental lesions. There is a clear need for randomised controlled trials of treatment of FSGS.

2

Prognostic Factors for Lupus Nephritis

D. Adu

Queen Elizabeth Hospital, Birmingham, UK

The prognosis for lupus nephritis has improved substantially over the last two decades. Nevertheless at 10 years, 10–20% of patients are in renal failure or dead and many patients will have treatment related side effects such as sustained amenorrhoea. Knowledge about prognostic factors assists physicians in their choice of treatment and provides patients with information on possible outcomes. Patients with proliferative glomerulonephritis (WHO III and IV) tend to have a

worse outcome for renal function when compared to patients with milder lesions although with current treatment the difference in survival is minimized. In most studies the prognostic factors associated with the development of renal failure include renal impairment at diagnosis, an incomplete response to treatment with cyclophosphamide and prednisolone, relapses (especially nephritic flares), anaemia and black race (possibly as a surrogate marker for poor socio-economic status or genetic predisposition to severe disease). Histological correlates for a poor outcome include the chronicity index (although this has been disputed) and the presence of cellular crescents. Our own study showed that the index of chronic damage predicted progression to renal failure better than the WHO Class of glomerulonephritis and suggested that prognosis was determined in large part by histological damage at diagnosis. Survival in WHO Classes III and IV is improved by the addition of cyclophosphamide to steroids although cyclophosphamide increased the risk of infertility.

3

Xenotransplantation

A. JF d'Apice

St. Vincent's Hospital, Melbourne, Australia

The worldwide shortage of human organs/tissues for transplantation and the consequent increasing waiting list for transplants has fueled interest in alternate sources. Adult and fetal stem cells are the favoured novel approach for many types of cellular transplants but they are unlikely to solve the problems faced by patients awaiting solid organ replacement. Xenotransplantation and various mechanical therapies are therefore being explored for kidney, heart and liver replacement. There has been a major resurgence of interest in xenotransplantation in the last 10–15 years following the development of the capacity to generate genetically modified pigs.

Pig-to-human (primate) transplants undergo hyperacute rejection because of the presence of naturally occurring anti-Gal antibodies which react with the Gal- α 1,3-Gal epitope present on pig tissue. This is followed by activation of the complement cascade, endothelial activation and damage and activation of the coagulation cascade with subsequent ischaemic necrosis of the graft. This can be overcome by transgenic expression of human complement regulators (DAF, CD46 and CD59) on the endothelium of the pig graft. Unfortunately grafts protected from HAR by this approach are still rejected by a process called acute vascular rejection (AVR), which appears to be initiated by anti-Gal antibodies and frequently involves intravascular coagulation.

Recently, pigs lacking the Gal- α 1,3-Gal epitope have been generated by in vitro homologous recombination in fibroblasts and cloning by nuclear transfer. These piglets are viable and sufficient numbers for transplant studies should be available towards the end of the first quarter of 2004. Initial studies probably will be performed using Gal

KO (alone) donors and results with these will determine whether additional genetic modifications, such as complement and coagulation regulator transgenes, are also required.

4

Application of Sorbents in ARF

R. Bellomo

Austin Hospital, Melbourne, Australia

The application of sorbents to the treatment of acute renal failure (ARF) is theoretically attractive. It could make it possible for physicians to remove substances that are currently beyond the reach of blood purification therapy, including some protein bound mediators or mediators of a molecular size that makes removal impossible with current dialysis/filtration membranes. However, the use of sorbents by direct hemoperfusion is limited by the problems of bioincompatibility which induces thrombocytopenia, leukocyte activation and, in the case of charcoal, hypocalcemia and hypoglycemia. A possible approach to adsorption without the problems of bioincompatibility resides in the separation plasma from blood and the perfusion of plasma through a sorbent with plasma regeneration. This approach, which can be called coupled plasma filtration adsorption (CPFA) has been tested in vitro and in vivo in animal models of sepsis and found to reduce mortality and remove a variety of potential inflammatory and immunosuppressive substances from blood. In the light of these findings, a pilot study of CPFA was conducted in patients with ARF and sepsis. In these patients, CPFA was found to be safe and effective in inducing a significant improvement in blood pressure and a reduction in vasopressor support with a short-lived period of intervention. These effects were associated with important changes in the property of plasma such that its immunosuppressive effects as seen in all patients with septic shock at the time of treatment were essentially removed. Furthermore, monocyte responsiveness to endotoxin stimulation was restored. Nine out of 10 patients with septic shock survived. These results suggest the need to further study adsorption techniques in ARF and sepsis.

5

Strategies to Improve Peritoneal Membrane Longevity

P. Blake

London Health Sciences Centre,
University of Western Ontario, London, Canada

Peritoneal membrane deterioration is one of the leading causes of technique failure in long-term PD patients. There are a variety of mechanisms that underlie this deterioration, including infection, bioincompatibility of solutions and, perhaps, inflammation related to uremia. With regard to solution composition, toxic effects may be related to the solution's low pH, hyperosmolarity or lactate buffer. The best evidence, however, is that exposure to dialysate glucose and its associated glucose degradation products (GDPs) is the key factor

and that this is mediated to a major degree by vascular endothelial growth factor (VEGF) induced neovascularization of the peritoneal membrane.

Strategies to decrease peritoneal glucose exposure include maximal use of non-glucose based solutions, avoidance of more hypertonic glucose solutions, salt and water restriction, high dose loop diuretics and residual renal function preservation. Strategies to decrease glucose toxicity include sterilization of glucose solutions at lower pH, facilitated by multi-pouch bags and/or bicarbonate buffer. Another membrane preservation strategy is avoidance of peritonitis. Future strategies might include inhibition of VEGF pathways, systemic or local anti-inflammatory strategies and gene therapy.

6

The Unmet Needs in Hemodialysis: Important Variables Influencing the Quality of Dialysis

A. Bosetto

Gambro Renal Products, Medolla, Italy

The formal definition of a quality standard regarding the management of chronic hemodialysis treatment has been the aim of a number of studies and initiatives. Despite the enormous progress achieved so far we are far from a real worldwide consensus on how to set appropriate standards of care and therefore to be able to define objective quality goals. Many aspects are involved such as:

- appropriate prescription: adequacy and dry weight definition;
- treatment outcome versus physiology needs in intra-dialytic, inter-dialytic and long term perspectives;
- vascular access approach is one of underlying problem areas which poses severe conditions to long term quality of care;
- an increased attention to the quality of life of patients;
- the socio-economical variables related to the sustainability of dialysis patient related costs.

Available technologies provide additional tools to make visible and measurable, and then rationalize, a number of facts which were previously just known in qualitative terms. The only chance was to appreciate them a posteriori because of their consequences. With the help of modern techniques it is furthermore possible to intervene selectively optimizing each specific therapy goal: catabolites removal, ions balance, acid-base control, water removal and cardiovascular stability. This applies to therapy prescription, on-line session parameters monitoring, advanced therapy schemes, daily dialysis and automated dialysis management toward clinical targets.

Biofeedback Technologies: Are We on the Right Track?

A. Bosetto

Gambro Renal Products, Medolla, Italy

In the conventional clinical practice the correctness of meeting desiderated targets is left to clinical analysis, judgement and long term patient observation. This may not be optimal in many cases when facing rapid variation of patients' intra-dialysis and inter-dialysis status, for instance during the development of an hypovolemic collapse. Today new methods of process control of dialysis therapy make on line monitoring of short term interrelation of patient and therapy delivering system possible. This is in general obtained by means of sensors, measure techniques and models, which determine before, during and at the end the treatment the effect of the delivered therapy in terms of transport phenomena, energy, compartments water equilibrium and refilling. Sensors have to be reliable and simple to use. They may be placed on the extra-corporeal circulation system (blood tubing set) and inside the dialysis machine (spent fluids) because in general they give the additional value of relevant information without the burden of specific handling or manoeuvres. They make a better use of available windows of observation of circulating blood and patient related plasma chemistry. By integrating information coming from sensors, model prediction and on-line monitoring of dialysis session, a very efficient way to trace, get real time alarms and assess quality of therapy can be formalised and made available. The use of this information to adjust in real time various parameters (ultrafiltration rate, conductivity, temperature, etc), within a feedback concept, translates the usual technical set process into the prescription of the physiological targets, which are more meaningful in clinical practice. In conclusion biofeedback results in an powerful additional toolset to obtain patients well being.

Patient Selection for PD: APD vs CAPD

E.A. Brown

Imperial College London,
Charing Cross Hospital, London, UK

The demands, social and medical, on a patient with renal failure vary during their time on treatment; the dialysis modality therefore also needs to change over time. The initial selection is therefore not going to be the same as one made later during the patient pathway, e.g. when there is no residual renal function, or when a patient may have become more socially dependent. Selection of the correct modality for an individual patient at any time is a two way process – the patient needs to understand the pros and cons of the different dialysis modalities, and the healthcare team need to know about the lifestyle of the patient.

The differences between APD and CAPD can be divided into medical and social. The frequent cycles overnight with long day dwells not only leave a patient (or carer) free during the day but also result in higher clearances (needed in patients who have lost residual

function) and greater ultrafiltration in patients with high membrane permeability. Intra-abdominal pressure is lower if PD is performed with the patient supine; APD is therefore indicated during in patients with recurrent fluid leaks or hernias. Thus many patients starting on CAPD will change to APD during their time on PD.

EAPDOS (European APD Outcome Study) has shown that anuric patients can be maintained successfully on APD. The majority of patients reached the creatinine clearance target of 60 L/wk/1.73 m² and an ultrafiltration target of 750 ml/24 h; ultrafiltration was also independent of membrane permeability status.

PD Access: Current Technology and Optimizing Management

E.A. Brown

Imperial College London,
Charing Cross Hospital, London, UK

Successful PD is dependent on successful access. Various catheter designs and insertion techniques have been developed to try to avoid the principal complications of PD catheters, namely infection, hernias, leaks and catheter non-function.

Varying configurations of PD catheters have been developed with the main differences being at the intra-abdominal end (straight or coiled) and at the extra-abdominal portion (straight, swan-necked). Coatings to the catheter have also been tried to reduce biofilm formation. Results from trials comparing different catheter designs have been conflicting suggesting that minimizing complication rates is more dependent on centre experience than catheter design.

The success of PD catheter insertion is also dependent on center experience. The results of trials comparing the various techniques – surgical laparotomy, percutaneous and laparoscopic will be reviewed. Complication rates and successful implantation rates using traditional surgical techniques often compare poorly with percutaneous insertion. More and more centres are inserting PD catheters laparoscopically, with some suturing the catheter into the pelvis at the time of initial insertion. There is increasing evidence that this may be the optimal method of catheter insertion but this will of course be dependent on local resources. The various techniques of correcting catheter migration will also be reviewed – again, laparoscopic techniques are emerging as the optimal management.

Advances in Delivery of Peritoneal Dialysis

E.A. Brown

Imperial College London,
Charing Cross Hospital, London, UK

Over the last few years there have been considerable clinical advances improving the quality of peritoneal dialysis itself and improving the quality of life of the patient. These improvements have required technical changes in the way PD is delivered.

Examples of changes in PD delivery are:

- Y-system: enables 'flush before fill' thereby reducing incidence of peritonitis.
- Cycler machines: smaller, safer, easier to use – enabling more patients to use APD for social or medical reasons.
- Overnight bag exchange device: 'Quantum' – makes it easier for patients to do an extra exchange overnight.
- Double or triple compartment bags: essential for delivery of bicarbonate fluids and allows more flexibility of prescribing CAPD; also allows glucose fluid to be sterilized at lower pH thereby reducing production of glycated end products.

Various IT developments have also improved monitoring of PD both for the individual patient and for the healthcare team coordinating a PD unit.

There needs to be a balance, however, between our desire for technical advances, many of which can be expensive, and keeping PD simple for the patient and economic for healthcare systems to use.

11

Australian Situation and Future Strategies

R. Bryant

Royal College of Nursing, ACT, Australia

This paper will explore the nursing workforce situation in Australia including the relevant findings of two reviews of nursing reported in 2002. The attractiveness of nursing as a profession will be explored and the supply of nurses graduating from university will be explored. The Government's response to the undersupply and its policy on recruitment of overseas nurses will also be presented. The results of benchmarking surveys of nurses in Australian hospitals will be discussed as a snapshot of where nursing is situated in Australia. Solutions to recruitment and retention of nurses and the implications of these initiatives will be reported upon. The Magnet Recognition Program and the research supporting this program will also be discussed as one long term solution which is known to be effective.

12

Best Practices in Dialyzer Reprocessing

W. Carlson

Minntech Corporation, Minnesota, USA

Dialyzer reprocessing has been widely practiced since the implementation of dialysis as a chronic therapy. Numerous studies have noted the safety and efficacy of the practice and standards have been in place for many years to assure on-going safety.

The success of a reprocessing program is indicated by financial outcomes, as measured by increased reuse averages, and clinical outcomes, as measured by accepted clinical indicators. This presentation examines the best reuse practices as demonstrated by favorable reuse and clinical outcomes. These best practices involve dialyzer rinsing and handling, heparinization and treatment management, post-treatment

dialyzer handling and dialyzer reprocessing and have a major impact on both reuse and clinical outcomes.

13

Recurrent and de novo Renal Disease in Renal Allografts

J. Chapman

Westmead Hospital, NSW, Australia

Recurrent disease is the third most important cause of graft loss over a ten years in the ANZDATA experience with only chronic allograft nephropathy and death with a functioning graft exceeding it in importance. Over a ten year period amongst 1,839 transplants with a primary diagnosis of GN, 82% were biopsy proven and 52 were lost to recurrent GN 8.4% (5.9–12.0%). The majority of graft failures were caused by MCGN, FSGS and IgA nephropathy with recurrence rates of 14.4, 12.7 and 9.7% respectively. Recurrence was also observed with Membranous and ANCA associated GN, but the risk is low in SLE, scleroderma, familial GN, anti-GBM transplanted with negative anti-GBM antibodies and non-IgA mesangioproliferative GN. The risk factors for recurrence (type of GN, PRA and male sex) are largely unmodifiable. Graft failure risk may be reduced by avoidance of positive anti-GBM or ANCA tests at the time of transplantation, avoiding retransplantation of patients who have lost their first graft to recurrent disease and HLA matching of both LRD and CAD transplants. Avoidance of recurrent renal disease other than GN is also relevant in Reflux nephropathy and Renal and Urothelial cancers. The former may be reduced or avoided through prophylactic surgery or antibiotics, while the latter requires 2–5 years of patience to ensure that recurrent malignancy does not occur.

Treatment of recurrent disease (especially FSGS) with Cyclophosphamide, steroids and plasmapheresis has been reported, but there are no controlled data demonstrating efficacy. Use of bilateral native nephrectomy remains controversial.

The percentage of grafts lost from recurrence of GN and thus its importance will continue to rise with time after transplantation.

14

Nutrition and the Kidney Transplant Patient: Targets for Clinical Monitoring and Management

S.S.S.W. Chee

Department of Nutrition & Dietetics,
Faculty of Allied Health Sciences,
National University of Malaysia, Kuala Lumpur, Malaysia

End stage renal disease is associated with considerable co-morbidity and a diminished quality of life. Successful transplantation of the kidney into a patient with renal failure restores near-normal kidney function and is expected to correct the nutritional abnormalities arising from ESRD. Both the patients and doctors think that one of the major benefits of transplantation is an end to dietary

restrictions required for therapy during ESRD and dialysis. While kidney transplant offers the recipient a new lease on life, however it is not without caveats. Continual development in and advancements in immunosuppressive and combination therapies have significantly improved long-term survival rates after kidney transplantation. This has led to an increased concern about the long-term complications associated with transplantation, which can impact quality of life negatively. The implications of proper nutrition therapy are far-reaching. Immunosuppressive therapy used to maintain renal allograft function especially glucocorticoids, calcineurin inhibitors (cyclosporin and tacrolimus) and sirolimus are associated with hypercatabolism, obesity, hyperlipidemia, glucose intolerance, hypertension, hyperkalemia, hyperphosphatemia, hypomagnesemia and bone disease. Post-kidney-transplant patients are at greater risk for cardiovascular disease, diabetes mellitus, cancer, and osteoporosis than the general public. The medical healthcare team treating kidney transplant candidates are challenged to include prevention of chronic diseases that have strong nutritional components. This paper reviews nutrition therapies and monitoring targets for complications in kidney transplantation and advocates that patients and their family members must work together with the medical team to successfully deal with the long-term effects of transplantation.

15

NFK/K-DOQI Guidelines for Cardiovascular Disease in Hemodialysis Patients

A.K. Cheung

University of Utah, Utah, USA

The National Kidney Foundation in the US has convened a workgroup to develop K/DOQI Guidelines on Cardiovascular Disease in Dialysis Patients. The workgroup is comprised of nephrologists, two pediatric nephrologists, a cardiologist, general internist, nutritionist, social worker, exercise physiologist, geneticist, nephrology nurse and an evidence review team. The project started in year 2001 and the document is due for submission for publication in year 2004. The document will encompass the evaluation and treatment of cardiovascular end organ diseases, including cardiac diseases, cerebrovascular diseases and peripheral vascular disease. In addition, the management of various established and potential cardiovascular risk factors are addressed. The target population is exclusively patients on chronic hemodialysis or peritoneal dialysis. Both adult and pediatric patients are included; however, kidney transplant recipients and chronic kidney disease patients not requiring dialysis are excluded. The highlights of the current draft will be presented.

16

Developing Outcome Measures that Link Nursing Impact to Patient Outcomes

J.S.F. Chow

Liverpool Health Service, Sydney, Australia

Evidence based practice is now almost institutionalised in most western countries, especially in Europe, the United Kingdom, North America and Australasia. Many of these countries have established centres for evidence based health care, evidence based medicine and evidence based nursing. Considerable time and effort has been devoted to the development of clinical practice guidelines derived from evidence based medicine, in the hope that these will serve as both a valuable educational resource and a means of enhancing the quality, appropriateness, consistency and cost-effectiveness of health care. However, the impact of such guidelines on clinicians and their practice needs to be recurrently evaluated. All clinical practice guidelines provide clinical audit tools to support practice change target measurement. The guidelines recommend audit processes be instituted and usually offer suggestions for appropriate audit measures. This paper provides information on a number of guidelines and how some of the recommended targets of clinical practice are being audited. To ensure effectiveness in changing clinical practice improved patient outcomes must be measured by outcome measures such as surveys, observational studies, auditing aggregated data, benchmarking data against historical or national/international data. This paper presents ways that nurses can act strategically to ensure clinical practice guidelines are relevant, accurate and applied. It also highlights how nurses can use these opportunities to identify gaps in knowledge or evidence, and initiate relevant clinical research.

17

Peritoneal Dialysis: Practices to Improve Patient Outcomes – The Nurse's Role in Improving Patient Outcomes

J.S.F. Chow

Liverpool Health Service, Sydney, Australia

The main issue facing peritoneal dialysis clinical practice today is how to prolong technique survival, now that infection and dialysis adequacy issues are coming under better control. A number of innovations in PD fluid biocompatibility will hopefully translate into long-term sustained improvements in technique survival. Alternate peritoneal dialysis solutions have been introduced, bicarbonate based buffered PD fluids to replace lactate, fluids containing Icodextrin and amino acids instead of glucose as the osmotic agent, low sodium fluids to improve filtration, low calcium fluids to restore calcium balance, fluid to prevent glucose degradation product formation and PVC free systems produced to avoid the accumulation of plasticisers such as DEHP, which are 50 times higher than WHO recommended safe levels. Automated peritoneal dialysis continues to be a popular choice of treatment for patients with end stage renal disease. New approaches included timely start of dialysis and combined peritoneal and haemodialysis therapy. Dialysis nurses are constantly facing the

challenges of integrating these new treatment options into patients' dialysis regimens to improve patient outcomes and lifestyle. This presentation will examine the scope of PD nursing practice in integrating evidence based clinical practice, research and new initiatives in evaluating new products, monitoring effectiveness of treatment therapy, therapy modelling, data collection, management and interpretation and patient education in this continuous evolving environment with advanced technologies.

18

Treatment of Steroid Resistant Membranous Nephropathy

W. Couser

University of Washington, Washington, USA

Membranous nephropathy (MN) remains the most common cause of idiopathic nephrotic syndrome in adult Caucasian populations and progresses to ESRD in one third of cases. Significant progress has been made in understanding the pathogenesis of MN which is now believed to involve deposition of autoantibody to podocyte membrane antigens leading to sublytic C5b-9 attack on podocytes stimulating local production of oxidants, proteases, CTGF and TGF- β . However, translation of this information into new treatments for MN has been slow. Relevant to this has been the inability to establish any reliable way to monitor immunologic disease activity coupled with the recognition that proteinuria, the only clinical measure of disease, may persist long after deposit formation ceases.

Several prospective, randomized trials have demonstrated little or no benefit from corticosteroid treatment alone. However, the benefits of non-specific proteinuria reducing therapy with ACEI or ARBs, or both, in reducing progression are well established in MN. Most attention has focused on the utility of non-specific cytotoxic drug therapy with either cyclophosphamide or chlorambucil in inducing remissions in MN, and these regimens are clearly beneficial in selected patients. MMF has also seemed beneficial in a few patients. However, these agents have significant toxicity, particularly in patients with renal impairment. Cyclosporine is also effective in inducing remission, although relapses are common. However, the future is likely to see the emergence of increasingly more specific and less toxic therapies for this antibody/complement mediated disease including more specific T and particularly B cell inhibitors, agents that block complement activation at both glomerular and interstitial sites, anti-oxidants and others. The rationale and current status of each of these types of therapeutic agents in the treatment of MN will be reviewed.

19

Role of Complement (C) Activation in CKD Progression: A Therapeutic Role for Complement Inhibitors?

W. Couser

University of Washington, Washington, USA

Progressive kidney disease (CKD) is believed to occur through common pathways of tubulointerstitial injury that are independent of the initiating disease. The best established risk factor for progression is the level of non-selective proteinuria. Several mechanisms have been proposed by which increased protein filtration results in interstitial inflammation and fibrosis. We have utilized C6-deficient (C6d) PVG rats to examine the role of the C membrane attack complex (C5b-9) in mediating interstitial disease in several proteinuric disorders. Rats with aminonucleoside nephrosis develop progressive interstitial disease, with tubular deposits of C3 and C5b-9, which is largely prevented by C6 deficiency despite equivalent amounts of proteinuria. In the remnant kidney model of progressive, hemodynamically mediated CKD, both normal and C6d animals develop similar degrees of early glomerular hypertrophy, sclerosis and interstitial disease at one month. However, despite development of similar levels of proteinuria, C6d animals exhibit resolution of injury and improvement of renal function whereas C6 sufficient animals exhibit progressive interstitial disease.

Based on these observations, inhibitors of C activation may provide a useful therapeutic approach to treatment of proteinuric CKD by virtue of effects on interstitial rather than glomerular disease. Several approaches to C inhibition in man are being pursued including design of synthetic molecules with C5 inhibiting properties, use of recombinant C regulatory proteins and development of antibodies that inactivate C proteins. The current status of this approach in the treatment of CKD will be reviewed and future clinical applications discussed.

20

Role of Socio-Demographic Characteristics in Defining Proteinuria: Insights from NHANES III

G.C. Curhan

Harvard Medical School, Massachusetts, USA

Microalbuminuria and macroalbuminuria are strong independent risk factors for cardiovascular disease, progression of renal disease, and all-cause mortality in both diabetic and non-diabetic men and women. In fact, proteinuria may be a stronger indicator of future cardiovascular events than systolic blood pressure or serum cholesterol. Detecting microalbuminuria is an important screening tool to identify individuals at high risk and who should be treated aggressively to reduce their risk of adverse events. While the gold standard is measurement of 24 hour urinary excretion of albumin, a more convenient and widely used method is the urinary albumin:creatinine ratio (ACR). A number of organizations have published definitions of abnormal urinary albumin excretion as measured by the ACR, but these guidelines do not take into account characteristics that might influence

creatinine excretion such as sex. The availability of the ACR has greatly improved our ability to examine risk factors for microalbuminuria as well as those factors that affect the ACR. In this talk, I will review the epidemiology of proteinuria based on data from the US based Third National Health and Nutrition Examination Survey.

21

The Case for Prevention

K. Edwards

National Kidney Foundation Singapore, Singapore

Chronic diseases represent the major burden on healthcare systems, families and society. They are the leading causes of death and disability worldwide. Although chronic diseases can be prevented or their onset delayed, factors that put people at risk for them are prevalent in many societies and are increasing as emerging economies become more affluent. Many people have at least one modifiable risk factor for chronic disease such as smoking, low levels of physical activity, poor dietary habits or overweight and obesity. Many chronic diseases share common modifiable risk factors and as such individuals are often at high risk for several major diseases simultaneously. This is one of the most significant challenges to overall population health. Chronic diseases also constitute the major demand on the health care system, and given the costs and social implications there is a need to establish integrated disease prevention strategies to mitigate the burden of these diseases. The fact that many chronic diseases share common causes represents an opportunity, not only for chronic disease prevention, but also for savings in healthcare costs, improved quality of life, and decreased morbidity and mortality. The major behavioral risk factors of poor diet, inactivity, smoking and stress contribute to obesity, hypertension, dyslipidemia and impaired glucose tolerance, all of which increase the risk of chronic diseases. Chronic disease prevalence increases with age and tends to develop over a long period and as societies become more affluent and life expectancy increases these diseases are manifest. There is international evidence that risk factor prevalence can be modified across entire populations, but an intensive, coordinated and comprehensive approach is required to achieve this. The experience of establishing an integrated primary and secondary disease prevention strategy in the Singapore context will be examined with discussion on the applicability of this model to other societies – its strengths and limitations.

22

Resource Rationalization: Cost Implications in Successful Management of Dialysis Care

K. Edwards

National Kidney Foundation Singapore, Singapore

Managers need to look further than simple cost cutting and consider a range of other operational parameters to ensure the effective management of dialysis services. Cost alone is not an indicator of

effectiveness and must be examined in conjunction with patient satisfaction, clinical outcomes and improved utilization and efficiency of all available resources. Complicating the goal of more efficient operational management is the fact that, for a range of reasons, the delivery of dialysis services can vary between and among patients, and between centers, even in the same organization. This needs to be taken into account by managers, as understanding how such variation affects service delivery increases the opportunities for more focused and successful improvement and restructuring programs. Dialysis care providers have often participated in managerial solutions that have promised to significantly change their operations, and historically such managerial innovations had disciples who led the process to its eventual demise as popularity for the concept waned, before the organization embraced the next management fad. This cycle of change is problematic because it is often made independent of a clear and consistent planning process and an assessment of the organizational impact and acceptance of change. This presentation examines the experience of undertaking a restructuring program for dialysis services at NKFS, including the review, assessment, options analysis, acceptance testing, planning implementation and evaluation phases of the project. The factors that influence and measure the success of a restructuring program including performance management, cost effectiveness, patient and staff satisfaction and clinical quality will be discussed in light of the evaluation of the experience of NKFS. The process of internal benchmarking will be analyzed together with the opportunities and challenges of defining external benchmarks for operational effectiveness.

23

Molecular Pathogenesis of IgA Nephropathy

J. Feehally

Leicester General Hospital, Leicester, UK

IgA nephropathy (IgAN) is characterized by the mesangial deposition of polymeric IgA1 (pIgA1). Although macroscopic haematuria in IgAN is associated with mucosal infection, tissue and immunization studies indicate that the marrow rather than the mucosal immune system is the site of increased pIgA1 production in IgAN. Assessment of homing receptor expression on circulating lymphocytes indicates that this shift in site of production may be the result of alterations in the site-specific T cell control of IgA1 production.

Increases in serum IgA1 do not alone predispose to mesangial IgA deposition. No single antigen has consistently been associated with IgA1 deposition in IgAN. Structural abnormalities of IgA1 have been investigated as an explanation for mesangial deposition. Human IgA1 has a characteristic hinge region not found in other immunoglobulins. Changes in O-glycosylation of the IgA1 hinge region have now been shown in both serum and mesangial IgA1 in IgAN. Mechanisms by which altered IgA1 O-glycosylation favour mesangial deposition and subsequent glomerular inflammation are not yet clear although altered interactions with matrix proteins or mesangial cell IgA receptors have been implicated. The basis of altered O-glycosylation has not yet been identified; the proposition that there may be abnormalities of the glycosylating enzyme, β -1,3 galactosyltransferase, has not yet been confirmed.

It is probable that more than one mechanism will eventually be shown to provoke mesangial IgA1 deposition, and the concept that IgAN is a single disease entity will need re-evaluation.

24

Infection Control in Dialysis Units

L. Fischbach

Minntech Corporation, Minnesota, USA

Chronic hemodialysis patients have a high risk of infection for many reasons. The process of recirculating the patients blood out side the body on a routine schedule tends to give opportunistic organisms the ability to invade the body. Some of the factors that lead to patient infections include access to blood and body fluids, close environmental conditions, routine administration of drugs, the extensive use of sharps and needles and environmental conditions such as water and the dialysis room itself.

Hepatitis viral transmission is also of concern in dialysis facilities, both from patient to patient and patient to staff. The United States Center for Disease Control has made numerous recommendations on the prevention and reduction of hepatitis in dialysis some of which will be discussed. Some of the differences between hepatitis B and C will also be discussed.

The implementation of a comprehensive infection control program is necessary to reduce the potential for transmission of infection in the dialysis unit. Elements of a infection control program should include, room design, waste disposal, sharps control, drug administration, supplies, gloves and hand washing, separation of patients and the use of standard (universal) precautions, along with infection control procedures.

25

Standards to Improve the Dialysis Treatment

L. Fischbach

Minntech Corporation, Minnesota, USA

Most aspects of the dialysis treatment are controlled by procedures developed by the dialysis staff. However, there are certain aspects of the treatment that can and should be regulated through the use of standards. Standards can be used to help develop universal procedures over a large number of dialysis facilities. By standardizing procedures it is possible to utilize the benefits and experiences from one unit to another or even from one country to another. Thus if a problem is found standards are one way to define a problem and give ways to keep the problem from harming patients in other units.

Some of the parts of the dialysis treatment that are standardized include: water treatment, reuse of hemodialysis, and the making and quality of dialysate. There are also standards directed at manufacturers that can help the user understand and better the dialysis treatment.

Some countries have been working to introduce standards to regulate the reuse of dialyzers. Because the practices varied widely from facility to facility, and since there is such a large potential to do harm to patients if shortcuts are made, the Ministries of Health from these countries wants to establish a uniform safety standard. This can and is being done in many countries.

This talk will help put the use of dialysis standards in prospective and show how it is possible to develop standards that can be used to improve the quality of the dialysis treatment in your country.

26

Atherosclerotic Renovascular Disease – An Approach to Diagnosis

R. Foley

Nephrology Analytical Services, Minneapolis, USA

Clinical conditions that tend to co-segregate with ischemic nephropathy older age, abdominal bruits, the presence of other manifestations of atherosclerosis, kidney disease, azotemia induced by ACE-inhibitors, and asymmetry of kidney size. A standard assessment of renal function, including estimation of GFR and protein excretion rate are essential, and have been found to be more predictive of outcome than the degree of renal artery stenosis in some observational studies. Physiological studies assessing the renin-angiotensin system (such as peripheral plasma renin levels, captopril-stimulated renin levels, renal vein renin levels) have largely been abandoned, and most centers use relatively non-invasive arterial imaging tests (such as Duplex ultrasonography, magnetic resonance arteriography, computed tomographic angiography) as the first specific investigation in subjects considered high-risk, in whom intervention might be considered. Conventional arteriography, which is still considered the gold standard, is generally employed in situations when revascularization would be seriously considered, an area of immense controversy, which may be informed by the ongoing ASTRAL trial. Nuclear imaging studies, to measure total and differential glomerular filtration rate, are often recommended as a pre-requisite to arteriography. In practice, many patients undergo three different renal imaging studies, at different times, before a decision is made to perform arteriography (ultrasound, non-invasive arterial imaging testing, and isotope GFR estimation), which is unsatisfactory. Techniques, such as dynamic magnetic resonance imaging offer considerable promise, as a satisfactory single-step alternative.

27

Cardiovascular Disease in Chronic Kidney Disease: Risk Stratification and Management of CVD in CKD

R. Foley

Nephrology Analytical Services, Minnesota, USA

Patients with chronic kidney disease have higher rates of cardiovascular disease, and vice versa. For example, we recently compared

abnormalities of 9 treatable cardiovascular risk factors (smoking, obesity, hypertension, LDL-cholesterol, hemoglobin, C-reactive protein, glycosylated hemoglobin, homocysteine and urinary albumin/creatinine levels) according to stage of estimated glomerular filtration rate (GFR) in adult participants of the Third National Health and Nutrition Examination Survey. 64.3% had estimated GFR above 90 (Normal), 31.2% between 60 and 89 (Stage 2), 4.2% between 30 and 59 (Stage 3) and 0.3% under 30 ml/min/1.73m² (Stage 4). The number of risk factors rose with stage of kidney dysfunction; 33.2% of normals had zero, 34.4% one, and 32.4% had two or more risk factors; for Stage 2 the corresponding figures were 27.9%, 31.2%, and 39.9%; Stage 3: 2.2%, 19.9%, and 79.9% and Stage 4: 0%, 0%, and 100%. When adjustment was made for age, self-reported hypertension, cardiovascular disease, diabetes mellitus, ethnicity and other demographic factors, subjects with GFR below 60 were 2.0 (95% CI 1.5, 2.6) times more likely to have 1 and 6.9 (4.4, 10.9) times more likely to have 2 or more risk factors, compared to those with GFR above 60 ml/min/1.73 m² ($P < 0.001$). The presence of chronic kidney disease identifies a population with a notable burden of under treated cardiovascular risk factors. If it is accepted that cardiovascular risks are additive or multiplicative, these data suggest that patients with mild to moderate chronic kidney need more aggressive treatment of each individual risk factor than patients without.

28

Evaluation and Management of Nutritional Status in CKD

D. Fouque

University of Claude Bernard Lyon, Lyon, France

Patients suffering from chronic kidney disease (CKD) commonly present with some degree of impaired nutritional status. This trend further aggravates with the progression of renal insufficiency, and it is not uncommon to record low energy and protein intakes even before ESRD. The maintenance dialysis treatment adds its own catabolic action thus raising the minimal dietary requirements to higher levels. Most observational studies report intakes much lower than required, which in turns may prevent improvement in nutritional status or allows for further aggravation of malnutrition.

In 2000, the American NKF has produced a comprehensive Clinical Practice Guideline for Nutrition in Chronic Renal Failure. This analysis was done based on a thorough literature search and analysis according to the upmost standards for evidence-based criteria. In this lecture, the adult guidelines will be presented, with reference to the evaluation of dietary intake, body composition assessment, biological parameters, composite indexes and the frequency of their respective measurements. Supervision of patients food intake and the need for individualized patient nutritional care plan will be presented. The minimal nutritional requirements will be addressed, with specific emphasis on protein and energy intakes. Enteral and parenteral nutrition will be considered, as well as other potential anabolic treatments. Implementation of these guidelines should be done by a global diffusion and local adaptations according to local nutritional customs and regulations. As for many international publications, it is expected that five to ten years will be necessary for most patients to benefit from them.

29

Management Strategies for Vasculitis: An Update

R.J. Glasscock

David Geffen School of Medicine at UCLA, California, USA

The management of renal-limited or systemic vasculitis has undergone remarkable changes in the last decade. The discovery of anti-neutrophil cytoplasmic auto-antibodies (ANCA) has facilitated these developments. Vasculitis is being recognized earlier, before irreversible injury has occurred, and monitoring of ANCA levels may aid in the avoidance of relapses. Oral or intravenous 'pulses' of glucocorticoids (GC) combined with an alkylating agents (usually cyclophosphamide, CP) have become the mainstay of therapy, despite the absence of placebo controlled, randomized trials. Proof of superior efficacy of intravenous 'pulse' GC over oral GC therapy in the induction of a remission is lacking. Originally, it was believed that prolonged CP (one year) was required to induce a lasting remission, however, controlled trials have suggested that shorter courses of CP (3 months) with conversion to long-term azathioprine (AZA) are both safe and effective. Intermittent intravenous CP 'pulses' appear to be more effective than oral CP in inducing a remission and are associated with fewer episodes of leukopenia and infection, but due to a higher frequency of relapses, such treatment is no better than oral CP in terms of renal or patient survival. Adjunctive use of intensive plasma exchange may provide some added benefits in patients who have acute renal failure requiring dialysis at the time of diagnosis. The role of other agents, such as cyclosporine, anti-lymphocyte antibody, anti-TNF antibody, leflunomide, 15-deoxyspergaulin, methotrexate, and mycophenolate mofetil are currently being evaluated. Prevention of relapses is very important. Prophylactic antibiotics and intra-nasal mupirocin may reduce the risk of relapse. Serial monitoring of ANCA titers, clinical findings and markers of inflammation (C-reactive protein and ESR) are valuable. Recurrences in the renal allograft are quite uncommon.

30

Steroid-Resistant Nephrotic Syndrome

R.J. Glasscock

David Geffen School of Medicine at UCLA, California, USA

Steroid-resistant nephrotic syndrome (SRNS) must be viewed from several perspectives. First, the definition will depend on the age of the patient, the duration and intensity of treatment. Older patients with steroid-responsive lesions require longer periods of therapy (up to 24 weeks) in order to achieve remissions compared to children (who generally respond within 8 weeks). Second, the morphology of the underlying disease identifies disorders with a broad spectrum of natural history (e.g. spontaneous remissions; progression to ESRD) and potential responsiveness to adjunctive therapy. Third, the choice of management (conservative or aggressive) will depend on the stage of disease at the time of presentation (renal function, degree of

persistent proteinuria and irreversible changes renal biopsy) and the evidence-based utility of various adjunctive therapies (such as alkylating agents, calcineurin antagonists, purine antagonists). Among the primary renal diseases causing the nephrotic syndrome 5–15% of minimal change disease (MCD), 95% of membranous glomerulonephritis (MGN), 50% of focal and segmental glomerulosclerosis (FSGS), 80–100% of membranoproliferative glomerulonephritis (MPGN), 100% of fibrillary glomerulonephritis (FGN), and 50% of mesangial proliferative glomerulonephritis (MesPGN) (including IgA nephropathy) are thought to be steroid-resistant. Patients with SRNS due to primary renal disease who present with serum creatinine values above 3.0–3.5 mg/dL usually fail to respond to adjunctive therapy and often relentlessly progress to ESRD. All patients with SRNS due to primary renal disease should have blood pressure controlled to <130/80 mmHg, preferably with angiotensin converting enzyme inhibitors and/or angiotensin receptor antagonists. A concomitant reduction in protein excretion to <1.0 g/day should be an additional goal of such therapy, which if attained will often retard the rate of progression of the disease to ESRD.

31

The Pathogenesis of Lupus Nephritis: An Update

R.J. Glassock

David Geffen School of Medicine at UCLA,
California, USA

Based on its immunopathology lupus nephritis (LN) is thought to be the consequence of antigen-antibody complexes (immune complexes) deposited from the circulation and/or formed in situ. Aberrant T-cell and non-antibody B-cell dependent mediated injury has also been suggested. Evidence from animal models and clinical studies have strongly supported a self-antigen driven expansion of auto-reactive B-cells, both T-cell dependent and independent, in the development of a broad array of auto-antibodies to cellular constituents, including native (double-stranded, ds) DNA, nucleosomes, chromatin and histones. The antigen-antibody systems involved in LN are still a matter of controversy. Recent evidence strongly suggests that nucleosomes, perhaps exposed to the immune system by abnormalities in apoptosis, are critically involved. In addition, circulating stimulators of B-cell proliferation related to the tumor necrosis factor superfamily (Blys) arise and may promote auto-antibody production. Auto-antibodies to C1q seem to be required for the development or relapse of LN. Classical anti-dsDNA-dsDNA mechanisms may only explain a part of the picture, since renal injury can appear in their absence and treatments which selectively eliminate anti-dsDNA antibody formation (B-cell toleragens) are only partially effective. In situ formation of IC, resulting from the binding of histone containing nucleosomes to the glomeruli followed by a reaction with circulating anti-nucleosome auto-antibodies can occur independent of the deposition of circulating IC. B-cells can also directly injure the kidney, independent of release of antibody. Once IC are deposited or formed in situ in the glomeruli, activation of complement, via the classical pathway, and the release of a cascade of cytokines, contribute to capillary wall injury. Thus, LN is the consequence of multiple pathways and several self-antigen-auto-antibody systems, as well as direct cell-mediated (T-cell and/or B-cell) damage.

32

Current Outcomes on Peritoneal Dialysis (PD) – The Role of Integrated Care

R. Gokal

Manchester Royal Infirmary, Manchester, UK

After over 25 years of CAPD, the therapy has established itself as a viable treatment, comparable to haemodialysis for patients in end-stage renal disease. Outcome studies in the first four to five years show equivalent patient survival compared to haemodialysis (and some show advantages for PD in the first one to three years). Technique survival is improving with up to 50 to 60% survival at five years. Main cause for 'drop-out' in long-term patients remains peritonitis, membrane related problems (UF failure and solute clearance) and patient 'fatigue and related psychosocial factors'. Infection complications are decreasing and PD has certain cardiovascular, quality of life, hepatitis risk and transplant advantages.

It is recognised however, that best patient outcomes are experienced when PD, HD and transplant are used in an integrated manner where all therapies complement each other rather than being competitive. Used in this way, PD as an initial therapy, shows better patient outcome. The choice of modality however, is heavily influenced by non-medical factors (resource, physician bias, reimbursement) and cost of therapy. With current outcomes on PD, there is no reason, other than medical, to deprive patients of the choice of the PD therapy as an initial form of dialysis, in an integrated programme, assuming patient acceptance.

PD is now an accepted dialysis therapy with good outcome results and should be used in an integrated RRT programme, where patient choice and clinical parameters dictate therapy.

33

New PD Solutions, Biocompatibility and Peritoneal Membrane

R. Gokal

Manchester Royal Infirmary, Manchester, UK

The basis for peritoneal dialysis is the use of appropriate solutions intraperitoneally, to bring about removal across the peritoneal membrane of uraemic substances, fluid and correction of acidosis. PD solutions are therefore in constant apposition to the peritoneal membrane, potentially for many years, in a situation where the peritoneal cavity was not designed for such a purpose. It is not surprising that peritoneal membrane changes do occur with long term PD, coupled with the derangements from peritonitis.

Current standard solutions are bio-incompatible, being of low pH, high osmolarity, glucose based, lactate as a buffer and containing glucose degradation products (GDPs). All of these factors have an impact on membrane viability, resulting in deposition of AGEs and impairing host defence. The Peritoneal Biopsy Registry reports on histological findings with long term PD. This shows increasing fibrosis and vasculopathy, especially after 4 years of therapy.

More recently, newer solutions have emerged which, in the laboratory, are certainly more biocompatible. This includes bicarbonate

(totally or partially replacing lactate-normal pH), reduced GDP solutions with glucose (two to three chambered bags) and the replacement of glucose as an osmotic agent (Icodextrin – iso-osmotic; and amino acids). All these have distinct advantages, (easy fluid removal by Icodextrin and less infusion pain with bicarbonate). Whether used singly or in combination will lead to improved outcome in the long run remains to be seen. Studies are ongoing to assess their impact.

34

Continuous Flow PD (CFPD)

R. Gokal

Manchester Royal Infirmary, Manchester, UK

Current PD regimes (CAPD, APD) are limited by the amount of dialysis that can be delivered. While no dialysis modality, as currently practiced, approaches normality, there is little doubt that more dialysis does provide better outcomes, as is the case in daily, long hours haemodialysis. Attempts to increase solute and fluid clearance are beset by practicalities of prescription and quality of life in peritoneal dialysis. While it is possible to increase solute clearance on APD from CAPD, even that has its limits.

One way of increasing solute clearance is by increasing dialysate flow rates (increase number of exchanges and decrease dwell times). The extension of this idea would be to have continuous flow of dialysate, whereby dialysate inflow is simultaneously matched by outflow through a double lumen catheter; adequate mixing of dialysate is crucial. There is also the thorny problem of ultrafiltration (matching internal and external UF rates). There is limited human experience but animal studies and modelling predict marked increase in solute clearance (up to 8 fold increase compared to APD).

The problems are of a technical nature (catheter design, need for large volumes of PD fluid). This could be partly overcome by using online fluid regeneration at the bedside and technical developments of an exchange machine device. One can envisage its use in daily home dialysis, treatment of acute renal failure and dialysis ascites.

35

Towards More Biocompatible PD Solutions

R. Gokal

Manchester Royal Infirmary, Manchester, UK

The basis for peritoneal dialysis is the use of appropriate solutions intraperitoneally, to bring about removal across the peritoneal membrane of uraemic substances, fluid and correction of acidosis. PD solutions are therefore in constant apposition to the peritoneal membrane, potentially for many years, in a situation where the peritoneal cavity was not designed for such a purpose. It is not surprising that peritoneal membrane changes do occur with long term PD, coupled with the derangements from peritonitis.

Current standard solutions are bio-incompatible, being of low pH, high osmolality, glucose based, lactate as a buffer and containing glucose degradation products (GDPs). All of these factors have an

impact on membrane viability, resulting in deposition of AGEs and impairing host defence. The Peritoneal Biopsy Registry reports on histological findings with long term PD. This shows increasing fibrosis and vasculopathy, especially after 4 years of therapy.

More recently, newer solutions have emerged which, in the laboratory, are certainly more biocompatible. This includes bicarbonate (totally or partially replacing lactate-normal pH), reduced GDP solutions with glucose (two to three chambered bags) and the replacement of glucose as an osmotic agent (Icodextrin – iso-osmotic; and amino acids). All these have distinct advantages, (easy fluid removal by Icodextrin and less infusion pain with bicarbonate). Whether used singly or in combination will lead to improved outcome in the long run remains to be seen. Studies are ongoing to assess their impact.

36

Peritonitis in Automated PD: Diagnosis and Treatment Guidelines

R. Gokal

Manchester Royal Infirmary, Manchester, UK

Peritonitis continues to remain a major complication of peritoneal dialysis, accounting for significant therapy change to haemodialysis, treatment failure and significant hospitalisation.

There is evidence that APD peritonitis is less frequent than CAPD, probably related to the fewer number of breaks (exchanges). There are a few differences in managing APD peritonitis as compared to CAPD. These are related to diagnosis of peritonitis (identification of cloudiness of the fluid, especially in asymptomatic patients), culture of the fluid, change in dialysis regimes and antibiotic administration. The initial empiric antibiotic treatment of APD peritonitis is no different than that of CAPD, with a variety of antibiotic regimes advocated. For once daily administration of antibiotics, it is preferable for this to be done during the longest dwell. Results, from using the ISPD guidelines in the treatment of APD peritonitis, are good with nearly 80% success rate without the need to remove the catheter. Some advocate a change of APD to CAPD for ease of management, especially for in-patient treatment of episodes.

The outcome of gram negative and fungal peritonitis remain poor, especially when these are associated with catheter related infection. Prevention and successful treatment are essential. Prevention depends on good aseptic technique and exit site prophylaxis with Mupirocin. There appears not to be any role for prophylactic antibiotics.

37

An Analysis of Daily Haemodialysis Practice

T. Goovaerts

University Hospital St. Luc, Brussels, Belgium

Many recent studies have reported better outcomes with Daily Haemodialysis (HD) – Slow Nocturnal and Short Daily – as compared with thrice weekly Conventional HD.

Advantages such as better removal of solutes, increased dietary protein intake, reduced cardiovascular morbidity and mortality, greatly increased energy, increased quality of life and others have been described.

In the year 2000 we conducted a study on 14 patients, selected on a voluntary basis, to evaluate the influence on the nutritional status of a shift from Conventional HD to Short Daily HD.

We observed a highly significant increase in Lean Body Mass, while the total body weight remained stable.

More vascular access problems, higher dialysis costs – usually not reimbursed – could be considered as serious drawbacks of this modality. Reports however have shown that increased vascular access problems are not observed (which was also our observation) and that the global ESRD costs (drugs, hospitalisation) are decreased on Daily HD.

Conclusion: Daily (home) HD is the best Renal Replacement Therapy modality for many more patients. The results of our observational study and many other encouraging reports focussing on improved patient outcomes have convinced us to propose Daily HD at home as an additional choice to new patients entering our Pre-Dialysis Counselling Programme. Today most of our Home HD patients dialyse more frequently than 3 times weekly.

38

Analysis of the 'Buttonhole' Puncture Technique

T. Goovaerts

University Hospital St. Luc, Brussels, Belgium

Although the way of using an access has an influence on its survival, not many articles have been published on the puncture techniques of the AV fistula and no consensus on which technique to be used can be found.

The most common puncture technique is the 'rope ladder' technique, where the punctures are equally spread over the whole length of the fistula.

An alternative cannulation technique is the 'buttonhole' technique, where the fistula needles are inserted into exactly the same puncture site for each dialysis treatment. After a break-in period, the needle slides through an established path into the vessel.

The 'buttonhole' cannulation technique is certainly not new. Dr. Zyblut Twadorowski already describes the technique in the mid-seventies. It was originally used for patients with limited puncture sites, but proved to be efficient for other patients with native AV fistula.

In 1997, after a visit to Dr. Twadorowski's unit, we abandoned our 'rope ladder' puncture technique for the 'buttonhole' technique in all our haemo patients with native AV fistula who dialysed at home and in the Satellite Unit. Patients on daily dialysis have two pairs of buttonholes.

In accordance with the few published observations, the 'buttonhole' technique proved to be better for most of our patients: less pain, easy puncturing, less haematoma formation, no longer bleeding times and last but not least, less 'scar formation'; the latter point makes the technique preferred by all patients from esthetical point of view.

Conclusion: The 'buttonhole' cannulation technique rightly deserves to be THE preferred technique for many more patients.

39

Arresting the Progression of Renal Disease: New Knowledge and Future Trends

T.H. Hostetter

NIH – NIDDK, Maryland, USA

End stage renal disease (ESRD) has been increasing in the US for more than 20 years. Large costs result from this trend. This increase is caused by an aging population, a rising prevalence of diabetes, and better survival after myocardial infarction and stroke. However, these factors account for only about ½ of the increase in ESRD. Moreover, no increase in the size of the large pre-ESRD, chronic kidney disease (CKD) population can be discerned during the 1990s. Despite advances in treating CKD over the last 10 years, these strategies have been slow to be introduced into practice. The National Kidney Disease Education Program seeks to increase awareness of risk factors and modes of diagnosis and treatment among high-risk groups and their providers. Efforts include initiatives to improve laboratory reporting of kidney function, creation of materials for public and provide awareness and development targets and measures of their implementation.

40

The Role of Aldosterone in Progression of CKD

T.H. Hostetter

NIH – NIDDK, Maryland, USA

Blockade of the renin-angiotensin-aldosterone system has proven effective in retarding progression of renal disease and ameliorating heart failure. Attention has focused on the role of angiotensin II in propagating injury both by its hemodynamic and non-hemodynamic actions. Aldosterone has an established place as an injurious member of this system in heart failure. Several lines of evidence suggest that progressive renal disease is also adversely affected by aldosterone and that the current therapies with angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB) converting and dietary protein restriction also lower aldosterone levels. Thus, aldosterone, as well as angiotensin II (ANG II) appears to be instrumental in sustaining the destruction of residual kidney tissue as well as in aggravating the course of heart failure.

New Insights in Renal Osteodystrophy

K.A. Hruska

Washington University School of Medicine,
Missouri, USA

In an adynamic osteodystrophy and in an animal model, the metabolic syndrome is worsened by CKD and improved with exogenous BMP-7.

An osteodystrophy has not been defined in an animal model of the metabolic syndrome with hypercholesterolemia, hyperglycemia, vascular calcification and renal insufficiency. This syndrome complex is associated with increased mortality in chronic kidney disease (CKD). We hypothesized that the vascular calcification seen in these animals may be associated with alterations in bone remodeling, and changes in serum phosphorus and CaxP. Ten week old LDLR^{-/-} mice were either Sham operated or subjected to electrocautery of the right kidney followed in two weeks by left nephrectomy to create CKD, then randomized into 5 groups: Sham/Chow, Sham/High fat (15%), Sham/High fat/BMP-7 (10 mcg/kg q week), CKD/High fat, CKD/High fat/BMP-7. The mice fed a high fat/cholesterol diet developed hyperglycemia, hypercholesterolemia and intimal atherosclerotic plaques. All groups were maintained on their regimens for 12 weeks prior to sacrifice. BUN levels and iPTH were elevated equally in the CKD groups. Despite high iPTH levels, the osteodystrophy in the LDLR^{-/-} CKD high fat mice was an adynamic bone disorder (decreased ObN, MS/BS and BFR/TV). A similar osteodystrophy of milder degrees was observed in the Sham/High fat group. BMP-7 treatment did not affect iPTH levels but normalized the osteodystrophy, by improving ObN MS/BS and BFR/TV formation. Serum Pi levels were reduced from 16.4 ± 0.4 mg/dl to 10.1 ± 0.4 mg/dl with BMP-7 treatment ($p < 0.01$) in the CKD groups. This study demonstrates an adynamic bone disorder and hyperphosphatemia in LDLR^{-/-} animals fed a high fat diet which was reversed in BMP-7.

Molecular Genetics of Familial IgA Nephropathy

S.I.-H. Hsu

Genome Institute of Singapore, Singapore

IgAN has been widely touted as the most common form of inflammatory kidney disease in the world. Given the significant impact of IgAN on the incidence of end-stage renal disease in Southeast Asia, the Pacific Rim and worldwide, the current absence of serologic or molecular diagnostic tests, and the lack of specific and effective therapy for this inflammatory kidney disease, increased efforts are needed to elucidate the basic molecular mechanism(s) that mediate the development and progression of IgAN. A major tenet of modern molecular medicine is that when the pathogenesis of a disease process is understood at sufficient molecular detail, the development of clinically useful diagnostic and prognostic tests and the rational design of novel and increasingly specific drug therapies aimed at

target proteins involved in mediating disease pathogenesis, will become possible. This talk will present work by several international groups, including ongoing work at the Genome Institute of Singapore, to identify disease loci for familial IgA nephropathy by genome-wide analysis of linkage in both Caucasian and Southern Chinese multiplex families.

Evolution of Hemodialyzer Reprocessing

M.V. Hudson

National Nephrology Certification Organization (NNCO),
Sunnyvale, California, USA

Reprocessing of hemodialyzers began very soon after the start of chronic hemodialysis in the mid 1960s. It was done specifically for economic reasons. Notions regarding biocompatibility were not a consideration, primarily because the word had not been invented in relation to the dialyzer membranes.

At that time there were no automated reprocessing systems. And as the notion and the practice grew manual systems were the norm; they were facility designed and built. Also, all reprocessing was performed using untreated tap water. Reason: no one had any idea of the harmful effects of the various constituents dissolved and suspended in untreated tap water. Further, there were no accepted standardized procedures for sterilizing these units; every facility had it's own way of doing it with regards to type of sterilant. Strength of same, the duration of dwell time and the appropriate methods and materials for rinseout.

It must be remembered that the first 'workable' artificial kidney that was used on humans was developed by Dr. Willem Kolff in the late 1930s and early 1940s, his work had precursors. John Abel, et al of John Hopkins University in 1912 built a device to 'dialyze blood'. And there were others. Dr. Kolff's unit was a 'rotating circular drum' apparatus with a membrane wrapped around it that became known as a 'coil'. Although we are not certain that these membranes were 'reused' later versions were and the 'coil' became the workhorse of early chronic hemodialysis; to be followed by flat plate dialyzers called the 'Kiil'.

Our presentation will trace the evolution of the reprocessing of hemodialyzers, the development of standards for the practice, and the proliferation of patients being dialyzed on reprocessed hemodialyzers.

Home Haemodialysis: A Cost Effective and Quality Treatment Option

C.D. Hyde

Sydney Dialysis Centre, Northern Sydney Area Health,
Sydney, Australia

There are a total of 2,441 patients on dialysis in New South Wales (NSW), Australia and the anticipated growth in dialysis is 7–10% per annum for the next 20 years (ANZDATA 2003). A major review of dialysis services conducted in 1996 documented commitment by the

NSW State Government to ensure equity of access to dialysis services and this commitment is ongoing today.

Home dialysis modalities are considered the treatment of choice in NSW and as a result 458 patients were managing their own haemodialysis therapy in the home environment at March 2003 (ANZDATA 2003). The NSW State Government supports home haemodialysis by funding capital item equipment costs, consumables, nursing and maintenance expenses of the home haemodialysis program. Patients are required to contribute to start up expenses by installing appropriate plumbing for the dialysis machine and purchasing a suitable recliner chair and sundry items such as digital scales. Ongoing costs to patients are limited to pharmaceutical products.

Models of funding clearly demonstrate home haemodialysis programs are more cost effective than the alternative hospital and satellite haemodialysis services. There is also agreement in the literature that home haemodialysis is able to offer many potential benefits such as increased: survival; quality of life; independence; and rehabilitation. Currently the Sydney Dialysis Centre provides ongoing nursing and technical support to 145 patients who live in NSW. This paper will discuss the financial and logistical issues relevant to providing home haemodialysis services to patients who live in urban and rural areas of NSW.

45

Physical Assessment: Is it a Lost Art or an Underdeveloped Skill?

C.D. Hyde

Sydney Dialysis Centre, Northern Sydney Area Health,
Sydney, Australia

One of the fundamental roles of the registered nurse is to collect data that contributes to the initial diagnosis and ongoing assessment of the patient. Data collection skills may be as simple as counting the patients pulse rate or involve the manipulation of complex diagnostic equipment. Specialist nephrology nurses are also expected to incorporate the higher level skills of physical assessment into their every day practice. Post graduate nephrology nursing curriculum commonly acknowledges the importance of physical assessment in specialist nursing practice. As a result course content is directed toward facilitating the development of relevant knowledge and skills in the student. Fluid assessment, for example, is part of every day practice for the dialysis nurse. Patients arrive for treatment with a predetermined estimated ideal (dry) weight and it is the specialist nephrology nurses' responsibility to review the appropriateness of this weight given the specific clinical situation. So why is it that in recent times fluid assessment has, in many dialysis units, been reduced to routine documentation of the patients blood pressure and weight? Specialist nephrology nurses should be confident and competent in skills such as chest auscultation and jugular venous pressure assessment yet in many instances they seem reluctant to go beyond assessing ankle oedema.

This paper will review the aspects of physical assessment that should be part of the specialist nephrology nurses repertoire and will suggest reasons why nurses commonly evidence reluctance to claim these skills as their own.

46

Conservative versus Interventional Management in Atherosclerotic Renovascular Disease

P.A. Kalra

Hope Hospital, Salford, UK

Atherosclerotic renovascular disease (ARVD) is commonly associated with hypertension, CRF and progressive loss of renal function, and interventional procedures are often performed in an attempt to improve or control these conditions. However, outcomes are known to be variable, with up to 75% of patients manifesting no renal functional benefit after renal revascularization. The 3 RCTs that have been performed in ARVD patients have demonstrated only modest blood pressure reductions and no renal functional benefit with intervention. It is, therefore, questionable whether RAS lesions are actually causally linked to the hypertension and CRF seen in ARVD patients and emerging evidence provides explanation for these disappointing renal functional outcomes after intervention. Hence, epidemiologic studies have shown that baseline renal function is related more to the severity of proteinuria and renal histopathological (mainly hypertensive) injury, rather than to severity of proximal renal arterial narrowing in ARVD. Proteinuria and histopathological injury both predict progressive deterioration of renal function in ARVD, leading to the conclusion that pre-existing renal parenchymal (or 'intra-renal') injury is the usual arbiter of renal dysfunction in the majority of patients. This is supported by Doppler ultrasound studies which demonstrate that ARVD patients with high renal resistive index (due to severe intra-renal damage) are unlikely to benefit from intervention. However, in a minority of patients a severe RAS lesion will be responsible for potentially reversible ischaemic damage, and in the future our efforts should be directed to identifying this sub-group as they are the patients who will benefit from renal interventional procedures.

47

New Immunosuppressive Agents

B. Kaplan

University of Florida, Florida, USA

Several new immunosuppressive agents are currently undergoing clinical trials throughout the world. Some of these agents are quite novel in their mechanism of action while others are modifications of agents currently being utilized.

RAD is an mTOR inhibitor which broadly has similar characteristics to rapamycin. Clinical studies are being completed, the data to date indicates this compound is an effective agent with similar toxicities as rapamycin.

Myfortic is an enteric coated preparation of sodium mycophenolic acid. It is hoped that this formulation might have better GI tolerability than mycophenolate mofetil.

FTY720 has a unique mechanism of action. It causes 'homing' of lymphocytes, probably by modulating chemokine receptors. Clinical trials are ongoing.

LEA29Y is a co-stimulatory blocker. It is similar to CTLA4Ig but with a ten fold greater effectiveness and greater binding affinity for both CD80 (B7₁) and CD86 (B7₂).

Other agents to be discussed include FK778, JAK3 inhibitors, Campath, anti-CD45 and anti-Icam compounds.

48

Nutrition and Dialysis: The Asian Diet and Achieving Clinical Targets

T. Karupaiah

National University of Malaysia, Kuala Lumpur, Malaysia

For many patients with end stage renal failure maintenance hemodialysis and continuous ambulatory peritoneal dialysis are the major renal replacement therapy options. Both modalities are not as efficient as the normal kidney in supporting continuous and efficient removal of water and waste products. Malnutrition is the veritable skeleton in the closet of dialysis patients in Asia. Dietary recommendations to prevent protein energy malnutrition and control serum mineral levels are well established for the dialysis population. Dietary compliance to these nutrition guidelines is expected to achieve clinical targets that are surrogate measures of nutritional status.

Genetic differences, diet and lifestyle issues vary substantially between Western and Asian societies. In Asia, differences exist between economies, between communities, between lifestyles, between races, between religions and between cultures. Asian diets are said to be high in carbohydrates and low in fat compared to the Western diet's higher protein content. In truth, a diet is more than a representation of carbohydrates, protein, fat and micronutrients as eating patterns of people differ. In the context of a renal patient, the dietary prescription for dialysis should translate into the layman's language of food choice and food availability.

The nutrition care plan (NCP) for dialysis needs to account for the diversities in multiethnic Asian societies. Assessment, intervention, evaluation and monitoring are the cornerstones of the NCP and fundamental to achieving clinical targets that will help the patient achieve nutrition resiliency.

49

Renal Transplantation: Current and Future Directions

S. Kong

Singapore General Hospital, Singapore

Renal transplantation in Singapore has evolved tremendously since renal transplantation started in the seventies. The first major development was the opting out legislation, the first country in Asia to adopt such a legislation. Following this was the clinical interpretation act on the definition of death and now the discussion of amending the opting out legislation to include other organs and to also include medical causes of death. Live transplants have moved from

considering just related donors. Non-related donors can be considered on a case to case basis pending the necessary requirements that have been drawn up to safe guard donors, are met.

With the plateauing of cadaver transplants in most parts of the world, kidneys from live donors have now again become one of the main source for making up of the deficit of kidneys for transplant. Countries are turning to means of obtaining more live donors to support their transplant program. This has led to many discussions on ethical issues relating to live transplants. Some lessons can be drawn from countries who have managed to have a very successful live transplant program. With the limited source of organs, one just wonders the future direction of renal transplant. What new sources can we look towards and how can better immuno-suppression regime contribute?

50

Vascular Access Outcomes: Strategies to Increase Survival

K. Konner

General Hospital, University of Cologne, Cologne, Germany

Referring to the NKF-DOQI guidelines standards as first published in 1997, complications of vascular access are analysed in detail. Monitoring and surveillance techniques aim at an early diagnosis of dysfunctioning vascular access resulting in early elective revision before onset of thrombosis, may be by surgery or by interventional procedures. Most thrombotic events seem to be avoidable. Clear preference is given to clinical parameters in diagnosing the failing access. The pivotal role of cannulation is emphasized comprehensively. The best tools to care for a long-term function of vascular access are well trained fingers, ears and eyes. Technical equipment – except ultrasonographic techniques – is only used in selected cases. Thus, the rate of central venous catheters, emergency haemodialysis treatments, hospitalizations and expenditures can be reduced substantially.

Lifespan of vascular access is closely related to quality of life of our patients.

51

The Initial Creation of Native Arteriovenous Fistulae – Surgical Aspects and Their Impact on Practice of Nephrology

K. Konner

General Hospital, University of Cologne, Cologne, Germany

A highly welcomed goal, the increasing number of arteriovenous fistulae is defeated by a high rate of early failure – are there causes which can be identified for failure?

A potential contributing cause are strategies and details while planning and creating arteriovenous anastomoses. The 'simple' arteriovenous fistula is all but simple.

Construction of the anastomosis is a tool, not the aim of access surgery. Success also depends on selection of the optimal side, site and type of initial surgery. The aim is a fully and rapidly maturing fistula, a high flow construct, easily and repeatedly to cannulate for adequate hemodialysis therapy. Surgical details are illustrated to make verbal descriptions more clear.

The impact of a high quality of initial vascular access on the practice of nephrology is reviewed with respect to complications and adequacy of haemodialysis therapy. The role of the nephrologist in the care for vascular access is extensively highlighted.

Closing remarks define a vascular access team as the optimal option for future management of vascular access.

52

When to Choose Arteriovenous Fistulae or Grafts, Catheters and Prosthetic Devices?

K. Konner

General Hospital, University of Cologne,
Cologne, Germany

Long before the delivery of the NKF-DOQI Guidelines in 1997, common wisdom and experience stated that absolute priority in creation of vascular access in haemodialysis patients should be given to native arteriovenous (AV) fistulae. Nowadays, the problem is to adapt the old surgical techniques to the type of haemodialysis patients in 2003 that is characterised by advanced age, diabetic and hypertensive nephropathy with their preexisting damage of the arterial and venous vasculature. Grafts really play a role as second-choice procedures.

Early, timely referral to nephrologist and access surgeon to create primary AV fistulae can reduce the use of grafts as well as untunneled and tunneled catheters in initiating haemodialysis therapy. Nevertheless, a few patients need soft, tunneled, cuffed central venous catheters due to cardiac and vascular reasons.

Two types of prosthetic devices (ports) were introduced a few years ago. Since comparative studies are missed and preliminary results are more or less disappointing the indications.

53

Dialysate Quality Monitoring: System Validation from a Pharmaceutical Point of View

S. Krietemeyer¹, R.L. Marseiler²

¹Lauer Membran Wassertechnik GmbH, Germany

²Institut für Spitalpharmazie, Kantonsspital Basel,
Basel, Switzerland

For the first time worldwide water treatment for hemodialysis and distribution systems was validated according to GMP (good manufacturing practice) standards for *water for injection* (WFI) and/or *aqua purificata* (AP) from pharmaceutical industry. Pharmaceutical validation procedures were adapted to existing quality standards in hemodialysis in a way that system design, installation, operation and

product quality can be guaranteed to ensure best patient treatment. Existing system approvals according to the European medical device directive (MDD, 93/42 EC) were considered as starting points for the validation process.

In 2001 the Department of Nephrology at the 'Kantonsspital Basel' (CH) decided to install a new water treatment and distribution system for HD (35 beds) including a dead space free stainless steel loop piping, hot disinfection of the ring main and a central concentrate supply system. Installation had to be carried out without disturbing the ongoing HD treatment in the clinic. Because of evident technical similarities between the planned system and already existing pharmaceutical water treatment systems in the hospital, system validation was part of the tender for the new centre. Validation of the installation was performed under direction of the department of hospital pharmacy.

Validation of a complex water treatment could only be carried out in cooperation between the manufacturer and the operator. As a basic concept, validation followed the V-shaped model for specification and qualification as described in GAMP4: Guide for validation of automated systems. Validation process was split up in seven phases that provided necessary documentation to establish that the system performs in the manner defined in a 'Basis of Design'. A summary of milestones that were considered for this project have been: (1) User Requirement Specification, (2) Design Specification, (3) Design Results, (4) Design Qualification, (5) Installation Qualification, (6) Operation Qualification and (7) Performance Qualification.

As a result within a period of 8 months a complete validation program for water treatment in HD centres was developed and applied according to pharmaceutical GMP standards. The validated installation was capable of producing water that exceeds all existing quality standards for water for hemodialysis.

54

Measuring Cardiac Output, Blood Flow Rate and Recirculation – Major Presentation Points

N. Krivitski

Transonic Systems Inc., New York, USA

Access flow (AF) range as a function of location, type, gender, and access condition will be presented. The role of the vascular access dysfunction as a major source of hemodialysis patient morbidity will be addressed. The NKF K/DOQI guideline recommendations related to AF monitoring and thresholds will be discussed and illustrated.

Theory and practical implementation of different methods for measuring AR and AF will be presented with major attention to accuracy, reliability, and operator-independence of the results. The role of intra-access venous pressure in access surveillance will be examined and compared with AF surveillance. Relationship between AF surveillance outcomes and access stenosis, thrombosis, and economics will be addressed. Implementation of surveillance program from surgical access placement to successful intervention by PTA will be analyzed.

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in patients with end-stage renal disease (ESRD). The transonic methodology of cardiac output (CO) measurements will be

explained. Summary of literature focused on the relationship between CO and AF will be presented. The following clinical situations will be analyzed:

- prolonged high levels of AF leading to high CO failure;
- low cardiac index (CI) placing patients at risk for cardiovascular complications and heart failure;
- decrease in CI during hemodialysis to dangerously low levels due to inaccurate dry weight estimation and/or inadequate medication;
- relationship of sudden death phenomena and CI in ESRD patients.

55

The Role of Podocyte in CKD Progression

W. Kriz

University of Heidelberg, Heidelberg, Germany

Most diseases progressing to chronic kidney disease (CKD) start in the glomerulus. Among the glomerular cells, the podocyte represents a uniquely differentiated cell type which, in the adult, is incapable of regenerative cell replication. Thus, if podocytes are lost for any reason, they cannot be replaced by new cells. This is a central fact in glomerular pathology.

Functionally, podocytes have a major impact on (1) mechanical support, counter acting – together with mesangial cells – the high pressure gradients across glomerular capillaries, (2) size selectivity of the glomerular filter and (3) together with parietal epithelial cells – maintenance of the urinary space. Failure in these functions results in capillary expansion, protein leakage and formation of tuft adhesions, respectively. The latter represents the most serious consequence of podocyte failure. Formation of tuft adhesions may be effected either by affixation of parietal epithelial cells to the GBM (predominantly in degenerative glomerular diseases) or by podocytes fixing to the parietal basement membrane (predominantly in inflammatory glomerular diseases). Both events may lead to crescent formation either by misdirected filtration towards the interstitium (matrix crescent) or by epithelial cell proliferation at the capsular side (cellular crescent). Encroachment of these processes upon the tubule (via the urinary pole) may lead to obstruction of the tubule and separation from the glomerulus, thus to the loss of a functioning nephron. The tubular remnants undergo decomposition and are replaced by fibrous tissue in a steadily progressing manner. The glomerular remnants may survive for a longer time.

Conclusion: In our view, these are the two most important mechanisms leading to nephron loss subsequent to a glomerular disease.

56

Does Hypertension Cause ESRD?

W. Kriz

University of Heidelberg, Heidelberg, Germany

There is general agreement that glomerular hypertension is a major effector of glomerular damage and thus a major contributor to progression in chronic renal disease. On the histopathological level, the pressure induced step by step sequences of events have been elucidated in animal models, including genetic (fawn-hooded hypertensive rat; Milan rat) as well as experimental models (DOCA-salt-hypertension). Expansion of glomerular capillaries (predominantly of the first branches of the afferent arterial) accompanied by mechanical overchallenge of podocytes initiates the formation of vascular pole associated adhesions of capillaries to Bowman's capsule. This type of tuft adhesion is the committed lesion that progresses to segmental glomerulosclerosis. Thus, it is the vulnerability of podocytes to elevated transmural pressure gradients which crucially underlies the development of irreversible glomerular damage.

The mechanisms underlying the vulnerability of podocytes on a cell-biological level are less understood. Recent work of ours as well as others has demonstrated that podocytes are indeed sensitive to mechanical stress. In culture, podocytes respond with a dramatic reorganization of their actin cytoskeleton (Endlich, et al: JASN 2001;12: 413) and with a decreased readiness to proliferate (Petermann, et al: Kidney Int 2002;61:40). Even more recently, cDNA arrays showed changes in gene expression in podocytes induced by mechanical stress (cyclic biaxial stress) in vitro (Endlich, et al: FASEB J 2002;16:1850). Several differentially regulated genes were found among them and most prominent osteopontin (OPN). An upregulation of osteopontin mRNA was also found in glomeruli from DOCA-salt treated rats. In cultured podocytes, OPN coating resulted in a markedly diminished podocyte loss in response to mechanical stress. Thus, podocytes are sensitive to mechanical stress and have mechanisms to adapt to increased stress. However, overtaxing of podocytes in their supportive function in vivo will lead to podocyte failure and thus contribute to progression of chronic renal disease.

57

New Therapeutic Approaches for Lupus Nephritis

K.N. Lai

Queen Mary Hospital,
University of Hong Kong, Hong Kong

The optimal treatment of severe lupus nephritis remains unclear. Regimens consisting of steroid and cyclophosphamide (CYC) appear to be most effective. However, up to 15% of patients are refractory of CYC treatment and 30–50% still develop progressive renal disease. Moreover, infection and gonadal toxicity is a major concern of CYC used in patients of the reproductive age. More effective but less toxic regimens are being sought. Sequential treatment employing aggressive induction therapy and maintenance treatment will less toxicity is

the preferred approach for severe lupus nephritis. Mycophenolate mofetil (MMF) is a new immuno-suppressive agent that selectively inhibits activated lymphocytes and renal mesangial cells. Although the use of MMF in lupus nephritis is still in its preliminary stage, uncontrolled experience has confirmed the efficacy in patients with serious disease recalcitrant to conventional cytotoxic agents. Controlled studies, albeit small and lacking statistical power, have revealed that MMF is as effective as CYC or azathioprine in the induction of renal remission in the short term. Its value in the maintenance treatment is strongly favored in a recent clinical trial. Newer agents targeting at binding of anti-DNA, inhibition of T cell costimulatory pathways, and depletion of B cells have just been undergoing preliminary testing. These newer therapeutic approaches will potentially allow better treatment for lupus nephritis with less toxicity.

58

Management of Hepatitis in End-Stage Renal Disease

K.N. Lai

Queen Mary Hospital,
University of Hong Kong, Hong Kong

Hepatitis B virus (HBV) is the first culprit to strike hemodialysis centers since their beginning. It has been effectively controlled by active vaccination, screening of blood donors, the use of erythropoietin, and segregation of HBV carriers. To date, HBV remains an important cause of morbidity in endemic areas. Hepatitis C virus (HCV) is the most significant cause of non-A, non-B hepatitis, and is mainly transmitted by blood transfusion. The introduction in 1990 of routine screening of blood donors for HCV contributed significantly to the control of HCV transmission. However, an effective HCV vaccine remains an unsolved challenge. The vigilant observation of guidelines on universal precaution and regular virological testing are the cornerstone to the effective control of chronic hepatitis in the setting of hemodialysis.

HBV carriers receiving kidney transplantation have increased liver-related mortality. Preliminary data on the impact of lamivudine treatment on patient survival, the optimal time to start treatment, and the feasibility of discontinuing treatment have just been emerging. Preemptive lamivudine therapy based on serial HBV DNA levels and clinical monitoring improved the survival of HBsAg-positive renal allograft recipients. Treatment can be discontinued safely in selected patients after stabilization to minimize the selection of drug-resistant HBV mutants. In contrast, there is no available treatment of HCV infection after renal transplantation. Recent data suggest that dialysis patients waiting for a RT need to be treated with α -IFN because when HCV RNA clearance occurred, they experienced no relapse after transplantation despite chronic immunosuppressive treatment.

59

New Insights into the Pathogenesis of Diabetic Nephropathy

H.B. Lee

Soon Chun Hyang University, Seoul, Korea

Clinical trials have demonstrated that hyperglycemia plays a major role in the development and progression of diabetic vascular complications including renal injury. Hyperglycemia induces renal injury through complex overlapping pathways: formation of advanced glycation end products (AGE), activation of protein kinase C (PKC), and generation of reactive oxygen species (ROS) among others. Growing evidence suggests that ROS may play an important role in the initiation and progression of diabetic nephropathy. High glucose induces cellular ROS in glomerular mesangial and tubular epithelial cells. High glucose-induced ROS in mesangial cells can be effectively blocked by inhibition of PKC, NADPH oxidase, and mitochondrial electron transfer chain complex I suggesting that PKC, NADPH oxidase, and mitochondrial metabolism all play a role in high glucose-induced ROS generation. PKC appears to play an important role in the activation of NADPH oxidase and subsequent generation of cellular ROS. On the other hand, high glucose-induced mitochondrial superoxide overproduction activates PKC. Interaction of ROS and PKC thus amplify high glucose-activated signaling in diabetic kidney. High glucose-induced AGE, TGF- β 1 and angiotensin II can also induce cellular ROS and may further increase oxidative stress in diabetic kidney. ROS activate signal transduction cascade (PKC, MAPK and JAK) and transcription factors (NF- κ B, AP-1, Sp1 and STAT) and upregulate TGF- β 1 and extracellular matrix (ECM) genes and proteins. In addition to upregulating ECM synthesis, ROS may also play a critical role in decreased ECM degradation by inhibition of proteolytic system in the glomeruli and in increased ECM degradation by mediating TGF- β 1-induced epithelial-mesenchymal transition in tubular epithelial cells. Precise definition of ROS-activated signaling pathways leading to ECM remodeling in the kidney will allow better understanding of the final cellular responses to high glucose.

60

Optimizing Renal Care in the ICU

K.H. Lee

National University of Singapore, Singapore

Critically ill patients have a high incidence of acute renal failure which increases morbidity and mortality. It behaves the intensivist to avoid further renal insult and provide protective strategies for preserving renal function.

Pre-renal causes of renal failure should be eliminated with rapid and adequate resuscitation. Newer methods of invasive hemodynamics that emphasize volume measurements may be superior as a guide to fluid resuscitation. Avoidance of nephrotoxic agents will prevent further deterioration in renal function, e.g. aminoglycosides, calcineurin inhibitors.

Preventive measures utilizing dopamine has not been shown to be helpful. Diuretic therapy may be detrimental to ultimate outcome. Preventing contrast nephropathy is important and appropriate protective measures should be instituted. Methods and dose of renal replacement therapy impacts on outcome of renal failure as well.

Specific medical problems that lead to renal failure may need specific treatment: hepato-renal syndrome – treatment with terlipressin or liver dialysis with MARS™; large volume paracentesis with albumin replacement; hydration, mannitol and alkaline diuresis for rhabdomyolysis.

61

New Devices for Dialysis in the Critically Ill: The MARS™ System

K.H. Lee

National University of Singapore, Singapore

Liver dialysis for liver failure patients as a replacement therapy has been the target for many investigators. These devices can be classified into biologic and non-biologic devices. Biologic devices employ bioreactors that contain viable hepatocytes (either human or porcine) that attempt to replace the synthetic and detoxifying functions of the liver. So far, none of these devices are in widespread use, and are still experimental. Non-biologic devices are purely detoxifying and provide no additional synthetic benefits. One such system that has been approved for use in Europe is the MARS™ system. This consists of albumin dialysis with a method for recirculation.

MARS™ has been shown to significantly reduce the level of total bilirubin, bile acids, ammonia, and aromatic amino acids. It will also improve the outcome of patients with hepato-renal syndrome, and improve outcome in those with alcoholic hepatitis. Hepatic encephalopathy can also be improved. Many centres are using this as bridge to liver transplantation but survival without transplantation is poor if there is no spontaneous recovery of liver function. The device will lead to some hemolysis, and increase the clearance of antibiotics as well as glucose, especially when non-dextrose containing dialysate is utilized.

This is a costly procedure and its ultimate utility in liver failure remains to be defined.

62

Application of Sorbents in ESRD

N. Levin¹, J. Winchester²

¹Renal Research Institute, New York, USA

²Renal Tech, New York, USA

Current high flux dialyzers are limited in their ability to remove low molecular weight proteins because of the potential for protein loss. Adsorption represents an alternative approach for the removal of identified potentially toxic in high concentration substances such as β_2 -microglobulin, immunoglobulin light chains, angiogenin, complement

factor D, ubiquitin, etc., and their glycosylated analogues. Leukocyte functional abnormalities including apoptosis have been reported (Hörl) but these substances may have many other deleterious effects in ESRD patients. We and others have recently investigated a divinylbenzene polymer in bead form with a biocompatible PVP coating on the surface (RenalTech International, New York, NY). The adsorbent has a pore size distribution which achieves removal of molecules in the weight range 8–40 kDa. The mean bead size is approximately 600 μ and the surface for adsorption is 600 m²/g of dry resin. Another resin (Lixelle) cellulosic beads to which ligands trapping β_2 -microglobulin are attached (Kaneka Corporation, Osaka, Japan) hemoperfusion device has also been shown to reduce β_2 -microglobulin concentrations during extracorporeal treatment, with removal of β_2 -microglobulin and partial regression of dialysis related amyloidosis over 6 to 13 months; Homma (1995). Applications of the divinylbenzene device, in addition to chronic dialysis, include patients with sepsis and the syndrome of systematic inflammatory response due to the ability of this device to adsorb multiple inflammatory substances, including cytokines. Preliminary experience of the device in patients on chronic dialysis and experimental data on its use in sepsis will be discussed.

63

On-Line Clearance Monitoring

N. Levin, F. Gotch

Renal Research Institute, New York, USA

The on-line clearance (OLC) monitor provides accurate, reproducible measures of dialyzer function during the dialysis treatment. The technique, which measures conductivity clearance equivalent to Na⁺ and therefore to urea clearance requires an increase to about 150 mEq/L and then decrease of Na⁺ to about 135 mEq/L in the dialysate over a ~6 min period with measurement of dialysate flow rate (Qd) and ultrafiltration rate (Qf). Precise conductivity cells measure differences in conductivity at the inlet (Cndi) and the outlet (Cndo) of the dialyzer before and during the period of sodium administration. Conductivity clearance = $\{1 - \Delta C_{ndo} / \Delta C_{ndi}\} \cdot (Q_d + Q_f)$. This is an effective clearance, since any recirculation will result in a decrease in the gradient between dialysate and blood compartments therefore reducing clearance. This technique permits evaluation of clearance six times per treatment and permits early diagnosis of errors in needle placement or of clotting in the dialyzer. In order to calculate Kt/V the K from OLC is used in the urea kinetics program to obtain V. Using OLC, by reversing arterial/venous flow 100% recirculation results and access flow can then be calculated using the OLC machine. Regular measurement of access flow may permit early diagnosis of access stenosis. This device adds substantially to the assessment of dialysis adequacy and of vascular access management. Its application will be reviewed.

Acute Renal Failure in Developing Countries

S.Y. Lin

Huashan Hospital, Fudan University, Shanghai,
P.R. of China

Great changes have taken place in the causes of acute renal failure (ARF) in the past twenty years. In China, intoxication and epidemic hemorrhagic fever were two main causes in 1980s. Since 1990s, infection and renal parenchymal diseases have taken the place and the proportion of ARF after operation has increased significantly. The mortality rate is still high for several reasons such as more old patients, severe infection, high APACHEII score and multiple organ failure (MOF). Continuous renal replacement therapy (CRRT) has been widely used in the treatment of ARF, but the survival rate has not remarkably increased because most of the patients received CRRT are severe. With the development of renal biopsy, we have achieved a great many positive results because more ARF caused by rapidly progressive glomerulonephritis (RPGN) or acute tubulointerstitial diseases are diagnosed and treated rapidly. Studies of Shanghai Hua Shan Hospital show that high volume continuous veno-venous hemofiltration (HVCVVH) is applicable to patients with unstable hemodynamics and MOF for its benefit of improving hemodynamics and removing a great deal of cytokine. Studies also find that in addition to its ameliorating hemodynamics, HVCVVH can improve many pneodynamic parameters including Ppeak, mPaw, Ppat, WOBp and Cdyn. Chinese scholars also focus on the leading fields of blood purification like ascorbic acid dialysate ameliorating oxidative stress, liposome dialysate removing protein-combined toxins and the use of tumor necrosis factor (TNF) monoclonal antibody immunoadsorption in ARF caused by endotoxin.

ESRD Registries in China

S.Y. Lin

Huashan Hospital, Fudan University, Shanghai,
P.R. of China

Began in 1999, end-stage renal disease (ESRD) Registries in China cannot involve all the countrywide data for the vast land and the uneven distribution of population. The incidence of ESRD in Shanghai in 2000 was 122/pmp while it climbed to 174/pmp in 2002 and it varies from 95/pmp to 185/pmp in other areas of China. The main cause of ESRD is primary glomerulonephritis especially IgA nephropathy while the proportion of diabetic nephropathy is increasing with the percentage between 6% and 20%. According to the incomplete statistics, in China there are about 8–9 million people receiving hemodialysis and 8,000 people receiving continuous ambulatory peritoneal dialysis (CAPD) most with the age from 40 to 59. In the patients who receive dialysis, one year survival rate is 76.4% and five years survival rate is 51.4%. Erythropoietin (EPO) is widely used in China but the target hemoglobin is below 9.5 g/dl in most areas except big cities such as Beijing and Shanghai. Cardiovascular

complications are the primary causes of death. About 86% of 1,092 cases of ESRD surveyed in Shanghai suffered cardiovascular diseases and the patients who died of cardiovascular complications accounted for 20.23% according to the survey in 1999–2000. Blood pressure (BP) is not well controlled in the patients with ESRD and the survey in Beijing and Shanghai shows that the average BP is 158/96 mmHg.

Reverse osmosis is widely used in China but the quality of water for dialysis needs improving. Take the endotoxin in the water for example, of 56 dialysis units in Shanghai, 6 units are above 0.5 EU/ml. From 1999 to 2003, serum phosphorus of hemodialysis patients rose from 1.63 ± 0.71 to 2.21 ± 0.86 mmol/L and the product of calcium and phosphorus went up from 51.33 ± 11.63 to 65.10 ± 17.58 ($p < 0.01$), while serum calcium, intact parathyroid hormone (iPTH) and alkaline phosphatase (AKP) remained unchanged. More large and full scale ESRD Registries are now carrying on in China.

Microinflammation: Causes and Consequences

B. Lindholm

Karolinska Institutet, Baxter Novum, Stockholm, Sweden

End-stage renal disease (ESRD) is a state of chronic systemic inflammation as reflected by increased circulating levels of pro-inflammatory cytokines and acute phase proteins including C-reactive protein (CRP). The causes include: uremia per se, loss of renal function and reduced clearance of pro-inflammatory cytokines, co-morbidities such as persistent bacterial and viral infections, fluid overload and congestive heart failure, oxidative stress, accumulation of advanced glycation end-products, and genetic factors. The consequences are manifold and include: catabolism, anorexia, loss of lean body mass, and other manifestations of malnutrition as well as an accelerated atherosclerosis, vascular calcification and cardiovascular disease. Taken together the syndrome of malnutrition, inflammation and atherosclerosis (MIA) is associated with most premature deaths in ESRD patients, and this should be taken into account in redesigning therapeutic and preventive strategies to reduce the excessive mortality in ESRD patients.

Malnutrition, Inflammation, and Atherosclerosis: Therapeutic Options

B. Lindholm

Karolinska Institutet, Baxter Novum, Stockholm, Sweden

The malnutrition, inflammation and atherosclerosis (MIA) syndrome represents a major challenge for renal care specialists who often have focused on the dialytic therapy as such; however, the identification of the MIA syndrome as one of the most important predictors of clinical outcome in end-stage renal disease (ESRD) patients also provides new opportunities for significantly improving the markedly reduced life span of ESRD patients. The therapeutic options

should not be confined to only one or a few of the components of the MIA syndrome but should include a variety of therapeutic (and preventive) strategies. Co-morbidities such as cardiovascular disease with fluid overload, congestive heart failure and atherosclerosis should be adequately treated using a variety of pharmaceutical and dialytic tools. Inflammation is often caused by these co-morbidities as well as by persistent infections, and the latter must be identified and treated. Therapy directed towards various complications of ESRD but also against inflammation should be considered using antioxidative agents, angiotensin converting enzyme inhibitors and blockers, statins and peroxisome proliferators-activated receptor gamma agonists. Future strategies may include use of specific anticytokine therapy, inhibitors of formation of advanced glycation end-products (AGEs), and of vascular calcification. Better control of inflammation in ESRD will have far reaching consequences for the whole spectrum of diseases and complications which are responsible for poor prognosis of ESRD.

68

PD Adequacy in Automated PD: Measurement and Prescription Time

B. Lindholm

Karolinska Institutet, Baxter Novum, Stockholm, Sweden

Automated peritoneal dialysis (APD) is an attractive treatment modality for end-stage renal disease (ESRD) patients who may benefit from the medical advantages of a continuous dialytic therapy (associated with steady state control of uremic toxins, electrolytes, acid-base balance and fluid status) and the life style advantages of a home therapy with automatic exchanges during the APD session (allowing work and undisturbed social life during daytime). New prescription and monitoring tools which further simplify the therapy will be reviewed and discussed. Whereas the emphasis on dialysis adequacy was previously most focused on the removal of small solutes as reflected by KT/V urea and creatinine clearance, the emphasis today, following the publication of ADEMEX study, is more on fluid balance for which APD, if possible combined with icodextrin based dialysis fluid for the long dwell, should be an ideal therapy. Accordingly, the monitoring and prescription of APD should include assessment of net ultrafiltration as an important component of the APD therapy.

69

Nutrition, Inflammation and Peritoneal Dialysis: Current Thoughts

B. Lindholm

Karolinska Institutet, Baxter Novum, Stockholm, Sweden

With the publication of the ADEMEX and HEMO studies it has become apparent that incremental removal of small solutes with the dialytic therapy over and above what is achieved in most clinical programs, is not as crucial as previously thought. Instead, it has become clear that the presence of the malnutrition, inflammation and

atherosclerosis (MIA) syndrome is a much more important predictor of clinical outcome, as this syndrome is associated with most premature deaths in cardiovascular disease (CVD) in ESRD patients. Interestingly, there are strong links between the MIA syndrome and the peritoneal solute transport rate (PSTR). Thus, patients with MIA syndrome often have a high PSTR whereas patients with a high PSTR often present with signs of both local peritoneal inflammation and systemic inflammation. With the increased awareness of the clinical significance of the MIA syndrome, it is important to assess, treat and if possible prevent the different systemic components of the MIA syndrome as well as provide a more physiological peritoneal dialysis therapy, using new more biocompatible solutions. These solutions should have both local and systemic salutary effects, and one should aim at achieving a *global biocompatibility* of the therapy, rather than only focus on the local effects. It is likely that the recent advances in peritoneal dialysis solutions and prescription recommendations with more emphasis on non-glucose solutions and fluid removal will have a major impact on the clinical outcome of PD therapy.

70

A Practical Approach to Meeting Best Practice Guidelines for Dialysis Fluid Purity

E. Lindley

St James's University Hospital, Leeds, UK

The first volume of the European Renal Association's best practice guidelines for haemodialysis [1] included a section on dialysis fluid purity. Meeting the requirements of these guidelines can have considerable resource implications in terms of equipment, services, staff time and laboratory investigations. A clear understanding of local conditions and potential risks can be used to limit the cost of complying with guidelines.

In practice, the choice of water treatment equipment can be adapted to suit the quality and reliability of the local water supply, as well as the cost and availability of staff to carry out routine monitoring and maintenance.

Knowledge of the type and variation of the contaminants in the feed water, and of the characteristics of the components of the water treatment plant can be used to simplify laboratory investigations.

Careful examination of test results, together with appropriate risk assessments can be used to rationalise maintenance and monitoring schedules and avoid unnecessary tests.

The costs of microbiological analyses can be reduced by testing for bacteria and endotoxin in-house. A procedure for culturing water-borne bacteria can be set up very easily as can the LAL gel-clot method for measuring endotoxin levels. Where large numbers of endotoxin tests are required, it may be cost-effective to lease a kinetic analyser.

Reference

- 1 Expert Group on Haemodialysis: European best practice guidelines for haemodialysis (Part 1). The EBPG Nephrol Dial Transplant 2002;17(Suppl 7): 45–62.

Management of Hyperphosphatemia in ESRD

F. Locatelli

A Manzoni Hospital, Lecco, Italy

Hyperphosphatemia, together with low active Vitamin D levels and hypocalcaemia, is one of the major determinants of secondary hyperparathyroidism, which not only causes bone disease, but also significantly contribute to cardiovascular disease and mortality in CKD patients. Until recently, aluminium hydroxide and calcium salts have been used. Unfortunately, these treatments have serious side effects. The introduction of sevelamer hydrochloride as the first non-calcium, non-aluminium phosphate binder has initiated further development of calcium- and aluminium-free interventions. Lanthanum carbonate is a novel phosphate-binding agent that is currently under development; it is able to bind phosphate in the gastrointestinal tract and reduce the amount available for systemic absorption. A third development is polynuclear iron preparations, which are based on the observation that the solubility product of trivalent iron and phosphate is extremely low. These agents are still in the early stage of clinical development. MCI-196 (colestilan), an approved agent for the treatment of hypercholesterolemia in Japan, is another new non-calcium, non-aluminium phosphate binder under development.

In addition to phosphate control, treatment of secondary hyperparathyroidism often include Vitamin D. However, its use is clinically limited. Calcimimetics are a novel class of therapy that directly targets the G-protein coupled with Ca receptor in the parathyroid gland and increase the sensitivity of the Ca receptor to extra cellular calcium. At present Cinacalcet is the most promising of calcimimetics. This agent has a rapid onset of action after oral administration, causing a rapid and sustained reduction in PTH, without major changes in serum phosphorus and with a 3–4 percentage reduction in serum calcium.

New Erythropoiesis Stimulating Protein

F. Locatelli

A Manzoni Hospital, Lecco, Italy

Therapy with rHuEPO is a well established treatment for renal anemia. However, because of its relatively short elimination half-life, it generally must be administered two to three times weekly in most patients. In recent year the pharmacological research has tried to modify the existing rHuEPO in order to improve pharmacokinetic performance and allow a reduction in the frequency of administration. New erythropoiesis stimulating protein (NESP) was designed to contain five N-linked carbohydrate chains (two more than rHuEPO). Due to increased carbohydrate content, NESP has longer circulating half-life and a lower EPO receptor binding affinity. It has been evaluated in a large number of patients with renal anemia and in cancer patients and found to be effective in maintaining hemoglobin in CKD patients who were previously treated with rHuEPO when administered at a reduced dose frequency. No evidence of antibody formation to NESP has been detected thus far. A pegylated version of epoetin

beta, CERA, has been recently synthesized. Data from animal studies indicate that it has a prolonged half-life in comparison with rHuEPO that may allow less frequent administration. Preliminary results of phase II clinical trials suggest that this agent is effective in maintaining Hb levels after switching from rHuEPO therapy when the intermediate dose was used (0.8/150 µg at the following administration frequency: once every week, once every three weeks or once every 4 weeks). In recent years, a third molecule of rHuEPO was synthesized and was named epoetin-ω. It is a sialoglycoprotein with smaller amounts of O-bound sugars, less acidic and with different hydrophylity than the other 2 epoetins. Preliminary findings indicate that this agent is an efficient and safe therapeutic agent, possibly allowing to use lower doses in comparison with epoetin-α to maintain the same Hb target.

Haemodialysis Technology in Retrospective and Perspective

F. Lopot

General University Hospital Prague, Czech Republic

Haemodialysis (HD) as the most widespread and purely technology-based method of RRT is not likely to be replaced by any bioartificial device in the near future. Discussion on its past achievements and challenges for future development are thus fully legitimate.

In the past, significant progress has been made in many aspects of HD technology, such as on-line mixing of dialysis fluid of stable composition and high microbiological purity, UF controllers with biofeedback etc. Contrary to this, development of safety concept of HD machines has not kept pace with development of functional blocks. There is still a blood leak detector on each HD machine despite very low incidence of membrane rupture in today but no sensor to detect far more frequent clotting of blood in extracorporeal circuit, no sensor to detect haemolysis easily inducible by blood line kinking. Some aspects of technological development are conditioned by basic research in clinical field. This is especially true in still incomplete list of solutes to be removed. HD limitations in comparison to natural kidney are obvious. While the latter removes many solutes by active, carrier mediated transport, HD is a passive process which can manipulate the ratio of low- and high-molecular weight solutes removal by selection of membrane pore size distribution and to a lesser degree also by changing the blood flow and dialysate flow ratio. Some techniques of removal capacity maximisation have been given up without appropriate clinical trials (Bellhouse vortex mixing dialyser), some have not yet been attempted at all (counter-current principle of the Henle's loop).

Biocompatibility issues have so far been oriented to biochemistry and molecular biology. Physical aspects of biocompatibility (shear stress, turbulence on blood side etc.) has not received appropriate attention.

Also automated determination of optimal 'dry weight' is still waiting for a break-through idea. The presentation will discuss current status and anticipated development in selected areas of dialysis technology.

Quality of Vascular Access for Haemodialysis – Still an Unmet Need

F. Lopot

General University Hospital Prague, Czech Republic

Creation of the external A-V shunt and later subcutaneous A-V fistula in the early sixties opened the way for dialysis treatment of chronic renal failure. However, key role of vascular access (VA) in dialysis adequacy was not appropriately appreciated at that time and surgical procedures were the prevailing corrective measures in failing VA. Later the first VA quality (VAQ) monitoring programmes were developed based on either pressures (first dynamic later also static) or recirculation (RN) measurement. Development of percutaneous correction techniques, namely balloon angioplasty (PTA) called for more proactive preventive monitoring. This was greatly facilitated by the invention of VA flow (QVA) evaluation from forced recirculation (RX) measured at reversed needles (Krivitski method). Since 1995 plethora of such QVA evaluation methods has been developed – thermodilutional, optodilutional or ultrasonic dilution RX measurement, complemented later by QVA calculation from on-line measured ionic dialysance at normal and reversed needles connection and by the variable flow Doppler method. Although QVA proved to be the most reliable parameter for early detection of a stenosis, combined QVA/RN enables to diagnose wider spectrum of VA anatomical anomalies. However, evidence that the VAQ monitoring programmes are really prolonging access patency is still considered weak by some. While most of those programmes are focused on timely detection of low-flow accesses, the opposite condition – access with QVA occasionally in excess of 2 l/min – usually receives much less attention. Yet it is obvious that high QVA leads to unphysiologically high cardiac output which may compromise cardiac performance especially in patients with heart disease. None of the existing renal registries has ever correlated cardiac mortality and QVA in general dialysis population. Catheter-like subcutaneous permanent access devices may prove to be the final solution of this problem due to their minimal impact on patients' haemodynamics.

Key Issues in Exercise for Dialysis Patients

W.M. Low

National Kidney Foundation Singapore, Singapore

End stage renal disease patients on dialysis can benefit from participating in regular physical activity and exercise. These benefits include improved management of their medical conditions as well as improvements in quality of life and independence. The National Kidney Foundation of Singapore's (NKFS) exercise programme addresses 4 key issues in helping patients to exercise.

1. **Programme Goals.** Given the demographics of the NKFS patients, the goals of the exercise programme were determined to be the development of functional fitness. This would contribute towards an improved ability to carry out activities of daily living, and enhanced quality of life.

2. **Risk Management.** ESRD patients often have medical co-morbidities that raise the risk of injury or medical event when exercising. The NKFS has introduced a system to grade each patient's medical fitness prior to participation in the exercise programme.
3. **Functional Fitness Components.** In developing all-round functional fitness, patients receive an individualized exercise prescription based on the components of: flexibility, strength, cardiovascular fitness, and balance. The latter is important given the deconditioning of most patients and the prevalence of bone disease.
4. **Measuring Outcomes.** Functional fitness outcomes are measured using a 5-test battery, facilitating customisation of exercise prescription, patient motivation and goal-setting.

Parenteral Iron – A Double-Edged Sword

I. Macdougall

King's College Hospital, London, UK

Not long after the arrival of recombinant human erythropoietin therapy in the late 1980s, came the realisation that iron supplementation was mandatory in patients receiving this treatment. Furthermore, in many patients (particularly those on haemodialysis), oral iron supplementation was insufficient to meet the demands of the proliferating bone marrow, and thus intravenous iron became the treatment of choice in many patients. IV iron supplementation proved to be beneficial not only in those patients who appeared to be iron-deficient, but it also augmented the response to erythropoietin therapy even in patients who appeared to be iron-replete. There have, however, been concerns that parenteral iron may evoke a number of adverse effects, such as acute reactions, enhanced susceptibility to infections, and increased oxidative stress. Non-dextran-containing-iron preparations, such as iron sucrose and iron gluconate are safer than iron dextran, which carries a risk of potentially life-threatening anaphylaxis. The evidence for an increased risk of infections and oxidative stress comes largely from in vitro studies, and there are no scientifically robust clinical studies which suggest any detrimental effects to the patient. Although these theoretical risks cannot be ignored, at the present time it is apparent that the benefits of intravenous iron supplementation outweigh any potential adverse effects.

Erythropoietin Resistance and the Role of Anti-Erythropoietin Antibodies

I. Macdougall

King's College Hospital, London, UK

The vast majority of patients treated with erythropoietic therapy show a satisfactory response with a progressive increase in haemoglobin. Around 5–10% of patients, however, show some resistance to erythropoietic therapy, and within the last couple of years it has become apparent that a very small number of patients may develop

severe resistance to EPO as the result of the development of anti-erythropoietin antibodies. This causes pure red cell aplasia (PRCA), which is a condition characterised by a sudden loss of response to EPO, with the haemoglobin falling to around 5–6 g/dL and rendering the patient transfusion-dependent. The white cell and platelet counts are usually normal, but there is a profound decrease in circulating reticulocytes to less than $10 \times 10^9/L$. Bone marrow examination usually shows a severe reduction in erythroblasts to less than 5% and/or red cell maturation arrest. The neutralising antibodies cross-react with all commercially-available erythropoietic products as well as endogenous erythropoietin. The cause of the antibody generation remains obscure at the present time, but it is apparent that more than one factor is involved, and it is certainly more common with the subcutaneous rather than the IV route of administration. It is also generally believed that immunosuppressive therapy may accelerate recovery.

Since EPO-associated PRCA is so rare (<1 in 10,000 patients treated) and has only recently been recognised, much information on this condition is lacking. A recent Editorial in *Nephrology Dialysis Transplantation* (January 2004 issue), however, summarises our current state of knowledge on PRCA, and provides recommendations on its diagnosis and management.

78

Prevalence, Causes and Management of Hypertension in India

M.K. Mani

Apollo Hospital, Chennai, India

Hypertension is a very common disease in India. Recent surveys indicate a prevalence of 26.78% in men and 27.65% in women aged over 20 in Mumbai, and 22.1% in men and women over 20 in Chennai. Only 37.3% in Chennai were aware of being hypertensive. Of those who knew, only 50% were on treatment, and of them only 40% were under control. 31.9% of high income subjects and 16.1% of low income were hypertensive ($p < 0.001$) and hypertensives had a higher BMI than normotensives (24.4 and 22). Prevalence in rural areas is significantly less, but still high (5.6%) in rural Tamil Nadu, and the trend is rising in both cities and villages.

Control of hypertension is essential. WHO figures indicate that mortality from circulatory illness in developing countries has risen from 16% in 1985 to 24% in 1997. Much of this is due to hypertension, and can be prevented if BP is well controlled. However, control is bad in cities and even worse in the average rural community because the poor cannot afford to pay for medicine. Current Government policy in its Primary Health Centres (PHC) is to provide treatment for only a few days at a time. Patients will not go to the PHC for chronic illness because they cannot afford to lose a day's wages every week. The only solution to this is to take up a domiciliary programme to detect and treat hypertension in the home.

Renal disease is the most common cause of secondary hypertension, but only 2% of hypertensives have renal disease.

The Kidney Help Trust has achieved tight control of hypertension in 96% of subjects using reserpine, hydralazine and hydrochlorothiazide, which are the cheapest available anti-hypertensive drugs. A domiciliary programme using trained preventive health workers

enables easy detection and treatment at low cost. It is recommended that hypertension and diabetes be treated on a domiciliary basis using the simple workable model established by the Kidney Help Trust.

79

Oxidative Stress in ESRD

Z.A. Massy

University of Picardie-CHU Amiens, Amiens, France

New, reliable oxidative stress markers are present in the plasma of ESRD patients, indicating that ESRD is evidently a pro-oxidant state. However, several questions related to ESRD oxidative stress remain largely unresolved. First, the relative importance of each type of oxidative stress in ESRD patients is insufficiently evaluated. Only two recent studies have addressed this issue, and both suggested that chlorinated stress played a central role in these patients. Second, the prevalence of oxidative stress among ESRD patients remains undetermined, since there is a very few population-based studies available. Third, although the link between ESRD oxidative stress and inflammation is emerging as a key factor contributing to the genesis of oxidative stress in these patients, its pathogenesis remains poorly defined. Fourth, data favoring the involvement of ESRD oxidative stress in uremic toxicity are still limited. Finally, while two recent pilot studies demonstrate that treatment of ESRD patients with antioxidants reduces cardiovascular events, information related to the pharmacokinetic characteristics of antioxidants, as well as their efficacy to prevent oxidative stress, are still fragmented in ESRD patients. All together, existing data suggest the prominent role of ESRD oxidative stress in uremic toxicity; however, to obtain definitive evidence further studies are certainly required.

80

Risk Factors for CVD in CKD

Z.A. Massy

University of Picardie-CHU Amiens, Amiens, France

Despite many therapeutic advances in CKD patient care, CVD morbidity and mortality remain high. A number of modifiable CVD risk factors, either traditional or specific to CKD patients, seem to contribute. These patients are most likely to be exposed to CVD risk factors for a long period of time, starting when they had their renal disease. It is therefore of capital importance to provide adequate intervention(s) as soon as possible in order to obtain effective cardiovascular prevention. Such preventive treatment is most likely to be multifactorial. However, the recommended targets of cardiovascular risk factors remain to be validated by evidence based data, since only few randomized, controlled intervention trials examining these questions have been conducted in these patients. Meanwhile, it is reasonable to assume that the risks associated with CVD and the benefits of correcting such factors in CKD patients are at least comparable with those in the general population. Evidently, it is clear such a classical

approach is not sufficient, and further clinical trials are warranted in order to optimize cardiovascular prevention in CKD patients.

81

Implications of the ADEMEX Study

S.K. Mujais

Baxter Healthcare Corporation/Renal Division, Illinois, USA

Cumulative evidence from outcome studies in patients on peritoneal dialysis suggest that peritoneal Kt/V, when used as a single parameter to examine dialysis adequacy, has very limited impact on patient survival and occurrence of morbid events. This is likely due to a convergence of factors among which figures primarily the uninformative nature of Kt/V. This parameter when used in isolation cannot differentiate between underdialysis and appropriate dose provision. To achieve this goal, simultaneous examination of protein catabolic rate and analytes concentrations are required. Additionally, the current doses of dialysis may when examined at a group level be in the ranges that are survival neutral. It is the purpose of this presentation to argue that the approaches to dialysis adequacy in peritoneal dialysis need to be expanded from the uninformative reliance on a single measured parameter, to a more comprehensive approach both on the level of solute clearance and the level of overall care. From the aspect of solute clearance, metabolic correction in relation of the protein catabolic load should guide the dose of therapy. While minimal guidelines for dose of dialysis may be helpful, it is certainly not sufficient to ensure adequate care. From a outcomes optimization standpoint, attention to reduction in cardiovascular risk, correction of comorbidities, enhancement of nutrition, prevention of bone disease and correction of anemia, need all to be addressed concurrently.

82

Pathology of Encapsulating Peritoneal Sclerosis and its Non-Surgical Treatment in Japan

M. Nakayama

Tokyo Jikei University, Tokyo, Japan

The growing incidence of encapsulating peritoneal sclerosis (EPS) been reported recently in Japan, and it is an urgent issue to establish preventative measures for EPS development at present. In this paper, we describe our observational results regarding to the risk of EPS development. Our findings have revealed that long-term CAPD is a risk factor for EPS development after being transferred to hemodialysis from PD, and in most patients, the peritoneal function is characterized by long-standing high-transport state. The laparoscopic findings revealed the involvement of fibrin exudates for the process of EPS development. Since the degree of vasculopathy found in the peritoneum has a close relationship with the duration of PD treatment as well as the increased peritoneal solute transport state, we hypothesize that the development of peritoneal vasculopathy has an important role for the EPS primary pathology.

In terms of EPS treatment, we present the clinical outcomes of steroid therapy and the peritoneal lavage maneuver which have been reported in Japan.

83

Chronic Kidney Disease: Definition, Evaluation and Treatment

R.G. Nelson

National Institutes of Health, Arizona, USA

Chronic kidney disease is a major public health problem affecting millions of people worldwide. Improving outcomes for those with chronic kidney disease requires a coordinated approach to prevention of adverse outcomes through defining the disease and its outcomes, estimating disease prevalence, identifying early stages of disease and antecedent risk factors, and detecting and treating populations at increased risk for adverse outcomes. A growing body of evidence indicates that the adverse outcomes of chronic kidney disease can be prevented or delayed through appropriate treatment, particularly if treatment is initiated in the early stages of chronic kidney disease.

In keeping with its longstanding commitment to improving the quality of care delivered to all patients with kidney disease, the National Kidney Foundation launched the development of clinical practice guidelines that encompass the entire spectrum of kidney disease. The kidney disease outcomes quality initiative (K/DOQI) guidelines permit a more accurate assessment of the true implications of abnormal kidney function and the prevalence of associated illness. Furthermore, they offer guidance regarding appropriate therapeutic interventions based on critical review of the current scientific evidence.

84

The Hidden Truth of Microbiological Quality in Dialysis Water Systems

R. Nystrand

Bio-TeQ Nystrand Consulting, Malmö, Sweden

Water used for dilution of hemodialysis concentrates is to meet official quality recommendations. Several recommendations exist. So far the situation is quite clear, if you forget that there is little harmonization between the recommendations.

But how to analyse? A number of different *cultivation techniques* are in use. Unfortunately they do not have the same efficiency. The differences can be 2–4 logarithms.

Much is spoken about the *water quality*. But, what about the *water system quality*? Few microorganisms will live in the water, most organisms will be on surfaces and they are difficult to prove. Underestimation up to 10,000 times is present when the total microbial content in a water system is calculated.

Is it possible to secure a certain water quality at any time in such systems?

The difficulties in performing good microbiological analysis make it obvious that there are huge amounts of microbiological analytical records which have little to do with the reality.

In order to have a quality assurance in water systems it is necessary to have a good disinfection strategy. The disinfection is not only including the single disinfection procedure but also most important, the *frequency* of disinfection.

All what is said about water and water systems is also valid for central concentrate systems, both central bicarbonate concentrate systems and central acid concentrate systems. Special microorganisms colonize these kinds of systems and consequently special cultivation techniques are to be used.

When the hidden truth about the real microbiological quality is exposed, there is a good bit of thinking to be made.

85

The Impact of Exercise on Dialysis Effectiveness

P. Painter

University of California, California, USA

Physical functioning and physical activity are very low in patients with ESRD treated with dialysis. There is adequate evidence that providing education and encouragement to engage in physical activity, physical functioning improves. Emerging data suggests that low levels of physical functioning as measured by self-report and objective laboratory testing are independent predictors of morbidity and mortality. Likewise, lack of participation in regular physical activity is an independent predictor of death in dialysis patients. Thus, every effort should be made to increase participation in regular physical activity with the goal of increasing physical functioning, quality of life and outcomes.

Physical activity recommendations and encouragement should become a routine part of the medical care of patients with ESRD.

86

Future Approach to the Prevention of the Progression of Diabetic Nephropathy

H.-H. Parving

Steno Diabetes Center, Gentofte, Denmark

Approximately 40% of diabetic patients develop diabetic nephropathy characterized by: Persistent proteinuria, increasing blood pressure, decreasing filtration power and a high risk for cardiovascular events. The following risk factor for developing diabetic kidney disease has been identified: HbA1c, blood pressure, urine albumin excretion rate within the normal range, increased lipids, smoking, retinopathy and gender. Many of these variables also act as progression promoters, i.e. risk factors for losing filtration power in patients with diabetic kidney disease. Improved glycemic control and blood pressure reduction particularly with ACEI and ARB's has been demonstrated

to have a beneficial effect on the development and progression of diabetic kidney disease. Moderate protein restriction has a benefit on progression of diabetic kidney disease. Smoking is playing a significant role particularly for the development of diabetic kidney disease while the impact for progression is less documented. The data of lipid lowering therapy is conflicting in relation to the development and progression of diabetic kidney disease. Multifactorial risk factor intervention is particularly beneficial to diabetic patients in relation to initiation and progression of diabetic kidney disease and other vascular manifestations. Potentially new treatment modalities in preventing and treating diabetic nephropathy will be discussed.

87

Showing the Gaps: A Critical Review of Vascular Access Technologies

H.-D. Polaschegg

Medical Devices Consultant, Koestenberg, Austria

In the technical industry automatic and often computer controlled processes have replaced manual work resulting in reduced cost and improved quality. The processes used for the development, production and after sales support of industrial products are described by ISO9000 and other standards. These standards are also applicable to services, e.g. medical treatments.

Vascular access operations still rely mostly on the craftsmanship of the surgeon resulting in a wide range of reported access patencies. The design of products for vascular access, e.g. catheters is often based on opinion of experienced clinicians rather than hydraulic knowledge.

The use of technology for the improvement of medical treatments requires knowledge of the relevant parameters. Devices and methods for access flow measurement were developed when the correlation between access flow and access patency became known. No methods based on quantifiable parameters exist yet allowing the prediction of flow or failure rates for new accesses. The published strategies for choosing appropriate vessels for fistulas will be discussed in terms of hydraulic and mechanic properties.

Using general knowledge of hydraulics and with the help of in vitro measurements the author has falsified frequently published opinions regarding flow in cannulas, through side holes of catheters and catheter locking solutions. The underlying physical laws, the measurements and consequences for future product developments will be discussed.

88

Fluid Removal for Congestive Heart Failure: A New Task for Dialysis Clinics?

H.-D. Polaschegg

Medical Devices Consultant, Koestenberg, Austria

Congestive heart failure (CHF) is the only form of heart disease still increasing in frequency. According to the American Heart

Association, CHF is the 'Disease of the Next Millennium'. Mild chronic CHF is currently treated with drugs including angiotensin converting enzyme (ACE) inhibitors, positive inotropic agents, diuretics, digitalis, and, more recently, β -blockers. Chronic CHF tends to deteriorate and patients may experience an abrupt, severe deterioration in heart function, termed acute congestive heart failure. Much higher doses of the same drugs as in chronic CHF are used requiring hospitalization of the patient and treatment in the ICU.

Slow continuous ultrafiltration (SCUF) has been used successfully for the treatment of acute CHF. It has been found that relapse after ultrafiltration treatment is delayed for a much longer period as compared to conventional drug treatment. The machines currently used for this treatment are complicated requiring specially trained personnel. The treatment is usually done in the ICU.

The author has participated in the development of a novel device allowing SCUF in an outpatient setting using peripheral blood access. This device which uses an air free extracorporeal circuit with a smooth flow path has the size of a large infusion pump. The only parameter that needs to be adjusted by the operator is the ultrafiltration rate. Problem free continuous treatment for more than 12 h has been reported. In the future this device may be used not only for the treatment of acute CHF but also for the treatment of severe chronic CHF. Hemodialysis clinics may be suitable for providing this treatment because of their experience with the organization of chronic blood treatment.

89

Technologies for Cost-Effective Home and Daily Dialysis

H.-D. Polaschegg

Medical Devices Consultant, Koestenberg, Austria

Daily haemodialysis is related to superior patient wellbeing as compared to regular dialysis. Reduced patient morbidity has been reported to reduce the total cost of daily dialysis to the cost of four regular treatments. The cost of the additional treatments is partially compensated by the reduced cost for medication and hospitalization.

Two modalities for daily treatment are currently popular: Overnight and short dialysis at home and short dialysis in the clinic. Standard haemodialysis machines are used for both modalities today. Standard machines are designed for a wide range of treatment modalities. For daily dialysis machines can be simplified allowing cost reduction.

For the clinic, the author proposes a central delivery system for 'raw-dialysate' containing the minimum concentration of all dialysate solutes. Additional solutes are added patient specific by bedside monitors. The bedside monitors control ultrafiltration and comprise simplified air-free extracorporeal circuits allowing fast setup by the patient. This approach does not require any technical novelties. This system can be designed employing readily available technology.

For overnight dialysis at home, dialysis machines can be made smaller and less noisy by reducing peak dialysis flow to 300–500 mL/min (as compared to 800–1,000 mL/min). 'True' integration of the reverse osmosis unit for water treatment reduces the number of hydraulic components and allows energy savings.

The use of modern technology for the hydraulic circuit (piezo-electric pumps and valves and optimized rotary pumps) allows reduction of size and saves energy.

90

The Chronic Renal Insufficiency Cohort (CRIC) Study

M. Rahman

Case Western Reserve University, Ohio, USA

Objectives: The overarching aim of the CRIC study is to establish an enduring, collaborative research group capable of examining hypotheses concerning disease etiology, diagnosis, health outcomes, and health services utilization among a cohort of patients with chronic kidney disease (CKD). The two main hypothesis are (a) a set of non-traditional risk factors is associated with both progression of CKD and the development of ESRD and (b) a set of non-traditional risk factors is associated with cardiovascular (CVD) events and measures of CVD progression in the setting of CKD.

Research Plan: This is a prospective cohort study of 3,000 racially diverse adult patients at 7 clinical centers across the US, with mild to moderate CKD. Half of CRIC participants will have diabetes, their ages will range from 21–74 years, and their estimated glomerular filtration rate (GFR) at entry will be stratified by age.

Methodology: Baseline evaluation will include estimation of renal function (by iothalamate clearance in a subset), assessment of sociodemographics, prior comorbidity and treatment, psychosocial attributes, quality of life, prior health care resource utilization as well as anthropometry and selected biochemical measures. Subclinical CVD will be detected using EKG, ankle brachial index, echocardiography, and electron beam CT scans (in a subset). Patients will be seen at yearly intervals. Renal outcomes include reductions in GFR and level of proteinuria and end-stage kidney disease. CVD outcomes include clinical CVD events and progression of subclinical CVD.

Significance: The CRIC study is expected to identify risk factors for CKD and CVD events among patients with CKD and to develop predictive models that will identify high-risk subgroups. Improved recognition of etiological factors will permit development and testing of interventions to reduce the burden of advanced renal failure and cardiovascular morbidity and mortality.

91

Risk Factors for Proteinuria in a Multiracial Southeast Asian Population

S. Ramirez

National University of Singapore,
National Kidney Foundation Singapore, Singapore

With the epidemic rise of ESRD in multiple regions of the world, there is an urgent need to implement programs to address this increasing burden of kidney disease. We illustrate a public health approach using the program of the NKF Singapore that incorporates stepwise primary, secondary and tertiary strategies for prevention.

This presentation discusses the factors associated with proteinuria in a large multi-racial Asian population who took part in a screening program aimed at the early detection of renal disease. Out of 213,873 adults who participated, 189,117 with complete data were included.

Malay race, increasing age, both extremes of body mass index (BMI), self-reported family history of kidney disease (FKD), and higher SBP and DBP measurements, even at levels still classified as within the normal range, were independently associated with dipstick positive proteinuria. The odds ratios (OR) for proteinuria increased progressively with age. There was a J-shaped relationship between BMI and proteinuria (OR of 1.3, 1.00, 1.3, 1.6 and 2.5 for BMI $\leq$ 18.00, 23.00–24.99, 25.00–27.49, 27.50–29.99 and $\geq$ 30.00 kg/m², as compared to BMI of 18.01–22.99 kg/m², respectively). OR for proteinuria by SBP and DBP were significantly increased beginning at levels of 110 mmHg and 90 mmHg, respectively. In addition, the Malay race had a significantly higher OR for proteinuria as compared to the Chinese (OR of 1.3). Finally, FKD was significantly associated with proteinuria (OR of 1.7), whereas FDM and FHTN were not. Indeed, when family history was analysed by cluster, isolated FKD remained a significant determinant of proteinuria and the magnitude of the effect was not significantly different than that observed in the presence of co-existing FDM or FHTN. This is the first study to evaluate factors associated with proteinuria in an Asian population. The epidemiologic study of renal disease in this population suggests that risk factors for renal disease may differ significantly across racial groups.

92

End-Stage Renal Disease in Australia and New Zealand: The ANZDATA Registry

G. Russ

Queen Elizabeth Hospital, Australia

The ANZDATA Registry has collected information on patients receiving chronic treatment for end-stage renal failure by dialysis or transplantation in Australia and New Zealand since the 1960s. At the 31st of December 2002 there were 658 per million of population (PMP) in Australia and 686 in New Zealand receiving renal replacement therapy. 292 per million in Australia and 283 per million in New Zealand had a functioning kidney transplant. In 2002, 94 patients per million in Australia and 115 per million in New Zealand commenced treatment. The mean age at commencement of treatment was 59 years and 55 years in the two countries respectively. In Australia, 26% of new patients had glomerulonephritis attributed as the cause of their renal failure and 26% had diabetic nephropathy. In New Zealand diabetic nephropathy accounted for 45% and glomerulonephritis 23%. In Australia there has been an increase in the number of prevalent dialysis patients by approximately 6% per year. The majority of these patients (71%) were out of hospital, with 37% dialysing at home and 36% in satellite centres. 16% of all prevalent dialysis patients are using continuous ambulatory peritoneal dialysis and 8% automated peritoneal dialysis. For New Zealand, the dominant mode of dialysis is peritoneal (40% CAPD, 8% APD). The transplant rate in 2002 was 31 and 30 PMP in the two countries respectively. The living donor transplant rate was 39% and 41% in each country. For primary cadaver grafts performed in 2001 in Australia, the 12 month patient and graft survival rates were 94% and 91% respectively. The five year survival rates for operations performed in 1996 were 85% and 76%.

93

Options of Renal Replacement Therapy in Developing Countries

B. Rutkowski

Gdansk Medical University, Gdansk, Poland

Renal replacement therapy (RRT) is becoming more and more wider used in treatment of ESRD patients throughout the world. In 1990 nearly 0.5 million people underwent this kind of therapy, in 1996 – 1.0 million and in 2001 nearly 1.5 million. It has to be underlined that availability of this kind of treatment is unequivocal throughout the world. There are countries with over 1,000 patients per million inhabitants on RRT (Japan, USA). On the other hand in Africa or Asia there are regions where this type of treatment is still in very initial stage. It is visible especially in countries with huge populations like India, China or some countries located in Central Africa. Also in Russia availability of RRT is still limited. Nevertheless during the period of last 10 years in all these regions similarly like in Central and Eastern Europe significant progress was achieved in this matter. One of the best examples is Poland, where after political and economical liberation number of RRT patients was increased by four times. It is worth to emphasize that worldwide epidemic of ESRD patients with diabetic nephropathy and elderly people is noted. According to the predictions presented in the literature over 2.5 million of ESRD patients will need RRT in 2010. Predicted increment of ESRD population without any doubts will cause not only medical but mainly economical problems for health care systems throughout the world. Education of medical community, wider implication of adequate conservative treatment delaying renal failure, peritoneal dialysis and/or preemptive renal transplantation are necessary to rationalize expenses and enable further progress in this matter.

94

New Results from the International Dialysis Outcomes and Practice Patterns Study (DOPPS)

R. Saran

University of Michigan, Michigan, USA

The DOPPS is a prospective, longitudinal, observational study of hemodialysis (HD) patients currently enrolling patients in 12 countries (7 European countries, Australia, New Zealand, Canada, Japan and the United States). DOPPS is not designed as a registry of all HD patients; rather, representative HD facilities are randomly selected in each participating country and a random sample of patients is recruited at each facility. In DOPPS I (1996–2001) there were >52,000 HD patients listed on the census for mortality analyses, and >17,000 sample patients from whom detailed data was collected by comprehensive questionnaires. In DOPPS II (2002 onwards), data on approximately 35,000 census patients, and between 10,000–11,000 sample patients has been collected thus far (with a goal of eventually obtaining 15,000 sample patients for long term follow-up). The Data Coordinating Center is at URREA, in Ann Arbor, MI, USA. DOPPS has, as its chief aim, the identification of practice patterns that are associated with

improved outcomes for HD patients after extensive statistical adjustments. In particular, detailed data on comorbidity and medication use is a major strength of DOPPS. The major outcomes being examined are mortality, hospitalization, vascular access and quality of life. Data from some of the recently published papers from DOPPS will be presented, in addition to important recent unpublished findings that are very likely to influence practices related to hemodialysis around the world.

95

New Insights on the Pathogenesis of Acute and Chronic Rejection

M.H. Sayegh

Brigham and Women's Hospital, Massachusetts, USA

The most common cause of late allograft failure, excluding death with a functioning graft in the case of kidney transplantation, is a clinicopathologic entity termed chronic rejection, a feature common to all solid organ transplants, including kidney, heart, lung, pancreas and to a lesser extent, liver. Morphological findings associated with this process include progressive narrowing of hollow structures within the allograft, regardless of whether they are vessels (heart and kidney), bronchioles (lung) or ducts (pancreas and liver). Despite extensive research, the precise mechanisms responsible for the characteristic pathological changes seen in chronic rejection remain unclear. Both alloantigen-independent and alloantigen-dependent mechanisms have been shown to be responsible for the development and progression of chronic rejection, although it is clear that the alloimmune response predominates. Alloantigen-independent factors include organ injury secondary to brain death in the donor, ischemia/reperfusion injury, cytomegalovirus (CMV) and other infections, hypertension, hyperlipidemia, cellular senescence, and toxicity of immunosuppressive medications. These factors likely act in concert with the alloimmune response and may not of themselves be sufficient to effect the characteristic changes seen in chronic rejection. Indeed, several lines of clinical and experimental evidence support the critical role of the alloimmune response in initiation and progression of chronic rejection. These include the influence of HLA matching, the impact of acute rejection and under-immunosuppression, and most importantly, in the experimental models, the prevention of chronic rejection when tolerance is induced. The immunopathogenetic mechanisms of chronic allograft rejection and new approaches to therapy will be discussed.

Reference

Womer KL, Vella JP, Sayegh MH: Chronic allograft dysfunction: Mechanisms and new approaches to therapy. *Semin Nephrol* 2000;20(2):126–147.

96

Challenges to Achieve Immunosuppression-Free Long-Term Engraftment

M.H. Sayegh

Brigham and Women's Hospital, Massachusetts, USA

Achieving clinical transplant tolerance has been a longstanding goal of transplant biologists. Its attainment would allow patients to be spared from the non-specific immunosuppression that is currently required, with all the associated adverse drug effects, and should also prevent the significant graft loss due to chronic rejection, thus optimising the lifespan of the transplanted organs. However, achieving tolerance remains an elusive goal at the present time, despite a wealth of experimental data relating to this subject.

The aim of clinical tolerance is not to achieve complete unresponsiveness towards the graft, but rather to induce a non-destructive immune response towards it, in the presence of generalised immune competence. Operationally we define it as the absence of acute and chronic rejection with indefinite graft survival and normal graft function, in an immunocompetent host. This is achieved through the silencing of alloreactive T cells by exploiting the physiological mechanisms of tolerance, which usually serve to prevent autoimmunity.

The most significant hurdle is how best to achieve and measure tolerance. There are numerous manipulations in rodent model systems that appear to induce long-lasting donor specific tolerance. Ultimately, the most successful of these strategies will need to be tested on large animal models (including non-human primates) so that the safety and efficacy of the regimen can be validated prior to being tested in the clinical setting. There are a number of examples of clinical transplant tolerance that have been already been achieved in humans. These include patients who have stopped or were withdrawn from their immunosuppressive drugs and not lost their grafts, patients who received total body irradiation as induction therapy, and patients who received combined bone marrow and kidney transplants from the same donor. The Immune Tolerance Network (www.immunetolerance.org) approved and is currently conducting several new tolerance protocols in human kidney and islet transplant recipients and plans are underway to expand this to liver transplantation. The next major hurdle is knowing when we have achieved tolerance. Accurate immunological and molecular assays to measure such tolerance are required, so that we can monitor its induction and its breakdown, should that occur. It is possible that a panel of assays will be required to provide an adequate immunological profile that no test could achieve singly. Finally, other important hurdles include issues of infections, chronic rejection, patient selection etc. will be discussed.

97

Genetic and Genomic Approaches to CKD Progression

J.R. Sedor

Case Western Reserve University Ohio, USA

The incidence of end-stage renal disease (ESRD) is increasing worldwide despite efforts to slow progression of chronic renal failure

(CRF) by controlling blood pressure and hyperglycemia. Two available therapies for ESRD, dialysis and transplantation are expensive and are at best palliative. Recently, data from several laboratories have demonstrated that ESRD is under substantial genetic control, and efforts to identify these genetic determinants are underway. Identifying genes for ESRD pathogenesis has several goals. First, understanding the genetic basis of ESRD offers a means to clarify the mechanisms that result in kidney pathobiology. Second, better and new treatments for prevention of progression of CRF to ESRD may be developed. Third, individuals at risk could be identified early in their course and targeted for intensive therapy. Finally, the products of genes causing disease become target molecules for gene therapy. We discuss data from our laboratories, which employ two different molecular genetic strategies for identifying ESRD pathogenesis genes. In contrast to traditional experimental design, both approaches are hypothesis-generating, identifying candidate molecules for further study, rather than hypothesis-driven and may provide novel insights into mechanisms of renal disease progression.

98

Diabetes Management: Dealing with the Epidemic

E. Strock

International Diabetes Center, Minnesota, USA

Diabetes is a common, costly and serious chronic disease affecting an estimated 300 million individuals worldwide. Over the past decade the prevalence of diabetes has increased by 33%. This rapid growth is seen in all ages and across all ethnic groups, with a significant increase in the number of children and adolescents now diagnosed with type 2 diabetes. This is of particular concern throughout Asia. Diabetes is the leading cause of end stage renal disease accounting for over 43% of cases. New standards for diabetes care have been established in many countries, however these standards are not being met. Studies have shown that diabetes-related complications can be minimized or prevented through good metabolic control. New therapeutic options for treating diabetes and related complications have expanded tremendously in the past five years including new oral agents used alone or in combination and as well as short and long acting insulin analogues, however they continue to be underutilized. Staged Diabetes Management (SDM) is a systematic, evidence-based approach to diabetes care and education which has been shown to significantly improve metabolic control and reduce complications. SDM has been implemented in over 25 countries worldwide. Nurses have utilized SDM in collaboration with physicians to improve outcomes with their patients. This session will focus on the role of nurses in the prevention and management of diabetes. An update on current diabetes therapies and management strategies focusing on treatment-to-target approaches, will be provided. Strategies for prevention of diabetes and diabetes-related complications will be presented. Participants will have the opportunity to apply new knowledge through interactive case studies.

99

Evolution of Daily Dialysis and its Clinical Benefits

J. Tattersall

St. James's Hospital, Leeds, UK

Daily dialysis has been used for over 30 years. Until recently, it has not been a main option due to the increased inconvenience to the patients and perceived cost.

Recently the poor long-term outcome for standard dialysis has been much discussed. Much of the mortality of dialysis patients is related to inadequate homeostasis of fluid, blood pressure, calcium and phosphate.

Unless assisted by significant renal function, intermittent dialysis is unable to maintain fluid and blood pressure homeostasis. With standard thrice-weekly dialysis, small solute clearance cannot be greater than around 12% of normal renal function.

In theory, daily dialysis is capable of overcoming these limitations to a great extent. By reducing fluid and solute accumulation between dialysis, daily dialysis is functionally closer to normal kidney function.

In the last few years, technological advances have made daily dialysis easier to deliver. There is mounting evidence to support superior clinical outcomes.

100

Medical Software Design: Regulatory and QA Issues

J. Tattersall

St. James's Hospital, Leeds, UK

Medical software is increasingly used to control medical devices and inform medical decisions. Where the software is an essential part of the medical device (embedded software), it is clearly a safety-critical component of the device and subject to regulatory approval.

Stand-alone software to present clinical data and inform medical decisions is equally critical and ubiquitous. In its simplest form such systems include on-line access to laboratory or other patient information. More complex systems handle pharmacy prescriptions, electronic patient records and clinical decision-support tools such as urea kinetic modelling.

Medical software must be capable of being repeatedly updated or adapted to incorporate new medical knowledge. These changes may undermine the original planned specification and have major impact on safety. Modern software is increasingly designed using 'Agile' methodologies to be more easily and safely adapted in the future. This means that comprehensive documented planning of the software is not possible, posing challenges for regulation and QA.

Object-oriented design, automated testing and formal project management methods are increasingly seen as desirable or essential for safety.

The new regulatory standard AAMI SW68 attempts to address these issues by requiring that the software is designed within a certified quality system and includes demonstrable risk-assessment. The standard covers both the initial development and the process of

maintenance, documentation, configuration, verification and problem resolution.

101

Technology System to Support Clinical Outcomes

J. Tattersall

St. James's Hospital, Leeds, UK

Clinical staff are expected to make correct decisions at the appropriate time. This requires staff to have up to date knowledge of all aspects of medicine and the patient's condition and to have sufficient time to consider the options.

In the busy clinical department computer-assisted decision-making has the potential to help achieve this ideal.

A specific aspect of care can be managed automatically to achieve a desired outcome. Examples include the management of renal anaemia, dialysis adequacy and blood lipids using a computer algorithm.

Large amounts of data can be assessed by decision support software to produce a probable diagnosis or recommended action. This may become increasingly necessary, as decisions become guided by complex genetic information.

Defined data may be checked automatically to alert for potential problems or to plan management. Examples include automatic checking and alerting of out-of range laboratory results, identification of patients with renal failure in the community from laboratory results and checking for interactions between prescribed drugs.

As we increasingly rely on these systems, safety and legal aspects are important. Keeping the technology up to date with new medical knowledge, managing increasingly complex systems and integrating an increasing number of systems will be challenging.

102

Clinical Implications of Impure Dialysate and Techniques for Ensuring Ultra-Purity

J. Tattersall

St. James's Hospital, Leeds, UK

For many years, it has been recognized that dialysis patients have a greatly increased risk of developing and dying from heart and vascular disease.

Similarly, dialysis patients are at an increased risk of malnutrition and this also increased mortality. A low serum albumin has been considered as a marker of malnutrition and is strongly predictive of reduced survival. Recently, low serum creatinine, a marker of reduced muscle mass has also been shown as a strong predictor of reduced survival.

There is increasing evidence that heart and vascular disease, muscle wasting and malnutrition are linked to, and may be entirely or partly caused by, chronic inflammation. This is a state of chronic over-stimulation of the immune system, which is normally involved

in the response to infection. This causes various changes, including, atherosclerosis, muscle wasting, change in liver function, anorexia and muscle wasting.

Dialysis patients have been shown to be in a state of chronic inflammation and that this may be due partly to impurities in the dialysate, which pass through the dialyser membrane into the blood.

Methods for removing these impurities include an appropriate water treatment, adequate disinfection of the dialysis machine, water treatment and delivery system and ultrafiltration of the dialysate at point of use. Dialysate purity should be monitored and managed to ensure optimum survival for the haemodialysis patient.

103

Role of Wireless Communications and Telematics

J. Tattersall

St. James's Hospital, Leeds, UK

Standard computer and network hardware is designed for offices. In the hospital, the standard system, which delivers data by wired connection to a desktop computer is suitable for clerical, administrative or secretarial offices, but is less suitable for clinical areas. Clinical workers in hospital, require mobile or bedside access to data. This is easiest to implement using mobile computers (such as a Tablet PC or PDA) connected to the network wirelessly using IEEE 803.11. Clinical workers in the community may connect by mobile phone.

Standard desktop computers in the clinical area may need to be moved occasionally to make room for other equipment or beds. In this setting the wireless network is most appropriate, since rerouting the network wiring is expensive and disruptive.

Wireless data communication is potentially less secure than wired communication, especially when the public mobile phone system is used. This is an important consideration when clinical data is being transmitted or if the system communicates with the main hospital system. Wireless networks can implement sophisticated security but this requires careful planning.

Wireless network access points and wireless communication cards for computers and peripherals are marginally more expensive than the wired equivalents. However, the wireless system can be cheaper overall when the cost of wiring is taken into account.

Transmission of data from equipment (such as dialysis machines) and voice (e.g. from Smart Phones) over the wireless network is also possible and increases its usefulness.

ANCA-Associated Vasculitis: Insights from the European Vasculitis Study Group (EUVAS)

J.W.C. Tervaert

University Hospital Maastricht, Maastricht,
The Netherlands

ANCA-associated vasculitis (AAV) is frequently associated with glomerulonephritis. During the last decade EUVAS proposed a system of clinical subgrouping based on the presence of kidney involvement or not. Patients with kidney involvement can be divided into severe renal involvement (serum creatinine $>500 \mu\text{mol/L}$), moderate renal involvement (serum creatinine between $120\text{--}500 \mu\text{mol/L}$) and early renal involvement (serum creatinine $<120 \mu\text{mol/L}$). Standard therapy of these patients consists of prednisolon and cyclophosphamide. In patients with severe renal involvement, the addition of plasma exchange was found to be superior to pulse solumedrol as induction therapy. For patients with moderate renal involvement, after induction of remission switch to azathioprine as compared to continuation of cyclophosphamide is equally effective and probably induces less toxicity in the long run. For patients with early renal involvement, cyclophosphamide can be replaced by methotrexate (15–25 mg once per week). Cyclophosphamide in all these trials has been given orally. Whether oral cyclophosphamide can be replaced by intravenous pulse cyclophosphamide is currently being studied. Furthermore, the duration (2 years vs. 4 years) of azathioprine maintenance therapy is under study. Whether other drugs than azathioprine, such as methotrexate, MMF and/or anti-TNF, are more effective for maintenance therapy remains to be studied. In patients that are refractory to standard therapy intravenous immunoglobulins, anti-T cell and anti-B cell therapy has been proven to be effective. Whether these expensive drugs can reduce the total costs of vasculitis-related hospitalizations (over 150 million per year in the USA) is not yet certain.

Cytokines and Adhesion Molecules in Renal Vasculitis

J.W.C. Tervaert

University Hospital Maastricht, Maastricht,
The Netherlands

In renal vasculitis analysis of cytokine and adhesion molecule action has been studied by analysis of in situ expression of the molecules in tissues and on circulating cells and by measuring serum levels both in patients and in experimental animal models. Development of vasculitis relies on dynamic interactions among leukocytes, endothelial cells and extra cellular matrix proteins. Serum levels of proinflammatory cytokines are increased during active disease. Proinflammatory cytokines such as tumor necrosis factor- α , interleukin-1 and interleukin-8 have been shown to induce expression of ANCA target antigens on the surface of human leukocytes. Furthermore, these cytokines induce leukocytes to adhere and to migrate through endothelial cells.

Both T-helper 1 and T-helper 2 type cytokines are involved in the pathophysiology of renal vasculitis. Experimental animal models, however, demonstrate that T-helper type 2 cytokines are protective against crescent formation. In kidney biopsies up regulation of ICAM-1 and VCAM-1 is found. Serum levels of soluble ICAM-1, VCAM-1 and E-selectin are elevated in untreated active renal vasculitis patients but not during remission. Therapeutic studies have been performed in animal models. In humans, until now, only anti-CD18 and anti-TNF therapy has been demonstrated to be effective in a proportion of patients.

Update on the Therapy of IgA Nephropathy from Japan

Y. Tomino

Juntendo University School of Medicine, Tokyo,
Japan

The committee on IgA nephropathy of the Special Study Group on Progressive Glomerular Disease, Ministry of Health, Labor and Welfare of Japan published new clinical guidelines for the diagnosis and treatment of patients with IgA nephropathy in Japan. Patients with IgA nephropathy are divided into the following four groups at the time of renal biopsy: (a) Good prognosis group: almost no possibility of dialysis; (b) Relatively good prognosis group: possibility of dialysis is relatively low; (c) Relatively poor prognosis group: dialysis is likely to be required within 5–20 years; and (d) Poor prognosis group: the possibility of dialysis within 5 years is high. Based on these clinical guidelines, the committee on IgA nephropathy performed a multicenter trial on adrenocorticosteroids (PSL). IgA nephropathy patients were divided into two groups: PSL plus dilazep hydrochloride (anti-platelet drug) (PSL) group (33 patients) and dilazep hydrochloride alone (36 patients) (dilazep) group. All these patients showed creatinine clearance (CCr) levels of more than 70 ml/min. The mean level of urinary protein excretion after one or three years of treatment ($0.92 \pm 1.21 \text{ g/day}$, $0.82 \pm 1.03 \text{ g/day}$) was significantly lower than that before the start of treatment ($1.39 \pm 0.81 \text{ g/day}$) ($p < 0.05$) in the PSL group. There were no significant differences in the mean level of CCr before and after one to four years of treatment in the PSL group. It appears that combination therapy with adrenocorticosteroids and dilazep hydrochloride was effective for patients in the mild stage (relatively good prognosis and relatively poor prognosis groups) of IgA nephropathy. Furthermore, I will discuss the efficacy of tonsillectomy and steroid pulse therapy in such patients.

Service Quality Measurement – An Essential Process to Improve Quality of Care

N. Venkataraman

National Kidney Foundation Singapore, Singapore

Tracking service quality levels within the organization is a key process in many industries. The healthcare industry is no exception. Evidence exists that a majority of adverse events, arising out of human factors, are within the control of the service provider. There is a strong link between satisfaction and safety from the patients perspective. The need for minimizing human error in a clinical setting has been well documented and healthcare service providers have effectively used information technology to address some of these issues. The SQuest tool, developed in 2001, incorporates measurement of customer perceived service shortfalls and can be used by management to sustain continual quality improvement programs. Service attributes and criteria for measuring the quality of services need to be carefully defined before a SQ measurement process is initiated. The tool should be flexible, simple and easy to use. In the case of a multi-racial and diverse patient population, a multi-lingual feature would be appropriate. This is important as customer perceptions are key to the measured SQ levels. Use of patient advocates in the data capturing process is helpful especially in an elderly patient group. An online version of the SQ measurement tool will greatly assist in process implementation as this allows customer assessment away from point of care. Data should be analyzed periodically for implementing corrective and preventive actions and linked with the performance score-card for clinical services. The philosophy is 'what gets measured gets done' and this ensures a consistent output by all service providers, internal and external, to continually improve the overall quality of care.

Outcome of Puncture Technique in Fistulae and Grafts

J.-P. Van Waelegheem

University Hospital Antwerp, Belgium

Successful long-term hemodialysis depends to a large extent upon a trouble-free vascular access (VA). Not only the creation but also the use and maintenance of the VA by patients and nurses strongly determine the outcome of the VA.

The puncture technique is one of the most critical manipulation of the whole hemodialysis treatment. Also the conditions and materials used may play a very important role.

We studied the management of the VA in 1,385 European patients within the research board of the EDTNA/ERCA. The ropeladder ($n = 334$) and the area puncture ($n = 358$) techniques were most popular in comparison with the single button hole ($n = 139$) and the multiple button hole ($n = 133$) techniques. Although the ropeladder technique showed the lowest VA complications compared to the other techniques we are convinced that the single button hole technique is

the preferred technique for many types of VA. Moreover the use of ropeladder technique is only possible in forearm fistulae with long vascular tracts. In all other types of VA such as the elbow brachiocephalica construction, the upperarm fistula and even the AV graft, the use of single button hole technique is preferred. In high pressure fistulae and grafts we change puncture place every month to avoid bleeding and false aneurismata formation.

The use of metal needles showed the lowest complications 16% compared to teflon catheters 27%. Also the patient nurse ratio had an impact on vascular access complications. Dialysis units with a patient ratio of 7 or higher showed significantly more flow problems and thrombosis.

In conclusion, the puncture technique should be selected according to the anatomy and type of AV fistula or graft. Moreover, materials for cannulation and staff conditions also may play an important role in VA outcome.

The Genetics of Familial Focal Segmental Glomerulosclerosis

M.P. Winn

Duke University Medical Center, North Carolina, USA

Focal and segmental glomerulosclerosis (FSGS) is a pathological entity which is a significant cause of end-stage renal disease (ESRD). More than 20% of individuals with ESRD have FSGS in the US. All ethnicities are affected. The diagnosis of FSGS is based on areas of glomerular sclerosis and tuft collapse that are both focal and segmental on renal pathology. Proteinuria, nephrotic syndrome and frequently the progressive loss of renal function are the clinical hallmarks of this disorder. At present, there are no consistently reliable treatments for FSGS with response rates estimated at less than 30–50%. FSGS has primary (idiopathic), secondary and familial forms. Advances in molecular genetics technology and mapping, including high-throughput genotyping for genomic screening, provide powerful tools for the analysis of renal diseases. Genes associated with many familial renal disorders that lead to ESRD have been isolated; these include Alport's nephropathy, familial juvenile nephrolithiasis and polycystic kidney disease. Recently, three genetic mutations causing hereditary forms of nephrotic syndromes have been described. These include nephrin (NPHS1), podocin (NPHS2) and α -actinin 4 (ACTN4). These genes are involved in the cytoskeleton of the podocyte or the slit diaphragm. Further understanding of the molecular pathogenesis of these mutated genes will provide additional insight into FSGS.

East Meets West Ethical Dilemmas for Nursing and Ways of Working Together Effectively: Impact in Asia

K. Yetti

University of Indonesia, Jakarta, Indonesia

The development of nursing profession is influenced by several factors. One of those is education. The milestone of nursing education in Indonesia had been developed in early 1960s, where the nurses were trained in a tertiary education to be graduated at diploma level. However, the bachelor program was initiated two decades later, which was in 1985; and master program in certain area of nursing has been started four years ago. Within this 40 year the nursing profession in Indonesia has been trying to struggle the fact of having left behind. To improve the role of nurses to become nurse provider, nurse manager, nurse educator or nurse researcher, nurses in Indonesia faces some limitation. These limitations might be different from their colleagues in other countries. 180,000 nurses are registered in Indonesian Nurses Association, they spread out in thousand of islands. They differ in education, economical and cultural background. The limitation in English language to read and adjust the western literatures into Indonesian context exists. The situation is perceived as dilemma for nursing in Indonesia. In one hand, nurses in Indonesia are willing to move forward like their colleagues in western countries. On the other hand, many obstacles inter and intra profession has to be encountered and anticipated in order for nurses in Indonesia to achieve their professional identity.

socially acceptable methods and technology made universally accessible to individuals and families in the community through their full participation, and at a cost that the community and the country can afford to maintain at every stage of their development in the spirit of self reliance and self determination'. In Indonesia PHC is regulated as a part of Health Care System and is translated in several programs. The program of PHC in Indonesia is based on government priority in health through community participation. However, the main focus of PHC in Indonesia is aimed at solving the very basic of community health problems such as diarrhea, malnutrition or immunization. Dialysis and transplantation perceived as chronic illness problems that need high technology in its treatment. It is not perceived as a government priority. However, the Indonesian Nephrology Nurses Society (INNS) has been working on this issue and it will be completed in the near future. The aim of PHC program being formulated is to empower the patients and their families to be able to participate in their health care. The INNS realizes this aim is not as simple as it says. Several aspects, such as patients' life styles, economical, and cultural background have to be taken account. Moreover, the values and believes among health care providers toward nursing/health care will play an important role to conduct the PHC. These all need a 'bright' strategic in order to be accepted by the patients and families and especially by the health care providers. As the aim of PHC program is to empower the patients and their families, so some efforts should be created based on the limited resources.

Primary Health Care: Is Prevention the Solution to Limited Resources? The Case Study in Asia – The Competing Needs

K. Yetti

University of Indonesia, Jakarta, Indonesia

Primary Health Care (PHC) as defined at Alma Ata in 1978 is 'essential health care based on practical, scientifically sound and

Medical – Basic Science

112

Proteinuria Inducing Activity of Hemopexin

W.W. Bakker

University Hospital of Groningen, Groningen,
 The Netherlands

Human plasma hemopexin (Hx) is believed to act as a protective molecule against oxidative injury.

Previously, we observed that plasma Hx can induce proteinuria in rats in combination with affection of glomerular alterations identical to those observed in minimal change disease (MCD). Heat inactivation (HI) of Hx was able to prevent this effect.

To answer the question whether the Hx molecule per se or a contaminating plasma constituent is due to the putative enzymatic activity of Hx, we now prepared r-Hx by transfection of the human gene constructed by PCR techniques in the yeast *Pichia pastoris*, using primers covering the complete coding region of Hx. The gene product was analysed using affinity chromatography with anti-Hx IgG, PAGE and Western blotting.

Either r-Hx ($n = 9$) or HI-r-Hx ($n = 8$) was perfused into the left kidney of anaesthetized rats (100 μ g/ml saline) for 6 min followed by diluted rat serum (10.0 mg/ml saline) for 10 min. Using urether cannulation, urine was collected before and after 5.0, 10.0 or 15.0 min after perfusion, analysed for protein content (pyrogallol method), and calculated as mg per 24 h.

The results show a gene product of about 85 kD, identical with the 85 kD band observed in plasma Hx samples after staining with polyclonal anti-Hx IgG. HI-r-Hx showed an identical 85 kD band. After renal perfusion of either r-Hx or HI-r-Hx significant protein leakage is seen exclusively using r-Hx perfusion after 5, 10 and 15 min (6.23 ± 4.40 vs 3.62 ± 2.70 ; 36.13 ± 10.30 vs 2.76 ± 1.17 ; and 24.97 ± 2.90 vs 3.93 ± 1.40 respectively).

It is concluded that the Hx molecule, rather than some other unknown plasma constituent, is able to affect the glomerular filtration barrier leading to proteinuria. Since we recently detected enhanced Hx activity in subjects with MCD in relapse versus remission, we feel that an active isoform of plasma Hx may play an important role in the pathogenesis of MCD.

113

Renal Protective Effect of Pitavastatin on Spontaneously Hypercholesterolemic (SHC) Rats

X.M. Liang, M. Mune, H. Otani, Y. Tone,
 N. Hirasaka, S. Yukawa

Wakayama Medical University, Internal Medicine (III),
 Wakayama, Japan

Purpose: The renal protective effects of pitavastatin, a new 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor was examined in our study.

Methods: Spontaneously hypercholesterolemic (SHC) rats spontaneously develop hypercholesterolemia, proteinuria and glomerulosclerosis with age, and they finally die as a result of renal failure. In this study, 11 male SHC rats from 10 weeks of age were treated with pitavastatin at a dose of 100 mg/kg of diet, while another 11 male SHC rats received no specific therapy as controls. Body weight, urinary protein level, and serum constituents were evaluated every 4 weeks until the rats reached the age of 22 weeks old. Low-density lipoprotein (LDL) and high-density lipoprotein (HDL) were isolated at 22 weeks of age and the resistance of LDL and HDL to copper-induced oxidation was measured by continuous photometric monitoring of diene formation at 234 nm. At the end of the experiment, rats were studied for histology and immunohistochemistry.

Results: During the experimental period, body weights and food intake were similar in both groups. Pitavastatin treatment did not affect hypercholesterolemia but significantly reduced proteinuria (251 ± 40 vs. 320 ± 85 mg/24 h, $p < 0.05$, at 22 weeks) and preserved creatinine clearance (0.28 ± 0.018 vs. 0.20 ± 0.024 ml/min/100 gBW, $p < 0.05$, at 22 weeks). The treatment of pitavastatin prolonged the lag time of LDL and HDL to 126% and 153% respectively as compared with the control group at 22 weeks of age. The glomerulosclerosis index (SI) was significantly higher in the untreated control rats than that of the pitavastatin-treated group (138 ± 27 vs. 96 ± 22 , $p < 0.01$). Immunohistochemistry showed significant high numbers of ED-1 positive macrophage in the glomeruli and interstitium of control rats.

Conclusion: These results show that pitavastatin has renal protective effects in SHC rats independent of a cholesterol-lowering effect.

Participation of α -Smooth Muscle Actin-Positive Cells in Renomedullary Interstitial Cell Tumors

N. Kuroda, M. Toi, M. Hiroi, H. Enzan

First Department of Pathology, Kochi Medical School, Nankoku, Japan

Purpose: To elucidate the detailed histologic features and the origin of the constituting cells in renomedullary interstitial cell tumors.

Methods: We examined the histologic features of eight tumors from four patients and investigated the appearance of α -smooth muscle actin (ASMA)-positive cells in these tumors using immunohistochemistry.

Results: We considered that five tumors are cellular type and the remaining three as fibrous. Characteristic hyalinization was observed in two of the three fibrous tumors. All the tumors except for one fibrous type contained entrapped tubular cells. CD35-positive cells (dendritic cells) and ASMA-positive cells were observed in all the tumors, with a more frequent occurrence in the cellular type than the fibrous type. CD35-negative spindle cells were considered as fibroblasts or activated fibroblasts (myofibroblasts). The number of CD35-positive cells was higher than that of ASMA-positive cells. Additionally, the entrapped tubular cells showed the transition to spindle cells and some of them expressed for ASMA. With double immunohistochemical staining, there were some cells showing positive reactions for both CD35 and ASMA. Furthermore, an ultrastructural examination confirmed the presence of ASMA-positive filaments in the dendritic cells and myofibroblasts. The expression of TGF- β 1 was observed not only in the tumor cells and the collecting ducts surrounding the tumor but also in the entrapped tubular cells. In addition, the intensity of TGF- β 1 was stronger in/around the tumor than in the areas distant from the tumor. The positive cells were more numerous in the cellular type than in the fibrous type.

Conclusions: ASMA-positive cells appear in renomedullary interstitial cell tumors and some of the cells may originate in dendritic interstitial cells, fibroblasts (myofibroblasts), and entrapped tubular cells. Furthermore, TGF- β 1 may contribute to the formation of fibrosis in the tumors.

Multifactors in the Pathogenesis of Heredofamilial Kidney Disorders

W. Adiku, F.A.M. Shaheen, Y. Bounatiro, L. Menawy, I. Bounatiro, A. Bayrakdar, A. Al-Shamran, M. Obeid

Jeddah Kidney Center (JKC), Saudi Arabia

Abstract: Since its inception in 1989, our center has had a number of patients from various ethnic groupings. We discovered in course of time a number of families with two or more members who suffered from renal failure.

Fourteen (14) families were screened and we excluded during study, such disorders caused by known single gene inheritance

dis-orders like Alport Syndrome and Adult Polycystic kidney disease. The discovered renal diseases failed to show any autosomal or sex-linked pedigree inheritance, except that they clustered in the family with various degrees of expression and penetrance. The occurrence of primary as well as secondary nephritides caused by diabetes mellitus (DM), hypertension, effects of ethnic origin, age, parasitic, viral or microbial as well as other environmental toxic agents were considered. The role of HLA antigenicity in association with immune response to environmental factors, gene interactions, probable gene mutation effects all play a part in the individual susceptibility. Such added risk factors like parenteral consanguinity, existence of DM, hypertension and systemic diseases affecting parents and other close family members have also been found. We think the identification of mutant genes, minimizing of possible consanguineous marriages, reduction of environmental factors can help limit the impact of multifactorial and polygenic causes of familial renal disorders.

Effect of ALT-711, an 'AGE Cross-Link Breaker', on Renal Expression of NADPH Oxidase in *db/db* Mice

H. Ha¹, M.K. Kwon¹, R. Nagai², S. Horiuchi², H.B. Lee¹

¹Hyonam Kidney Lab, Soon Chun Hyang University, Seoul, Korea, ²Department of Biochemistry, Kumamoto University School of Medicine, Kumamoto, Japan

Background: Oxidative stress plays an important role in the development and progression of diabetic renal injury. NADPH oxidase has recently been suggested to be a major source for reactive oxygen species (ROS) in streptozotocin-induced diabetic kidney. Advanced glycation end-products (AGE) may increase oxidative stress through activation of NADPH oxidase. We, therefore, examined the effects of ALT-711 [(2-oxo-2-phenyl) ethyl-4,5-dimethylthiazolium chloride], an AGE cross-link breaker, on renal expression of NADPH oxidase in *db/db* mice, a model of type 2 diabetes.

Method: ALT-711 (2 mg/kg/day) or saline was administered intraperitoneally to 8-week-old diabetic *db/db* mice with stable hyperglycemia and control *db/m* mice for 12 weeks. Urinary albumin was measured by ELISA. Glomerular volume (VG) and relative mesangial area (RMA) were quantitated using a computer-assisted color image analyzer. Fibronectin (FN) and pentosidine protein expression in isolated glomeruli were analyzed by Western blot analysis. Subunits of NADPH oxidase in cortical tubules were measured by RT-PCR.

Results: Untreated diabetic *db/db* mice at 20 weeks of age had significantly increased VG, RMA, urinary albumin excretion (UAE), and urinary LPO compared to *db/m* mice of the same age. Glomerular FN increased 8-fold in *db/db* mice compared to *db/m* mice, pentosidine by 1.6-fold, NOX-2 mRNA by 2-fold, p47phox by 1.5-fold, and p67phox by 1.5-fold. NOX-4 mRNA expression in *db/db* mice was not altered compared to *db/m* mice. Treatment with ALT-711 effectively ameliorated all these changes in *db/db* mice without an effect on plasma glucose level.

Conclusion: This study provides evidence that AGE may increase oxidative stress in the kidney through upregulating NADPH oxidase and ALT-711 may prove to be a novel therapeutic agent in renal injury of type 2 diabetes.

Antioxidants and Inhibitors of Hexosamine Biosynthetic Pathway Prevent High Glucose Induction of Insulin Resistance on Inhibition of Angiotensinogen Gene Expression in Rat Immortalized Renal Proximal Tubular Cells

J.S.D. Chan, T.-J. Hsieh

Université de Montreal, Montreal, QC, Canada

Purpose: Angiotensinogen (ANG) is the sole substrate of the renin-angiotensin system (RAS), and RAS activation plays an important role in the progression of diabetic nephropathy (DN). We have previously reported that high-glucose (25 mM) induced insulin resistance on inhibition of ANG gene expression in rat immortalized renal proximal tubular cells (IRPTCs). The present study investigated whether reactive oxygen species (ROS) generation and/or activation of hexosamine biosynthetic pathway (HBP) might mediate high-glucose induced insulin resistance on inhibition of ANG gene expression in IRPTCs.

Methods: IRPTCs were cultured in monolayer. ANG mRNA expression were determined by specific reverse transcription polymerase chain reaction assay. p44/42 MAPK phosphorylation was determined by Western blot analysis.

Results: Pre-cultured of IRPTCs for 2 weeks in high-glucose or glucosamine (10^{-6} M) induced insulin resistance on inhibition of ANG gene expression and on activation of p44/42 MAPK phosphorylation. The effects of high glucose were blocked by antioxidants (taurine and tiron), inhibitors of mitochondrial oxidation (rotenone, TTFA, and 4-OHCA). Azaserine and DON (specific inhibitors of HBP) also blocked the high glucose effects whereas they failed to affect glucosamine-induced insulin resistance on inhibition of ANG gene expression and p44/42 MAPK phosphorylation in IRPTCs.

Conclusion: Our studies demonstrate that the high-glucose induction of insulin resistance on inhibition of ANG gene expression may be mediated, at least in part, via ROS generation and subsequent activation of HBP.

The Protective Effects and Type III Collagen mRNA Expression of Pedicled Omental Transposition in Rats with Experimental Glomerulosclerosis

D. Xinggang

Shanghai Second People Hospital, Shanghai, P.R.China

Objective: To investigate the effect of pedicled omental transposition on Type III Collagen mRNA in glomerulosclerosis rats.

Methods: We randomized 27 male SD rats control and glomerulosclerosis rats. Uninephrectomized rats were divided into two groups. Normal rats were put in the blank control group, glomerulosclerosis rats by adriamycin were divided into glomerulosclerosis group and pedicled omental transposition group. Renal histological examination

was performed, while Type III Collagen mRNA expression of cortex was assessed by Northern blot analysis.

Results: Pedicled omental transposition group could not only decrease the accumulation of extracellular matrix ($P < 0.05$), but also expression of Type III Collagen mRNA was lower than that in glomerulosclerosis group ($P < 0.05$). Changes in gene expression were accompanied by parallel changes in immunostaining for Type III Collagen. Pedicled omental transposition can reduce urinary protein ($P < 0.05$).

Conclusion: Pedicled omental transposition group decrease the accumulation of extracellular matrix and attenuates glomerulosclerosis through down-regulation of Type III Collagen mRNA expression.

The Study on Effect of Tripterygium Wilfordii Glycosides by Peripheral Blood Mononuclear Cells from Proteinuric Patients

D. Xinggang

Shanghai Second People Hospital, Shanghai, P.R.China

Purpose of the Study: To evaluate the role of apoptosis on the pharmacologic effects of Tripterygium Wilfordii Glycosides (TWG) in proteinuric patients.

Methods: 30 patients in glomerulonephritis with proteinuria were randomized to two groups, control and TWG groups using TWG (1 mg/kg/d) for 14 days. Apoptosis of peripheral blood mononuclear (PBMC) was detected by gel electrophoresis, HE staining and flow cytometry.

Results: After treatment by TWG, there were typical nuclear condensation and fragments, 'DNA ladder' was viewed on agarose gel, 'Sub G1' peak was recorded in DNA histogram of flow cytometry at two weeks.

Conclusion: These results suggest that TWG used to treat proteinuric patients can induce apoptotic of PBMC and may be one of the mechanisms for immune inhibition.

Renin-Angiotensin System Gene Polymorphisms and End-stage Renal Failure in IgA Nephropathy

K.-T. Woo, Y.-K. Lau, L.H.L. Choong, Y. Zhao, H.-B. Tan, F.-E. Liu, E.-K. Tan, H.K. Yap, S. Fook-Chong, K.S. Wong

Department of Renal Medicine, Singapore General Hospital, Singapore, Singapore

Gene polymorphisms in angiotensin-converting enzyme (ACE), angiotensinogen (AGT) and angiotensin II type 1 receptor (ATR) had been associated with IgA nephropathy (IgAN) and its progression. Several studies on Caucasian and Japanese had reported conflicting

results. We determined these polymorphisms in 118 Chinese patients with IgAN and 94 healthy Chinese to assess their clinical impact.

Genotyping was performed with DNA from peripheral leukocytes by PCR amplification of the polymorphic sequence, restriction enzymes digestion, separation and identification of DNA fragments. Clinical data at renal biopsy and status on renal function were also analysed.

ACE genotypes in controls was not significantly deviated from Hardy-Weinberg equilibrium. All IgAN patients ($p < 0.05$) and those with end-stage renal failure (IgAN-ESRF, $p < 0.05$) but not IgAN-nonESRF showed significant difference from controls with increase in the DD genotype. AGT and ATR genotype distributions were similar in controls and all patient groups. Compared with IgAN-nonESRF, IgAN-ESRF patients were not different in gene polymorphisms but had higher male prevalence ($p < 0.05$), increased serum creatinine at presentation ($p < 0.05$), more sclerosis ($p < 0.01$) and higher tubulointerstitial lesion score ($p < 0.001$).

Our data on Chinese patients suggest that ACE gene polymorphism may impact on IgAN initiation and its progression to ESRF. AGT and ATR gene polymorphisms have no apparent impact. Male sex, impairment of renal function at presentation, glomerular sclerosis and tubulointerstitial lesion remain useful as risk factors.

Clinical Nephrology

121

Urinary Screening of School Children for Hematuria and Proteinuria in Southeastern Iran

S.B. Simin, H. Jamal

Medical Science of University, Iran

Purpose of Study: Urine screening is one of the ways which can help in early diagnosis of kidney diseases. The goal of this study was to determine the prevalence of hematuria and proteinuria in asymptomatic school children.

Methods: For finding of these abnormalities the urine sample of children were collected in early morning and examined with dipstick immediately. It was done twice (for two days). For those abnormalities urine examination were followed with random urine Pr/Cr ratio assay and RBC count in high power field.

Results: This study was performed in 1,169 children and adolescent including 600 girls and 569 boys, in range of 7–15 years old of age. Urine abnormalities were detected in 2.2% of children.

Urine abnormality	Male	Female	7–9 y/o	10–12 y/o	13–15 y/o
Proteinuria	0.33	1.05	0.53	0.49	1.02
Hematuria	1	2.1	1.59	1.48	1.54

Conclusions: The results indicate that urine abnormalities in school children in the studied region are great important. Mass screening of school children seems to be necessary.

122

Clinicopathology Correlation in Lupus Nephritis (LN) in Children of Southern Iran

S.B. Simin, Gh. Hashemi

Meical Science of University, Iran

Purpose of Study: To study the incidence of different grades of renal involvement in SLE in medical center of southern Iran which is a referral center from S state.

Method: All children with accepted criteria of SLE which is proved by serological studies during ten years period (1990–2001) are included with fifty-nine and/or hematuria all had percutaneous renal biopsy, grading as WHO classes.

Results: Presenting findings were hematuria and proteinuria in 100% in grades II–IV–V.

Evaluated blood pressure in 81.8% of grade II, in 66% of grade III, in 72.2% of grade IV and in 33% of grade V. Renal failure in 9% of grade II, in 50% of grade III, in 40.4% of grade IV and none in grade V (Table 1).

45% of grade II to prednisolone and 36.1% to cyclophosphamide pulse therapy did response well. 66.7% of grade III response to cyclophosphamide and 11% of grade IV responded to prednisolone and 50% of them response to cyclophosphamide, but 13.6% did not go to remission.

66.7% of grade V response to cyclophosphamide well.

Table 1. Clinicopathologic correlation in LN

Grading	Hematuria	Proteinuria	Hypertension	RF	Pt(n)
I	75	87.5	12.5	0	8
II	100	100	81.8	9	11
III	83.3	83.3	66.6	50	6
IV	100	100	72.5	40.9	22
V	100	100	33	0	3

Conclusion: Most involvement in our group is grade IV with highest rate of hypertension and renal failure at presentation so these two finding beside urinary abnormalities can be accounted in early renal biopsy for grading and aggressive therapy in severe LN cyclophosphamide pulse therapy was an effective treatment.

123

Epotin® in the Management of Anaemia of End Stage Kidney Disease in Patients on Maintenance Haemodialysis

E.El Tayeb Abbas, R. Dham, D. Shaker, et al.

Division of Nephrology,
Saif Bin Gobash Hospital, UAE

Purpose of the Study: Recombinant human erythropoietin (rHuEPO) is effective therapy for anaemia of end stage kidney disease (ESKD). In this multicenter open study we assessed the efficacy and safety profile of a new (rHuEPO) alpha (Epotin®) manufactured in the Middle East, in treating ESKD patients on maintenance haemodialysis.

The study was conducted in 18 centers in 8 Middle Eastern countries and carried throughout thirteen weeks treatment period.

Methods: Patients on thrice weekly haemodialysis who have not been on erythropoietin earlier or were washed off erythropoietin for two weeks, having a haematocrit (Hct) of <27%, haemoglobin (Hb) <9 and fulfilling all subject's selection criteria were included. All patients were given (Epotin®) intravenously in a starting dose of 150 units/kg body weight per week in three equal doses postdialysis and titrated according to Hct response. All the influential factors including the iron status were monitored, managed and recorded.

Results: A total of 124 (ITT) patients were recruited, statistical analysis was performed on 85 (PP) cases (46 males: 39 females). The average duration since diagnosis as ESKD and enrollment to the study was 1,151 with a range of 4 to 4,351 days, while the average duration between diagnosis and initiation of haemodialysis was 84 with a range of 0 to 3,319 days. (Epotin®) raised Hb level as early as week three. An increase from a baseline of 7.58 (± 1.80) to 11.97 (± 1.72) g/dl was recorded in week 13 (P value = 0.0001); Hct followed to 36.28 ($\pm 5.78\%$) from 22.52 ($\pm 4.16\%$) (P value = 0.0001). A success rate of 85.8% was recorded considering an absolute increase in Hb of 2.5 g/dl (Hct of 7.5%) over the 13-week trial period as a target as per K-DOQI guidelines. Non responding patients were tested for antierythropoietin antibody and were found to be negative. No significant difference in response was noticed between females and males. The chronicity of ESKD did not affect the response to Epotin® when subgrouping the patients as those with ESKD for more than 3 years and those with less, even though long standing ESKD was associated with significantly more severe anaemia. A history of hypertension was reported upon study entry in 45 patients; blood pressure of those patients was stable throughout the study. Eleven patients developed mild hypertension. There was no incidence of thrombotic episodes, and consumption of heparin during dialysis sessions was stable. No dropouts were reported due to intolerance.

Conclusions: The new (rHuEPO) alpha produced in the Middle East, given intravenously is effective in treating anemia of ESKD in patients on maintenance haemodialysis. No difference in response between males and females, nor between patients with different levels of chronicity of ESKD was reported. No cases of PRCA were reported. Moreover, the side effect profiles were similar to other erythropoietins.

124

Darbepoetin Alfa (Aranesp®) at Extended Dosing Intervals Maintains Haemoglobin Concentrations in Dialysis Patients

R. Brunkhorst

Klinikum Hannover Oststadt, Hannover, Germany

Purpose of the Study: Darbepoetin alfa has a 3-fold longer half-life and greater in vivo biological activity than epoetin (rHuEPO). The efficacy and safety of darbepoetin alfa for the treatment of renal anaemia, given at extended dose intervals relative to rHuEPO, were assessed in a pooled analysis of 8 European studies.

Methods: Dialysis patients ($n = 5,520$) maintained on stable rHuEPO treatment for at least 8 weeks were switched to darbepoetin alfa at extended dose intervals, by the same route of administration

(intravenous [IV; $n = 1,788$, 32%] or subcutaneous [SC; $n = 3,732$, 68%]) and an equivalent dose based on peptide mass. Patients who previously received rHuEPO two ($n = 1,885$, 34%) or three ($n = 2,537$, 46%) times a week were switched to once-weekly dosing with darbepoetin alfa. Those who received rHuEPO once a week ($n = 1,098$, 20%) were switched to darbepoetin alfa once every other week. The dose of darbepoetin alfa was titrated to maintain haemoglobin (Hb) concentrations between 10 and 13 g/dL. The primary endpoint was the mean change in Hb concentration from baseline to evaluation (weeks 21–24).

Results: At baseline, mean Hb concentration was 11.51 ± 0.78 g/dL and remained stable between baseline and evaluation (-0.05 g/dL [95% confidence intervals {CI}: -0.09 , -0.02]). At the end of the evaluation period, 97% of patients remained on their assigned frequency of darbepoetin alfa administration. The mean weekly darbepoetin alfa doses for IV-treated patients at baseline were $27.40 \mu\text{g}$ (95% CI: 26.61, 28.21) and at evaluation $23.31 \mu\text{g}$ (95% CI: 22.50, 24.14). For SC-treated patients, they were $25.39 \mu\text{g}$ (95% CI: 24.89, 25.89) and $24.68 \mu\text{g}$ (95% CI: 24.09, 25.29), respectively. The IV:SC dose ratio of 1.08 (95% CI: 1.04, 1.12) at baseline and 0.94 (95% CI: 0.90, 0.99) at evaluation indicated similar dose requirements by both routes of administration. Darbepoetin alfa was well tolerated, and overall safety data were consistent with those expected for a population of dialysis patients.

Conclusion: Overall, these data confirm that the administration of darbepoetin alfa at extended dose intervals relative to rHuEPO effectively and safely maintains Hb concentrations in dialysis patients.

125

Once-Weekly IV Darbepoetin Alpha Maintains Haemoglobin Levels in Haemodialysis Patients Switched from Three-Times Weekly IV Epoetin

F. Carrera, A.I. Anunciada, C. Nogueira, J.G. Silva

Hospital SAMS, Department of Nephrology,
Lisbon, Portugal

Purpose of the Study: To evaluate whether haemoglobin (Hb) levels can be maintained in patients with end-stage renal disease (ESRD) receiving haemodialysis (HD), after switching from three-times weekly dosing with intravenous (IV) epoetin to once-weekly dosing with IV darbepoetin alfa.

Methods: Patients with ESRD, maintained on HD and ≥ 18 years of age, with no evidence of active bleeding, infection or inflammation were stabilized on epoetin therapy for an initial period of 6 months. IV epoetin was administered three-times weekly, with the dose titrated to maintain Hb within the range 11.0–12.5 g/dL. At Month 0, patients were randomized either to continue treatment with three-times weekly IV epoetin (control group) or to switch to once-weekly treatment with IV darbepoetin alfa (darbepoetin alfa group). 200 IU:1 μg was used to start patients who were switched from three-times weekly epoetin to darbepoetin alfa. Patients were followed up for a period of 10 months, during which time the dose of epoetin or darbepoetin alfa was titrated to maintain Hb in the range 11.0–12.5 g/dL. The primary efficacy parameter was the level of Hb

at the end of the study (Month 10) in the darbepoetin alpha group, compared with the control group.

Results: In total, 24 patients were randomized to the darbepoetin alpha group and 20 to the control group. At month 10, mean Hb levels in the darbepoetin alpha and control groups were 12.03 g/dL (95% confidence intervals [CI]: 11.57, 12.50 g/dL) and 12.41 g/dL (11.55, 13.27 g/dL), respectively ($P = 0.38$), representing a mean change in Hb from Month 0 to Month 10 of 0.12 g/dL (95% CI: -0.72, 0.96 g/dL) in the darbepoetin alpha group and 0.05 g/dL (-1.13, 1.23 g/dL) in the control group ($P = 0.91$). Serum ferritin was adequate in both groups throughout the study. Two patients from the darbepoetin alpha group and three from the control group died before study completion, but these deaths were not believed to be treatment-related.

Conclusion: Once-weekly dosing with IV darbepoetin alpha is as effective as three-times weekly dosing with IV epoetin in maintaining Hb levels in patients receiving haemodialysis.

126

Baseline Characteristics of European Dialysis Patients Receiving Treatment for Renal Anaemia

M. Kessler

CHRU de Nancy, Hôpital de Brabois,
Vandoeuvre les Nancy, France

Purpose of the Study: Data on practices in anaemia management are presented from baseline data from 8 European studies in 12 countries designed to investigate the efficacy and safety of darbepoetin alpha for the treatment of renal anaemia.

Methods/Results: All patients had received haemodialysis (HD) or peritoneal dialysis (PD) for ≥ 6 months, had a mean baseline haemoglobin (Hb) concentration between 10 and 13 g/dL, and had been stable on intravenous (IV) or subcutaneous (SC) rHuEPO therapy for ≥ 8 weeks. All patients had adequate iron stores (serum ferritin $\geq 100 \mu\text{g/L}$) or transferrin saturation ($\geq 20\%$). The total number of patients recruited was 5,520 (Nordic region, $n = 442$ [8%]; Germany, $n = 1,502$ [27%]; Austria, $n = 250$ [5%]; UK/Ireland, $n = 262$ [5%]; Spain, $n = 826$ [15%]; Italy, $n = 950$ [17%]; France, $n = 1,008$ [18%]; Portugal, $n = 300$ [5%]). The use of SC rHuEPO ranged from 40% (Germany) to 98% (UK/Ireland). 98% of patients were receiving HD and all patients were being treated with rHuEPO (61% rHuEPO α , 39% β). 20% of patients were receiving rHuEPO once weekly, 34% rHuEPO twice weekly and 46% were receiving rHuEPO three times per week. Across all regions, the mean baseline Hb level was 11.51 ± 0.78 g/dL (lowest: Italy [11.34 g/dL]; highest: Nordic region [11.81 g/dL]). The mean baseline Hb level for patients receiving IV rHuEPO was 11.46 ± 0.75 g/dL (lowest: UK/Ireland [10.86 g/dL]; highest: Nordic region [11.81 g/dL]), and for patients receiving SC rHuEPO it was 11.53 ± 0.79 g/dL (lowest: France [11.38 g/dL]; highest: Nordic region [11.81 g/dL]). Overall, 72% of patients had Hb levels ≥ 11 g/dL (range, 62% [Italy] to 84% [Nordic region]), and this proportion was similar for IV- and SC-treated patients.

Conclusions: These data show the widespread use of SC rHuEPO in populations of patients almost exclusively receiving HD, and that the management of renal anaemia with rHuEPO remains

suboptimal, even in this pre-selected population. Many countries fail to achieve the European Best Practice Guidelines target of $>85\%$ of patients with Hb ≥ 11 g/dL.

127

Renal Fas, Bax and Apoptosis in Schistosomal Hepatic Fibrosis: Relation to Nitric Oxide and Oxidative Stress

H.El Kashef Essam, A.El Aggan Hayam, M.B. Nahed,
M.E. Maha, F.K. Amal, M.El Batet Kamel

Faculty of Medicine, University of Alexandria,
Alexandria, Egypt

The present study was designed to evaluate the role of apoptosis and its regulatory proteins Fas and Bax, in the progression of renal disease in schistosomal hepatic fibrosis (SHF) in relation to the levels of nitric oxide (NO), transforming growth factor- β (TGF- β) and oxidative stress. Three groups of patients with SHF, 15 each (normo GI, micro GII and macroalbuminuria GIII) and 15 healthy control subjects were included in the study. Also, an experimental study was designed and included 90 Swiss Albino mice infected with *Schistosoma mansoni* (every 10 infected mice were sacrificed at 3, 5, 7, 8, 9, 10, 13, 15 and 20 weeks post-infection) and 10 non-infected mice were used as controls. Sera from all patients were analyzed for levels of nitrite, TGF- β , malondialdehyde (MOD), and superoxide dismutase (SOD). In the renal tissue, apoptosis was examined using the terminal deoxynucleotidyl transferase (TdT) nick end labeling method and detection of Fas, Bax, proliferating cell nuclear antigen (PCNA) and fibronectin were done by immunohistochemical technique. In patients, serum nitrite and MOD levels were higher and serum SOD level was lower in all groups of patients than in the controls and in GIII patients than in both GI and GII. Also, GIII patients showed a higher level in serum TGF- β than the other groups. Serum creatinine was positively correlated with serum nitrite, MOD and TGF- β levels and negatively correlated with serum SOD level ($P < 0.05$). Renal biopsies of GIII patients showed a significant increase in glomerular apoptosis, Fas and Bax proteins and fibronectin and in tubulointerstitial PCNA than in the normal renal tissues. In infected mice Fas, Bax, apoptosis, and fibronectin started to appear at 3rd, 13th and 7th week post infection respectively, they continued to increase till the 20th week. The PCNA decline gradually till the 20th week. Glomerular apoptosis was positively correlated with glomerular Fas, Bax, and fibronectin, serum creatinine, nitrite, TGF- β and MOD levels and was negatively correlated with PCNA and serum SOD level in GIII ($P < 0.05$). From this study it can be concluded that increased glomerular apoptosis with a decrease in cellular proliferation has a role in the development of glomerulosclerosis and the progression of renal disease was related to the increased levels of nitric oxide, TGF- β and oxidative stress.

Medullary Nephrocalcinosis and Hypercalciuria in a Patient with Osteogenesis Imperfecta

J.-M. Sung¹, C.-C. Hsieh², H.-L. Liu¹, F.-F. Chen³, J.-J. Huang¹

¹Departments of Internal Medicine, ²Department of Internal Medicine, ³Pathology, National Cheng Kung University Hospital, Tainan, Taiwan

Osteogenesis imperfecta (OI) is a connective tissues disorder of gene mutation of type I collagen and presents with fragile skeleton, blue sclera, and small thin teeth (i.e., dentinogenesis imperfecta), etc. We hereby reported a female with OI type IB and unusual medullary nephrocalcinosis (MN).

A 32 y/o female had the short stature (height: 152 cm). Several years ago, she had two episodes of wrist bone fracture after falling, but without sequela. In health examination, renal ultrasonography revealed hyperechoic medulla. Also, blue sclera and small thin teeth were noted. Bone mineral density showed osteoporosis grade II, and echocardiography was normal. She never took as calcium salts or vitamin D. Blood biochemistry showed calcium, 9.5 mg/dl; phosphate, 4.1 mg/dl, uric acid, 6.5 mg/dl. Arterial blood gas analysis was normal, and intact-PTH level was 29.3 pg/ml. Routine urinalysis revealed neither hematuria or proteinuria. Thyroid function test, ANA, anti-double strand DNA, and serum levels of complements were normal. Renal tubular function test with bicarbonate loading showed no tubular defect. Under the regular diet, daily urinary calcium excretion was 5.8 mg/kg and uric acid, 4.2 mg/kg. Intravenous urogram was normal, but CT scan showed MN. For hypercalciuria, she adhered to a low calcium (400 mg/day) and low sodium (100 meq/day) diet for one week. Urinary calcium level on fasting revealed 0.062 mg/100 ml glomerular filtrate, and after calcium load it was 0.48 mg/100 ml glomerular filtrate. Absorptive hypercalciuria was diagnosed. Renal biopsy revealed only mild tubulointerstitial inflammation.

Our case illustrated that MN can occur in mild OI patient without other precipitating factor. And absorptive hypercalciuria, which can be reversed by low salt and low calcium diet, was the underlying mechanism of MN in OI regardless of mild bone involvement. Whether the absorptive hypercalciuria a common in OI patients deserves further studies.

CVVH/CVVHD in Leptospirosis

K.P. Jayakumar

Department of Nephrology,
Govt Medical College Kottayam, Kerala, India

Leptospirosis is the commonest cause of acute renal failure in our institution. Myocarditis, hepatic encephalopathy and 'ARDS' (Acute Respiratory Distress Syndrome) like picture are the common causes of mortality in these patients. Capillary leak with additional complications in acute renal failure may progress to 'ARDS'. Hypotension is a common problem in patients with leptospirosis and renal failure

during hemodialysis. CVVH/CVVHD is found to be useful in leptospirosis with hemodynamically unstable patients. Mixed acid base disorder of metabolic acidosis and respiratory alkalosis in patients with leptospirosis is an indication of fluid in the lungs. Hence removal of fluids from lungs by ultrafiltration even in normotensives was found to be useful in reducing the morbidity and mortality. In this study the usefulness of ABG (Arterial Blood Gas analysis) in leptospirosis was studied in order to consider them for CVVH/CVVHD. All patients suspected to have leptospirosis (confirmed subsequently) with features suggestive of fluid in the lung clinically, radiologically or ABG showing metabolic acidosis and respiratory alkalosis were subjected to CVVH/CVVHD. Replacement fluid consisted of fresh frozen plasma, platelet transfusion or crystalloid solutions. End point was the disappearance of the respiratory alkalosis in ABG or disappearance of signs in the chest. In the last one year (2002) 30 patients of leptospirosis were subjected to CVVH/CVVHD. Sixteen of them were taken as they had hemodynamic instability and the rest 14 were taken as per our study protocol. 13 patients recovered from the study group and one died of hepatic encephalopathy. CVVH/CVVHD is useful in leptospirosis with 'ARDS' like picture and is a life saving procedure. Mixed disorder of metabolic acidosis and respiratory alkalosis is an indication of starting CVVH in leptospirosis.

Safety and Efficacy of Fluvastatin in Hyperlipidemic Patients with Chronic Renal Disease

G. Yasuda¹, N. Ogawa¹, G. Shimura¹, D. Ando¹, K. Shibata², S. Umemura²

¹Division of Nephrology, Center Hospital, ²Second Department of Internal Medicine, Yokohama City University School of Medicine, ³Minami Clinic, Yokohama, Japan

Purpose of the Study: There are few reports on the safety and efficacy of long-term treatment with statins in patients with chronic renal disease. We evaluated these subjects using fluvastatin.

Methods: The study consisted of a 4-week run-in period and a 48-week treatment phase with fluvastatin in patients with diabetic nephropathy or chronic glomerulonephritis. They were randomly allocated to a fluvastatin (20 mg daily)-treated group (n = 37) and non-fluvastatin-treated group (n = 40). Lipid parameters, myolysis-related indicators, 24-hour urinary albumin excretion and creatinine clearance were measured. Pharmacokinetic parameters were examined in 8 patients.

Results: Creatinine clearance and 24-hour urinary albumin excretion did not differ between the two groups during the study period. Peak serum concentration (C_{max}) was $141 \pm 67 \mu\text{g/L}$ with the mean AUC_{0-6h} of $341 \pm 149 \mu\text{g} \cdot \text{h/L}$. Fluvastatin decreased significantly ($P < 0.05$) serum total cholesterol (from 6.8 ± 0.2 to $5.7 \pm 0.1 \text{ mmol/L}$), low-density lipoprotein-cholesterol (from 4.4 ± 0.1 to $3.3 \pm 0.2 \text{ mmol/L}$), and apolipoprotein B (from 1.4 ± 0.1 to $1.1 \pm 0.1 \text{ g/L}$) concentrations in the fluvastatin-treated group which were lower than those in the non-treated group. Fluvastatin did not decrease serum triglyceride and high-density lipoprotein-cholesterol concentrations. During the fluvastatin treatment period, serum creatine

kinase, aldolase, and myoglobin concentrations did not change in both groups.

Conclusion: Fluvastatin improved abnormality of lipid metabolism in patients with chronic renal disease without serious side effects and accumulation in the serum, but it did not show direct renoprotective effects.

131

Changes in LDL, HDL Cholesterol and Lipid Peroxidation in IgA Nephropathy after Antioxidant Treatment

B. Deliyska, P. Angelova, A. Nedialkov, A. Rapondzhieva, V. Shurlev

Medical University, Sofia, Bulgaria

The aim of the study was to investigate the status of LDL, HDL cholesterol and circulating lipid peroxidation after antioxidant therapy by combination of 10 mg β -carotene, 40 mg Vitamin E, 100 mg Vitamin C and 50 μ g Selenium (Triovit, KRKA, Slovenia). Twenty-five patients with biopsy proved IgA nephritis received that drug one capsule daily as dietary supplement for 3 months. At the start and at the end of the study were provided routine laboratory examinations including also cholesterol, triglycerides, HDL and LDL cholesterol. Lipid peroxidation was established by thiobarbituric acid reactive substances (TBARS) and oxidative modification of HDL (HDL TBARS) and LDL (LDL TBARS). Levels of TBARS and LDL TBARS increased in whole group and levels of HDL TBARS decreased. TBARS decreased in 7 (28%) pts and LDL TBARS decreased in 5 pts (20%). HDL cholesterol was lower than normal range in 17 pts and it increased in 8 pts (47%). LDL was higher in 10 pts and its level decreased in 6 pts (60%). No correlation was observed between morphological changes and lipid peroxidation. Positive correlation was established between TBARS and LDL TBARS. Because of many factors that can affect free radicals production the value of examination of total lipid peroxidation appears to be limited. Our data suggest that antioxidant treatment does not changes significantly levels of TBARS and LDL TBARS, but modulates pathological changed HDL and LDL cholesterol in part of the patients with IgA nephropathy.

132

Monitoring of Neoral C₂ in Therapy of Severe Nephropathies: A Pilot Study

B. Deliyska, M. Bankova, A. Rapondzhieva, D. Svinarov

Medical University, Sofia, Bulgaria

Cyclosporine A (CyA) is used as a part of a pathogenic treatment for severe glomerulopathies, with concentration controlled dosage for optimal therapeutic management. Neoral C₂ monitoring is superior to C₀ monitoring in renal transplant patients. The aim of the study was to compare the monitoring of C₂ against C₀ for the Neoral formulation of CyA in 10 patients with severe glomerulonephritis. Patients were followed for 3 to 12 months. They also

received corticosteroids and cyclophosphamide in conventional and pulse doses. Whole blood CyA levels were measured before and 2 h post dose of Neoral at the steady state and drug levels were checked more than once, so 33 pairs of C₂ and C₀ concentrations were included in the study. The Neoral daily dose was 2.34 ± 0.64 mg/kg (1.2 to 3 mg/kg); C₀ level 93.9 ± 90.8 μ g/L (25 to 230 μ g/L); C₂ 754.8 ± 324.7 μ g/L (362 to 1,500 μ g/L). Individual concentrations were rated as therapeutic, low or high, applying a target range of 75–150 μ g/L, and 600–1,200 μ g/L for C₀ and C₂ respectively. Among the 12 low C₀ concentrations observed, 8 were paired with optimal C₂ levels and 5 with high C₂ levels; 4 of the 17 optimal C₀ levels were paired with low C₂ concentrations; 2 from three high C₀ were paired with low C₂ values. There were not significant differences in glomerular filtration rate, cholesterol, serum albumin and blood pressure at the beginning and at the end of the study. Proteinuria and episodes of hematuria were reduced significantly. No adverse effects were established during Neoral therapy. We conclude that C₂ monitoring of Neoral might have a place in the effort to optimise the therapy and avoid nephrotoxicity in patients with severe immune and autoimmune nephropathies.

133

The Role of Hypoalbuminemia as a Marker of Disease Severity in Women with Pregnancy Induced Hypertension

Y.O. Kim, S.A. Yoon, Y.S. Kim, B.S. Kim, H.C. Song, Y.S. Chang, B.K. Bang

Department of Internal Medicine,
The Catholic University of Korea, Seoul, Korea

Purpose: Preeclampsia, pregnancy induced hypertension, is considered to be associated with increased vascular permeability leading to albumin loss from the intravascular space. Although hypoalbuminemia frequently occurs in pregnant women with preeclampsia, the impact of hypoalbuminemia on maternal and fetal morbidity in preeclampsia is not well known yet.

Methods: This study included 392 preeclampsia patients. The patients were divided into hypoalbuminemia group (serum albumin <3.0 g/dl) and normal group (serum albumin ≥ 3.0 g/dl) based on the lowest serum albumin level during admission. And then we compared clinical factors representing maternal and fetal morbidity between two groups.

Results: Of the total 392 patients, 280 patients (71.5%) had hypoalbuminemia. Compared to normal group, hypoalbuminemia group had higher incidence of twin pregnancy (7.5% vs. 1.8%, $p = 0.030$), acute renal failure (12.5% vs. 3.6%, $p = 0.008$), severe proteinuria (≥ 3.5 g/day) (34.4% vs. 10.8%, $p = 0.002$), hepatic dysfunction (33.5% vs. 12.2%, $p < 0.001$), thrombocytopenia (37.8% vs. 19.6%, $p = 0.001$), respectively. As a comparison of fetal morbidity, the incidence of intrauterine growth retardation in hypoalbuminemia group was also higher than that in normal group (25.0% vs. 12.5%, $p = 0.011$) and birth weight in hypoalbuminemia group was smaller than that in normal group (2.5 ± 0.8 vs. 2.8 ± 0.8 kg, $p = 0.002$).

Conclusion: This data suggest that hypoalbuminemia frequently occurs in pregnant women with preeclampsia and it is associated with maternal and fetal morbidity.

Serum Albumin Level Correlates with Disease Severity in Patients with Hemorrhagic Fever with Renal Syndrome

Y.O. Kim, S.A. Yoon, Y.S. Kim, B.S. Kim, H.C. Song, S.Y. Kim, E.J. Choi, Y.S. Chang, B.K. Bang

Department of Internal Medicine,
The Catholic University of Korea, Seoul, Korea

Purpose: Hypoalbuminemia frequently occurs in hemorrhagic fever with renal syndrome (HFRS) but clinical significance of hypoalbuminemia is not well known. This study was designed to evaluate hypoalbuminemia as a marker of disease severity in patients with HFRS.

Methods: We evaluated the relationship between the serum albumin level and clinical parameters representing the disease severity in 144 patients with HFRS. The patients were divided into three groups based on the lowest serum albumin level; group I (normal serum albumin), group II (serum albumin <3.5 g/dl and ≥ 3.0 g/dl), and group III (serum albumin <3.0 g/dl).

Results: Forty-two patients (29.2%) were group I and 39 patients (27.1%) were group II and 63 patients (43.8%) were group III. Group III had a higher incidence in episode of hypotension, pulmonary edema, and pleural effusion than did group I and group II. The lowest serum albumin level was positively correlated with platelet count ($r = 0.505$, $p < 0.001$) and was negatively correlated with leukocyte count ($r = -0.329$, $p < 0.001$), and BUN ($r = -0.484$, $p < 0.001$), and serum creatinine ($r = -0.394$, $p < 0.001$), and AST ($r = -0.251$, $p = 0.002$).

Conclusion: Our data suggest that hypoalbuminemia frequently occurs in the acute stage of HFRS and serum albumin level is associated with the disease severity of HFRS.

The Estimation of Changes Frequency in Urine Analyses Comparing to Chlamydia Trachomatis Infections in Patients of Family Doctors' Practices

A. Steciwko, I. Pirogowicz, D. Kurpas, A. Mastalerz-Migas, I. Choroszy-Król

Family Medicine Department of
Wrocław Medical Academy, Poland

The appearance frequency of Chlamydia trachomatis infections varies between 11% and 38% in Poland depending on different data.

The aim of our investigation was the estimation of changes frequency in urine analyses comparing to Chlamydia trachomatis infections in patients of family doctors' practices.

1,000 patients were examined during 12 month. We made in all patients general urine analyses with the dipstick test (assessment of density, pH, presence of leucocytes, erythrocytes, protein, glucose, ketone, urobilinogen). Each patient filled up also a questionnaire on diseases symptoms, taken medicines, social-economic background, hygienic and sexual behaviour.

We selected the group of 200 patients to second stage of our investigation. These patients were examined with the immunological test on Chlamydia trachomatis infections that is very sensitive but low-specific. We characterized antibodies level in serum: IgA in dilution 1:16, IgG in dilutions 1:64 and 1:128.

We found after the questionnaires and tests analyses that: there is correlation between appearance of leucocyturia, dysuric symptoms and Chlamydia infections' frequency, quite often Chlamydia infections appears in the aged what can point at chronic nature of infections, Chlamydia infections more often appeared in the examined group in the aged living in bad social and hygienic conditions, with urinary system infections in anamnesis.

The next part of our investigation will be verification of selected patients' group with cervical swab in women and urethral swab in men.

Lanthanum Carbonate (Fosrenol®) in the Treatment of Hyperphosphataemia: Efficacy and Safety in Chinese Patients with End-Stage Renal Disease

S.-S. Chiang¹, W.-C. Yang², J.-B. Chen³, S. Stranks⁴, M. Gill⁴

¹Shin Kong Wu Ho-Su Memorial Hospital, ²Taipei Veterans General Hospital, Taipei, ³Chang Gung Memorial Hospital at Kaohsiung, Kaohsiung Hsien, Taiwan, ⁴Shire Pharmaceutical Development Ltd, Basingstoke, UK

Purpose of the Study: Lanthanum carbonate (LC) is a novel non-aluminium, non-calcium phosphate binder developed for the treatment of hyperphosphataemia. We report data from a recent trial that for the first time assessed the efficacy and safety of LC compared with placebo in Chinese patients with end-stage renal disease.

Methods: Following washout and an LC dose-titration phase, male and female haemodialysis patients were randomized to receive LC or placebo for 4 weeks. The primary efficacy endpoint was the serum phosphorus level obtained in the last week of treatment. Control of serum phosphorus to ≤ 5.6 mg/dL was the main secondary endpoint, and other measures included serum phosphorus, parathyroid hormone, calcium, and calcium $\times$ phosphorus ($\text{Ca} \times \text{P}$) product levels. Plasma levels of lanthanum were also measured throughout the study. The safety and tolerability of LC were assessed by monitoring adverse events and vital signs at each study visit.

Results: Mean serum phosphorus levels at the end of washout were 7.7 mg/dL ($\text{SD} = 1.5$, $n = 73$). At the end of the study, LC-treated patients had significantly lower phosphorus levels (5.1 mg/dL; $\text{SD} = 1.5$, $n = 30$) than those receiving placebo (7.2 mg/dL; $\text{SD} = 1.3$, $n = 31$; $P < 0.001$). In addition, a significantly higher proportion of patients receiving LC had controlled serum phosphorus levels, and $\text{Ca} \times \text{P}$ product levels were reduced in this patient group. LC was well tolerated; only one serious adverse event was reported and this was unrelated to LC treatment.

Conclusions: LC was shown to be an effective phosphate binder in Chinese patients, and treatment was well tolerated.

Lanthanum Carbonate (Fosrenol®) Phase II and III Studies: A Demographic Analysis

W.-C. Yang¹, A. Hutchison², W. Finn³, S. Stranks⁴, M. Gill⁴

¹Taipei Veterans General Hospital, Taipei, Taiwan,

²Manchester Institute of Nephrology and Transplantation, University of Manchester, UK,

³Department of Medicine, University of North Carolina, North Carolina, N.C., USA, ⁴Shire Pharmaceutical Development Ltd, Basingstoke, UK

Purpose of the Study: Lanthanum carbonate (LC) is a novel phosphate binder currently in development for the treatment of hyperphosphataemia in patients with end-stage renal disease. A number of studies have been completed on the efficacy and safety of LC in this patient population in the USA, Europe and Taiwan. In this presentation, we compare the patient demographics of these studies.

Methods: All of the studies were placebo-controlled, double-blind, randomized trials. An initial washout phase was followed by a 4- to 6-week LC titration phase. Patients were then randomized to receive 4 weeks of treatment with LC or placebo. Male and female patients were included, and all had received dialysis.

Results: The populations consisted of different racial groups; 100% of patients were Chinese in the Taiwanese study, 42% were black and 44% were Caucasian in the US study, and 95% were Caucasian in the European study. The dose of lanthanum required also varied between groups. Doses of $\geq 2,250$ mg/day were required by 75% of US patients, compared with $\leq 1,500$ mg by 82% of the European study population, and $\leq 2,000$ mg/day by 77% of the Chinese patients. This suggests that US patients may have had higher levels of dietary phosphate, which could affect dose requirement. The average body weight of the US patients was also higher than in the other trials. Average age was similar (50–60 years), and in all studies, LC treatment successfully controlled serum phosphorus levels (≤ 5.94 mg/dL in the USA; ≤ 5.6 mg/dL in Europe and Taiwan), and did not affect serum calcium or parathyroid hormone levels. Treatment with LC was consistently well tolerated.

Conclusions: A comparison of the study populations showed that they had diverse racial backgrounds. They also differed in average body weight, and the results suggest that titration enables the optimal dose of LC to be achieved. LC treatment was found to be effective for the management of hyperphosphataemia in this heterogeneous group of patients.

A 1-Year Study Comparing the Safety and Efficacy of Lanthanum Carbonate (Fosrenol®) and Calcium Carbonate in Dialysis Patients

A. Torres¹, M.E. De Broe², P.C. D'Haese²,
A. Hutchison³, C. Jones⁴

¹University of Canaries Hospital, Tenerife, Spain,

²Department Nephrology, Antwerp University, Belgium,

³Manchester Institute of Nephrology and Transplantation,

⁴Shire Pharmaceutical Development Ltd, Basingstoke, UK

Purpose of the Study: Hyperphosphataemia is a persistent problem in dialysis patients with end-stage renal disease. Calcium- and aluminium-based binders effectively reduce phosphorus levels, but have been linked with serious side effects. In this open-label study, we compared the safety and efficacy of long-term treatment with lanthanum carbonate (LC), a new phosphate binder, and calcium carbonate (CC), which is widely used.

Methods: Following a bone biopsy, patients were randomized to receive LC or CC. Doses were titrated to achieve serum phosphorus control (≤ 1.8 mmol/L). After 1 year of the treatment, a second biopsy was taken. Lanthanum and calcium concentrations in biopsy material were measured, and assessments during treatment included plasma lanthanum levels, and serum phosphorus, parathyroid hormone (PTH), calcitriol and calcium levels. Adverse events were recorded at each study visit.

Results: In total, 98 patients were randomized to receive LC ($n = 34$) or CC ($n = 34$); 68 patients completed the study. In both groups, phosphorus control was achieved (LC 1.79 ± 0.47 mmol/L; CC 1.65 ± 0.54 mmol/L), serum calcium and $\text{Ca} \times \text{P}$ product did not change from baseline, and calcitriol was maintained within the normal range. PTH levels decreased in CC-treated patients, but returned to pre-treatment levels by Week 52. The frequency of adverse events was similar, with the exception of hypercalcaemia (LC 6%; CC 35%). Bone lanthanum levels increased in both groups (maximum levels, $1.0 \mu\text{g/g}$ in CC patients, $5.5 \mu\text{g/g}$ in LC patients), and bone calcium levels were similar. Plasma lanthanum increased in LC-treated patients, and reached a steady state by Week 24.

Conclusions: LC controlled phosphorus levels, was well tolerated, did not affect PTH levels, and was associated with a reduced incidence of hypercalcaemia compared with calcium carbonate. These results confirm a previously published analysis of bone data from this study (D'Haese et al., 2003), which showed a general improvement in bone disease state during LC treatment.

In conclusion, LC showed similar tolerability and efficacy to CC over 1-year of treatment, but with a lower incidence of hypercalcaemia and with no effect on PTH levels. There was no evidence of plasma lanthanum accumulation, following achievement of steady state within 12 weeks in LC-treated patients.

Attitude of Patients to Phosphate Binders: Lanthanum Carbonate is Preferred to Conventional Agents in a Chinese Population

M. Cheung¹, R. Cheung¹, J. Anderson², M. Gill²

¹ISIS Research North Asia, Hong Kong, China,

²Shire Pharmaceutical Development Ltd, Basingstoke, UK

Purpose of the Study: Compliance with phosphate binders can be poor. We assessed the attitudes of patients to lanthanum carbonate (LC), a novel phosphate binder currently in development, and compared them with attitudes to available phosphate binders.

Methods: During a clinical trial of LC, 59 patients were interviewed, independently of the trial, using a semi-structured questionnaire. Data were captured anonymously by the study site coordinator and no patient identities were revealed. The trial consisted of a dose-titration phase with all patients receiving LC followed by a randomized, double-blind, placebo-controlled phase. As the interviews were undertaken before the unblinding of the trial, it was assumed that patients whose phosphorus levels remained unchanged or were reduced at the end of the placebo-controlled phase compared with the end of the titration phase were receiving LC. LC was given as either 250 or 500 mg chewable tablets.

Results: Before the trial, most patients (71%) were receiving calcium carbonate as a phosphate binder, alone (63%) or in combination with aluminium hydroxide (8%). During the trial, 44% of patients required fewer tablets than with their previous treatment and 27% required an equal number. Compliance with medication was greater during the trial than before (percentage who always took their treatment during vs. before trial: 63% vs. 41%). When asked to rate the trial agent against their previous phosphate binder, 61% of the patients preferred the trial agent compared with 17% preferring previous treatment. In those patients who were considered to be receiving LC as opposed to placebo, 71% preferred the trial agent to previous binders. The most common reasons cited for trial agent preference were taste (56%) and efficacy (36%).

Conclusions: LC was preferred by patients to their previous phosphate binder. Taste and efficacy were found to be important factors in determining patients' attitudes.

The Pharmacology of Lanthanum Carbonate (Fosrenol®): A New Non-Aluminium, Non-Calcium Phosphate Binder

S. Damment, I. Webster, M. Pennick

Shire Pharmaceutical Development Ltd, Basingstoke, UK

Purpose of the Study: Lanthanum carbonate (LC) has undergone extensive pre-clinical and clinical development as a treatment for hyperphosphataemia in patients with end-stage renal failure. Presented here is an overview of its non-clinical primary (desirable) and secondary (undesirable) pharmacology.

Methods/Results: In vitro experiments conducted over the pH range of the gastrointestinal tract showed LC to have similar phosphate-binding potency to aluminium hydroxide (AH), and significantly greater potency compared with calcium carbonate (CC) or calcium acetate (CA). At pH 3, LC bound 97.5% of phosphate vs. 86.8%, 0.0% and 0.0% for AH, CC and CA, respectively; at pH 5, LC bound 97.1% vs. 95.2%, 91.9% and 92.6%; and at pH 7, LC bound 66.6% vs. 68.0%, 6.2% and 99.9%. In 5/6th nephrectomized rats, LC was equipotent with AH and significantly more potent than CC or sevelamer at binding dietary phosphate, as indicated by marked reductions in urinary phosphate excretion (all agents dosed orally for 6 weeks at 1,000 mg/kg/day). In mice, rats and dogs, no direct effects on serum calcium, vitamin D or parathyroid hormone occurred at doses $\leq 2,000$ mg/kg. There were no effects on the intestinal transit time of a charcoal meal, fecal output and quality, or gastric mucosal integrity in rats given $\leq 1,000$ mg/kg, but reduced acidity occurred at doses > 500 mg/kg. In mice given LC $\leq 2,000$ mg/kg orally, no acute adverse central nervous system (CNS) effects were identified in an Irwin behavioural screen, or in screens assessing hexobarbital-induced sleeping time, proconvulsant activity, anticonvulsant activity or spontaneous locomotor activity. No long-term adverse CNS effects occurred in neurobehavioural screens in mice or dogs dosed for up to 62 weeks. In anaesthetized dogs, intraduodenally instilled LC ($\leq 2,000$ mg/kg) did not affect respiration, heart rate, blood pressure, left ventricular pressure or electrocardiograms, including QT and QTc intervals.

Conclusion: These studies indicate that LC is a selective and potent phosphate binder with a low potential for adverse secondary pharmacological effects.

The Pharmacokinetics of a New Non-Aluminium, Non-Calcium Phosphate Binder, Lanthanum Carbonate (Fosrenol®)

S. Damment, M. Pennick, M. Gill

Shire Pharmaceutical Development Ltd, Basingstoke, UK

Purpose of the Study: A series of studies to investigate the disposition of lanthanum (La) in animals and man was conducted to support clinical use in of end-stage renal failure patients.

Methods/Results: In animals, oral bioavailability was $\leq 0.0007\%$, with 99.4% ($\pm 5.25\%$) of an oral dose fecally excreted in rats ($n = 4$). Absorbed La (simulated in rats by intravenous dosing) was also excreted in feces ($96.9 \pm 1.12\%$ of recovered drug), with the majority ($93.6 \pm 8.17\%$) appearing in bile ($n = 5$). Urinary excretion was negligible in all species. In healthy human subjects, 0.000031% ($\pm 0.000038\%$) of a 1 g dose was recovered in urine ($n = 8$). Peak plasma La levels at steady state (1 g tid for 11 days) were similar in healthy individuals (0.42 ± 0.17 ng/mL) and dialysis patients (1.06 ± 1.04 ng/mL) ($n = 8$). Corresponding AUC_{last} values were 10.95 ± 4.11 and 31.05 ± 40.47 ng·h/mL. The predicted free plasma La concentrations are 1000× lower because $\geq 99.7\%$ is bound to plasma protein. In Phase II and III trials (doses up to 1 g tid), plasma La levels were constant over 2 years, confirming achievement of steady state, e.g. 0.572 ± 0.909 ng/mL after 6 weeks ($n = 699$), and 0.591 ± 1.129 after 1 year ($n = 275$). Median tissue La levels in animals after treatment for

up to 80 weeks indicated low retention in systemic tissues, the majority having median concentrations $<1 \mu\text{g/g}$ wet tissue (doses up to 2,000 mg/kg/day, $17\times$ a human dose of 3 g/day). There was no significant penetration into brain (median concentrations $<0.007\text{--}0.059 \mu\text{g/g}$). Concentrations in animal bone and liver achieved steady state with median levels of $1.84\text{--}8.15 \mu\text{g/g}$. Bone biopsies from dialysis patients ($\leq 3 \text{ g La/day}$ for 1 year) had La levels in the range predicted from animal studies ($2.10 \pm 1.36 \mu\text{g/g}$, vs. $0.103 \pm 0.166 \mu\text{g/g}$ in patients receiving calcium carbonate, $n = 49$ per group). Histomorphometry revealed no adverse effects on human bone, consistent with an absence of bone and other toxicities in long-term animal studies.

Conclusion: This pharmacokinetic profile is consistent with the good tolerability of lanthanum carbonate in pre-clinical and clinical studies.

142

The Toxicology of Lanthanum Carbonate (Fosrenol®), a New Non-Aluminium, Non-Calcium Phosphate Binder

S. Damment¹, P. Greaves², N. Downes³

¹Shire Pharmaceutical Development Ltd, Basingstoke,

²MRC Leicester, ³Sequani Ltd, Ledbury, UK

Purpose of the Study: An extensive programme of animal toxicology studies on lanthanum carbonate (LC) was conducted to support clinical evaluation and use in renal dialysis patients.

Methods/Results: LC was non-toxic to mice and rats at the maximum practical single oral dose of 2,000 mg/kg, equivalent to $17\times$ a clinical dose of 3 g lanthanum/day. Repeated oral administration of 1,500 mg/kg/day to mice and rats over their lifespan (99–104 weeks), or 2,000 mg/kg/day to dogs for 12 months, did not affect normal growth or behaviour. There were no changes in clinical pathology, ophthalmoscopy, electrocardiography or histopathology (40 tissues evaluated) to suggest any toxicities of concern for human use. LC exacerbated the spontaneous gastric pathology (adenomatous change) that occurs in aging CD-1 mice. No gastric pathology occurred at higher doses in the dog, a species in which the mode of administration (with food) and gastric environment more closely mimic those in man. Intravenous administration of soluble lanthanum chloride to mice, rats and dogs was similarly well tolerated. The liver was the only target organ identified at excessive doses, with mild-moderate inflammatory changes occurring at plasma lanthanum levels $\geq 20,000$ times the peak steady state plasma concentration in dialysis patients. Studies in rats and rabbits with oral LC indicated no potential for adverse effects on fertility, pregnancy, embryo–fetal or pre-/post-natal development. Furthermore, no potential to cause genetic damage was identified using in vitro microbial and mammalian test systems, or in two rodent micronucleus tests conducted in vivo by oral and intravenous routes. Rats with impaired renal function (5/6th nephrectomy) given 2,000 mg/kg/day for 13 weeks responded similarly to normal rats, except for the occurrence of reduced bone mineralization, an expected artefact of the phosphate depletion that occurs in this vitamin D compromised model with administration of high doses of any phosphate binder. No toxicity to bone occurred in any oral or intravenous study.

Conclusion: Overall, this toxicology programme predicts that LC will be well tolerated in clinical use.

143

Lanthanum Carbonate (Fosrenol®), a New Phosphate Binder, Demonstrates Favourable Pharmacokinetic Properties for Use in Patients with End-Stage Renal Failure

M. Pennick, S. Damment, G. Fiddler, M. Gill

Shire Pharmaceutical Development Ltd, Basingstoke, UK

Purpose of the Study: Lanthanum carbonate (LC) is a novel phosphate binder being developed for the treatment of patients with end-stage renal disease (ESRD) and hyperphosphataemia. Here, we review the extensive clinical trial programme that has been carried out to assess the pharmacokinetics of LC in healthy individuals and patients with ESRD.

Methods: Single- and multiple-dose pharmacokinetics of lanthanum ($\geq 3 \text{ g/day}$) were assessed in healthy volunteers and patients on dialysis in a number of clinical trials. Separate studies evaluated the effects of LC on the pharmacokinetics of warfarin, digoxin and metoprolol.

Results: Plasma lanthanum levels were consistently very low ($<1.1 \text{ ng/mL}$) when LC was given to healthy volunteers and dialysis patients. In a randomised, placebo-controlled trial in 9 healthy volunteers, mean C_{max} was $0.53 \pm 0.15 \text{ ng/mL}$ at treatment endpoint (5 days). Mean T_{max} was 4 h, and the terminal elimination half-life was approximately $36 \text{ h} \pm 7.02 \text{ h}$. Over the 7 days from the start of treatment, urinary lanthanum output was 0.000031% of the total oral dose. Renal clearance amounted to 1.5 mL/min. Timing of LC administration during or immediately after food intake had no important effects on the pharmacokinetics of LC in an open-label crossover trial ($n = 36$). Co-administration of citrate had no effect on the pharmacokinetics of LC in another open-label crossover trial ($n = 24$). In an open-label trial involving dialysis patients and healthy controls ($n = 18$), impaired renal function had no significant effects on LC pharmacokinetics. LC had no significant effect on the pharmacokinetics of warfarin, digoxin or metoprolol in open-label crossover trials ($n = 14$ in each trial).

Conclusions: The low absorption and predominantly non-renal elimination of LC, together with the lack of important drug–drug interactions with metoprolol, warfarin, digoxin and citrate, are important factors contributing to a good safety profile for clinical use in patients with ESRD.

144

Contrast Nephropathy due to Renal Angiography: Effects on Progression to End-Stage Renal Disease and One-Year Mortality

K.C. Garvan¹, K. Dita², G.D. Vesna¹

¹Mayo Clinic Rochester, MN, USA,

²Charles University, Hradec Kralove, Czech Republic

Purpose of the Study: Contrast nephropathy (CN) is associated with significantly increased morbidity, and in-hospital and long-term

mortality in patients requiring coronary angiograms. The aim of this study was to assess the incidence of CN and its long-term effects on renal function and mortality in patients with established renal failure undergoing renal angiograms.

Methods: We reviewed the cases of all patients who had interventional renal angiograms for resistant hypertension at Mayo Clinic between 1998–2003 and who had serum creatinines ≥ 2.0 mg/dL before the procedure. CN was defined as an increase in creatinine of 1.0 mg/dL or more within 7 days of procedure. We compared clinical outcomes and 1-year mortality rates between patients who did versus those who did not develop CN.

Results: We identified 62 patients who had serum creatinines >2.0 mg/dL before the procedure. All patients had angioplasty and 53 had at least one renal artery stent placed. Mean creatinine before the procedure was 2.5 (2.2–3.0) mg/dL. Mean systolic and diastolic blood pressures were 162 ± 32 and 81 ± 19 mmHg, respectively, while taking an average of 2.8 ± 0.9 blood pressure medications. Eight patients (12.5%) experienced CN and four of them (50%) required permanent hemodialysis compared to 16.7% (9/54) in the group without CN ($p = 0.05$). One-year mortality of 37.5% (3/8) was significantly higher ($p = 0.04$) in the group with CN compared to 7.3% (4/55) in the group without CN. We observed no difference between the groups with respect to age, sex, baseline creatinine and co-morbidities.

Conclusion: We report a 12.5% incidence of CN in patients who underwent renal angiograms and had pre-existing moderate renal insufficiency. Patients with CN were more likely to progress to end-stage renal disease and require permanent hemodialysis and had higher one-year mortality rate when compared to patients without CN.

145

A Large Cross Sectional Study in Type 2 Diabetics to Quantitate Non-Diabetic Kidney Disease Causing Early Renal Insufficiency

M.M. Bahadur¹, B.V. Gandhi¹, T. Aseem²

¹Jaslok Hospital and Research Center,

²Dr. BAM Hospital, Mumbai, India

Aim: To determine the prevalence of early Chronic Renal Insufficiency in patients with Type 2 diabetics nephropathy.

Study Design and Methods: Data of 1,360 diabetics registered in a large urban Diabetic and Nephrology clinic registry was studied. Only those having complete clinical examination, CBC, FBS, PPBS, Renal profile, Lipid profile, ECG, Fundus examination, test for microalbuminuria and 24 h protein estimation were analysed. Patients having serum creatinine more than 1.5 mg%, 24 h urinary protein more than 150 mg, micral positive, or diabetic retinopathy were excluded. 320 patients records met all inclusion and exclusion criterion. GFR was estimated for all these patients using Cockcroft and Gault formula. GFR less than 60 ml/min/1.73BSA was termed early renal insufficiency. All biochemistry was done on an autoanalysers, microalbuminuria by micral strips, fundus by direct and indirect ophthalmoscopy, fluorescein angiography where indicated.

Results: Low GFR less than 60 ml/min in the absence of microalbuminuria, macroalbuminuria, raised creatinine and diabetic retinopathy was detected in 9.9% cases.

Conclusion: It is usual to check for microalbuminuria and diabetic retinopathy as part of routine diabetic follow up to detect early diabetic nephropathy. This study highlights the presence of significant early renal insufficiency due to non-diabetic nephropathy. It is suggested that in addition to estimating serum creatinine, urine for microalbuminuria and fundus, GFR estimation should be done routinely in all diabetics to detect this group.

146

Dyslipidemia in Diabetes: Does it Alter in Overt Diabetic Nephropathy?

M.M. Bahadur¹, A. Vikram², P.K. Sharma³

Jaslok Hospital and Research Centre,

Dr. BAM Hospital, Mumbai, India

Aim: To study the significance of variation in Lipid Profile, if any, in patients with overt diabetic nephropathy v/s that in diabetics without overt nephropathy.

Materials and Methods: Records of total 1,359 diabetic patients were screened. Of these 1,286 patient whose complete lipid profiles were available were selected. Patients with Sr. creatinine of more than 1.6 mg% on 2 different occasion were placed in group A (overt nephropathy) ($n = 85$). Remaining patients ($n = 1,201$) who had a normal Sr. creatinine <1.6 mg% were placed in group B and served as controls for the nephropathy group. Dyslipidemia was defined as per ADA guidelines of Sr. TG >200 , HDL <35 for male and <40 for female, LDL-C >130 and Sr. total Chol. >201 all in mg%. The lipid profile was evaluated for both groups.

Results:

Lipid profile	Group A	Group B	(chi-sq. test)
T. Chol >201	41/85	628/1,201	>0.05 NS
TG >200	42/85	520/1,201	>0.05 NS
LDL-C >130	27/85	458/1,201	>0.05 NS
HDL <35	43/85	468/1,201	<0.05 Sig

Conclusion: In this large study in Indian population a significant finding is that those diabetics who develop renal failure have a further aggravation of dyslipidemia in the form of further reduction in their HDL levels as compared to those without renal failure. Markedly low HDL may be due to physical inactivity or uremic toxins interacting with the diabetic milieu. Statins form the first line drugs for treatment of diabetic dyslipidemia as per ADA recommendations. It is proposed that role of niacin and fibric acid derivatives in diabetic CRF needs reevaluation as these drugs are known to increase HDL levels.

Intravenous Darbepoetin Alfa (Aranesp®) Better Maintains Haemoglobin Levels in Dialysis Patients: A Steady State Analysis

J.L. Motellon

Amgen Europe, Lucerne, Switzerland

Purpose of the Study: Darbepoetin alfa has an extended half-life and greater in vivo activity than epoetin (rHuEPO). Data from two randomized controlled trials of darbepoetin alfa, performed in the USA and in Europe and Australia, were combined to investigate the efficacy of intravenous (IV) dosing with darbepoetin alfa at extended dosing intervals compared with rHuEPO, also administered IV.

Methods: Haemodialysis patients on a stable dose of rHuEPO were randomized to switch to darbepoetin alfa ($n = 303$) or continue with rHuEPO ($n = 401$). The initial dose of darbepoetin alfa was calculated to provide an equivalent peptide mass to the previous rHuEPO dose. Doses were subsequently titrated to maintain haemoglobin (Hb) within a target range of 10–13 g/dL and within -1.0 g/dL to $+1.5$ g/dL of the patient's baseline Hb. We present here data from weeks 21–24 of the studies, to demonstrate the effect of darbepoetin alfa on Hb concentrations as required by the study protocols to maintain Hb within the stated range. Mean ferritin levels were adequate in both groups.

Results: At baseline, mean Hb concentrations were 11.10 ± 0.68 g/dL in the darbepoetin alfa group and 11.18 ± 0.70 g/dL in the rHuEPO group. At weeks 21–24, mean Hb had increased by 0.10 g/dL (95% confidence intervals [CI]: $-0.04, 0.23$) in the darbepoetin alfa group, whereas in rHuEPO-treated patients, mean Hb had decreased by 0.19 g/dL (95% CI: $-0.30, -0.07$) a difference of 0.29 g/dL (95% CI: $0.11, 0.46$; $P = 0.0017$). Safety data were as expected in a dialysis population and similar between the treatment groups.

Conclusion: We conclude that IV darbepoetin alfa, administered at extended dosing intervals, is effective at maintaining Hb in haemodialysis patients.

Use of r-HuEPO in the Management of Anemia Due to CRF in Predialysis Diabetics – Early Experience from EPO Trial in Bangladesh

N. Islam¹, M.S. Hassan¹, M.A. Mansur¹, M.S. Islam¹, T. Ahmed¹, S. Ahmed¹, H.U. Rashid², M. Iqbal³

¹Nephrology and Immunology (BIRDEM),

²Nephrology, BSM Medical University,

³Nephrology, SSMC, Dhaka, Bangladesh

This on going study is designed to use erythropoietin (EPO) to increase hemoglobin in predialysis anemic diabetic subjects and to observe the required dose, response and outcome.

Forty anemic diabetics divided in two groups-EPO group ($n = 20$) receiving EPO with iron and Control group ($n = 20$) getting iron only were selected. They were evaluated at starting, during initiation (time

to reach target hemoglobin 11 g/dl) and at maintenance period (12 weeks after reaching target hemoglobin).

At starting both groups were matched for age, sex, BMI and different clinical/biochemical parameters. Initiation took 9 ± 3 weeks to reach hemoglobin 11 ± 0.2 g/dl in EPO group. At this time other clinical and biochemical parameters were similar between both groups. At the end of maintenance period (22 ± 5 weeks), both groups were evaluated again and found other parameters unchanged except improving hemoglobin status in EPO group. Different parameters at start and in the end of study between EPO and Control groups were hemoglobin 8.7 ± 0.7 vs 9.3 ± 0.8 , $p = \text{NS}$ and afterwards 11.8 ± 0.7 vs 9.5 ± 0.5 g/dl ($p < 0.001$); Serum creatinine 4.08 ± 1.7 vs 3.5 ± 1.6 , $p = \text{NS}$ and 4.2 ± 1.8 vs 4.6 ± 0.8 mg/dl, $p = \text{NS}$. EPO dose required in EPO group at three observation periods were -100 ± 20 , 93 ± 19 and later 62 ± 24 u/kg/week ($p < 0.001$).

In conclusion EPO therapy can safe and effectively raise hemoglobin in predialysis diabetics. The maintenance EPO dose is relatively low and renal with other biochemical parameters remain stable during treatment.

Concurrent Amyloidosis and Hodgkins Lymphoma Following Lymphomatoid Papulosis: Is There a Relationship? A Case Report

A.R.A. Amir, S.S. Sheikh

Dhahran Health Center, Dhahran, Saudi Arabia

Introduction: Hodgkin's lymphoma (HL) has been reported to occur infrequently in association with lymphomatoid papulosis (LP). On the other hand amyloidosis also may occur as a complication of lymphomas including HL but has never been reported in association with LP. We herein present an unusual case of LP who 3 years later developed concomitant HL as well as amyloidosis of his single kidney and brain leading to nephrotic syndrome, acute renal failure, coma and death within 3 weeks. In our patient the simultaneous development of amyloidosis and HL suggests that amyloidosis is secondary to LP, an association never reported before.

Material and Methods: A 74 years old male with 3 years history of LP presented with oliguria. He was found to have acute renal failure and 37 g of proteinuria. The patient had right nephrectomy done 27 years ago for a small nonfunctioning kidney. He was found to have paraaortic and mesenteric lymphadenopathy that were biopsied percutaneously. Despite supportive dialysis the patient continued to do poorly, went into coma and died.

Results: Biopsy of his single left kidney showed enlarged glomeruli completely replaced by amyloidosis confirmed by Congo red stain and electron microscopy. His paraaortic lymph nodes exhibited classic HL with CD 30 and CD 15 positive Reed Sternberg cells in a background of mixed inflammatory cells including prominent eosinophils. The CT scan of the brain was negative; however, the MRI showed multiple periventricular parenchymatous lesions and changes of cerebral amyloid angiopathy.

Conclusion: In this case the concomitant presentation of systemic amyloidosis and HL post LP suggests that amyloidosis is a late sequelae of LP, an association that is never reported before.

Plasmapheresis in Immunologic Renal Diseases

M.R. Ardalan¹, A. Ghafari²

¹Nephrology Department, Imam Hospital, Tabriz,

²Nephrology Department, Imam Hospital, Uromia, Iran

Purpose of Study: The last decade has witnessed a more vigorous reexamination of the efficacy of therapeutic plasma exchange. However the clinical efficacy of plasmapheresis for many renal disease is still controversial.

Methods: In this case series we studied 25 patients (11F, 14M), (12–70 years). 2 goodpasture syndrome, 7 HUS/TTP, 4 pauci-immune RPGN, 5 lupus nephritis, 4 acute renal allograft rejection and 3 patients with unknown crescentic RPGN. All patients received a mean of (8 ± 3) sessions, with mean of (2.5 ± 0.5) liter in each exchange, and also conventional treatments (cytotoxic drugs, prednisolone) and then we monitored response to this therapy.

Results: In anti-GBM group one died (lung hemorrhage), one became dialysis dependent. In HUS/TTP group 5 patients (0.71) had complete response (serum creatinin <2, one month after treatment), two became dialysis dependent. In pauci-immune RPGN all became dialysis dependant. In lupus nephritis group 2 patients had complete response (0.40) and 3 became dialysis dependant. In renal transplanted patients two respond completely and two of them lost their allograft. In unknown RPGN group one achieved complete response and two became dialysis dependent.

Conclusion: We had best response in HUS/TTP group. Lupus patients with mild renal involvement who had been received this therapy for another reasons had a good response (sever sensory neuropathy and antiphospholipid syndrome with Scr <3 mg/dl). In pauci-immune and in anti-GBM groups we did not have any response.

Two Methods of Oral Calcitriol Therapy in Secondary Hyperparathyroidism

M.R. Ardalan

Nephrology Department, Imam Hospital, Tabriz, Iran

Purpose of Study: Calcitriol (1,25-OH-D3) is an effective treatment for suppressing parathyroid hormone secretion in secondary hyperparathyroidism. In this study we observed the efficacy of two different models of oral calcitriol therapy.

Methods: 22 hemodialysis patients (47 ± 16 years) were included. The inclusion criteria: Intact PTH (iPTH) >300 pg/ml, serum phosphor (ph) <6 mg/dl serum calcium (ca) <1.1 mmol/l by random in group A. Patients were received calcitriol orally every night (0.5 µg), and in group B. Every other night (1 µg every 48 h) for eight weeks and then we compared this two groups.

Results: In group A we finally analyzed eight patients: pretreatment iPTH (654 ± 213.5 pg/ml), post treatment (iPTH = 208 ± 152). Pre and post treatment results for ca, ph, and bone alkaline phosphates were: 1.06 ± 0.15 vs 1.14 ± 0.10 mmol/l, 4.73 ± 1.26 vs 6.02 ±

1.77 mg/d ± 5411 and 1783 vs 579 ± 364 unit all in succeeding. In group B we finally analyzed seven patients, pretreatment and post treatment iPTH were 584.2 ± 191.8 (vs) 258.8 ± 167.1 pg/ml, and also they were 0.9 ± 0.1 vs 0.99 ± 0.12 mmol/l for ca, and 5.3 ± 1.5 vs 5.2 ± 1.5 mg/dl for ph and 615 ± 278.2 vs 519 ± 213 for serum bone alkaline phosphates.

Conclusion: There were significant difference ($p < 0.05$) between pre and post treatment iPTH levels in both groups, but this differences were not significant for bone alkalinephosphatase.

Real Time Sonography Guided Renal Biopsy

M.R. Ardalan¹, M.K. Tarazamani²

¹Nephrology and Dialysis Department,

²Radiology Department, Imam Hospital, Tabriz, Iran

Purpose of Study: Renal biopsy often require for accurate diagnosis of renal disorders dreaded complications, and also inadequate sampling may occurs in blind renal biopsies.

Methods: A 3.5MHZ probe was used. In prone position the lower pole of the kidney was found during end normal or deep inspiration, all by one radiologist and all biopsies were performed by one nephrologists. After skin anesthesia we inserted spinal needle which was guided by angled probe laterally, after it reached the capsule we measured the depth, after that we inserted the biopsy needle to this direction and depth and biopsy were taken out under real time sonography guidance.

Results: In this prospective study (Dec 2001–Jul 2003), 78 kidney biopsy performed. Three biopsies were unsuccessful and two without any glomerule. Mean depth of the renal cortex from the skin by spinal needles (51.1 ± 10.3) were greater (~8 mm) than sonographic measured (43.8 mm ± 10.8). Mean numbers of glomerules were 10, macroscopic hematuria occurred in two patients. Without any other major complications.

Conclusion: Real time sonography guided renal biopsy is a safe and accurate method for renal biopsy.

Encouraging Timely Specialist Referral in Chronic Renal Disease

A. Mondry¹, A.L. Zhu¹, Thuy Denise Vo², K. Hahn³

¹Bioinformatics Institute, Singapore, Singapore,

²Klinikum Solingen, Solingen, ³Praxis Karl-Harr-Strasse, Dortmund, Germany

Purpose of the Study: Guidelines recommend early specialist referral as late referral to nephrological care is associated with increased morbidity, mortality, and cost. Still, 22–51% of referrals need renal replacement therapy within 3–4 months. We hypothesize this is because these recommendations address the specialist, rather than the primary care providers (PCP).

Methods: In a single renal care center the potential of specialist intervention, especially in slowing progression of CRF, was introduced individually to some 250 local PCPs, and referral strategies were discussed. In order to overcome the PCPs' most commonly expressed fears, every referred patient was asked to report back to his PCP immediately after the initial specialist examination, and new medication was prescribed and allotted to the nephrologist's budget directly. A retrospective analysis compared the stage of renal disease in patients referred within three months before the introductory round (3Q 1997, group A, n = 18), and two years later (3Q 1999, group B, n = 50). Incipient renal disease (IRD) was defined as ECC >60 ml/min/1.73 m² on referral, CRF as 60 > ECC > 20 ml/min/1.73 m², and ESRD as ECC <20 ml/min/1.73 m².

Results:

Table 1. Referral pattern in 1997 and 1999

	N	IRD	CRF	ESRD
Group A	18	5 (28%)	5 (28%)*	8 (44%) [#]
Group B	50	14 (28%)	26 (52%)*	10 (20%) [#]

Chi-square test: overall significant at p = 0.096; for CRF *p = 0.077; ESRD [#]p = 0.062.

Conclusions: Individually addressing PCPs' ignorance and concerns significantly decreased late referral. This stresses the importance of enhancing the PCPs' problem awareness and knowledge of available resources and shows that timely referral indeed can be achieved.

154

SDS-PAGE for the Investigation of Acute Renal Failure

Y.-K. Lau, K.-T. Woo, T.H.C. Stephen, M.S. Sufi, C.-M. Chan, K.S. Wong

Department of Renal Medicine, Singapore General Hospital, Singapore, Singapore

SDS-PAGE is an excellent single test for investigating proteinuria. It can provide much useful information on the underlying renal problem. We studied the value of SDS-PAGE in the investigation of 9 patients with acute renal failure (ARF) to examine how closely SDS-PAGE may reflect the renal biopsy and clinico-pathological findings in patients.

Random urine samples were collected for SDS-PAGE analysis, performed on the PhastSystem (Pharmacia, Sweden) using PhastGel Gradient 8–25 and PhastGel SDS Buffer Strips.

Biopsies from the 5 cases of vasomotor nephropathy revealed acute tubular necrosis (ATN). The histological changes were reflected in the tubular proteinuria found by SDS-PAGE analysis of urines taken at the time of biopsy. Three cases of acute on chronic renal failure were not biopsied and the clinico-pathological diagnosis were affirmed with SDS-PAGE analysis showing 2+ or more tubular proteinuria. Another index of tubular proteinuria, α 1-microglobulin levels were measured elevated in these urines (>100 arbitrary units/l). The 9th case, an ARF recovering from Vioxx was also not biopsied and

SDS-PAGE showed only trace glomerular proteinuria. Thus in all 9 cases of ARF, SDS-PAGE analysis of urine correlated well with biopsy findings and with clinico-pathological diagnosis without biopsy.

SDS-PAGE analysis of urine is useful for the investigation of ARF whether patient has a biopsy or not. The test is not invasive, not expensive and easy to perform with dedicated instrument and ready-for-use reagents. With current emphasis on cost containment and evidence-based medicine, the role of SDS-PAGE test for the routine management of renal patients should be fully explored.

155

Losartan Reduces the Burden of ESRD: Implications from the RENAAL Study for the Western Pacific Region

J.C.N. Chan¹, K. Kurokawa², M. Thomas³, K.S. Wong⁴, S. Shahinfar⁵, G. Carides⁵, B.M. Brenner⁶, W. Gerth⁷

¹Prince of Wales Hospital, Hong Kong, ²University Tokai, Kanagawa, Japan, ³Baker Medical Research Institute, Melbourne, Australia, ⁴Singapore General Hospital, Singapore, ⁵Merck Research Labs, Blue Bell, ⁶Brigham and Women's Hospital, Boston, ⁷Merck & Co. Inc., Whitehouse Sta., USA

Background: Type 2 diabetes is one of the leading causes of end-stage renal disease (ESRD) in the Western Pacific Region. The RENAAL (Reduction of Endpoints in NIDDM with the AII Antagonist Losartan) study evaluated the renal protective effects of losartan versus placebo on a background of non-ACE-I/non-AIIA antihypertensive therapy in 1,513 patients with type 2 diabetes and nephropathy. Losartan reduced the primary endpoint (doubling of serum creatinine, ESRD, or death) by 16% (p = 0.02). Losartan reduced the incidence of doubling of serum creatinine by 25% (p = 0.006) and ESRD (29%; p = 0.002).

Purpose: To examine the potential effect of losartan on the burden associated with ESRD over 3.5 years in the Western Pacific Region.

Methods: New ESRD cases avoided is calculated by combining type 2 diabetes with nephropathy population estimates for countries in the Western Pacific Region with the percent absolute risk reduction of ESRD observed in RENAAL over 3.5 years. The number of ESRD days was defined as the length of time from ESRD onset until death or study end. ESRD free years is calculated by combining the population estimate with ESRD free days divided by the number of days per year.

Results: Compared to placebo, losartan reduced the cumulative incidence of ESRD by 6.3% (20.8–27.1%), and the number of days with ESRD by 33.6 (95% CI: 10.9 to 56.3, p = 0.004) per patient at risk. We estimate there are 1.81 million diagnosed type 2 diabetics with proteinuria (urine albumin/creatinine $\geq$ 300 mg/g) in the Western Pacific Region. Extrapolating RENAAL results to these patients, we may expect the addition of losartan to lead to a reduction of 114,000 ESRD cases and 166,400 fewer years with ESRD over 3.5 years.

Conclusion: If losartan treatment were extended to diagnosed patients with type 2 diabetes and nephropathy in the Western Pacific Region the benefits would be considerable.

Irbesartan Lowers Urinary Albumin Excretion through Hemodynamic Changes in Microalbuminuric Normotensive Diabetic Type 1 Patients

B. Draganov, S. Djurovic, A. Westheim, I. Os

Department of Medicine, Ulleval University Hospital,
Department of Pharmacotherapeutics,
University of Oslo, Norway

Purpose of the Study: To evaluate the effect of irbesartan, an angiotensin 2 receptor blocker (ARB), on urinary albumin excretion in normotensive type 1 diabetic patients with microalbuminuria.

Methods: Normotensive patients with type 1 diabetes mellitus with microalbuminuria, i.e. albumin/creatinine ratio (ACR) 3–30 mg/mmol, who had previously never been treated with antihypertensive drugs and never used ACE inhibitors (ACE-I) or ARB, were eligible for this pilot study lasting for 12 months that took place at a renal unit in a university clinic. A fixed dose of 300 mg irbesartan was given, and the patients followed for 3 and 12 months with respect to ACR, BP, inflammation mediators and growth factors. Data are given as median and Q1–Q3.

Results: Of the 47 patients that were screened, 36 were not eligible either because of ACR >30 mg/mmol, hypertension, or previously use of ARB or ACEI. Of the 11 (40; 32–44 years) who were eligible and followed for 3 months, 9 could be reinvestigated after 12 months. The ACR decreased from 9.0 (6.5 to 11.2) mg/mmol to 3.5 (2.5–6.0) and 1.8 (0.6–7.3) mg/mmol after 3 and 12 months respectively ($p < 0.001$). During the first 3 months all patients decreased in ACR, and 4 became normoalbuminuric. The decrease in ACR was accompanied by a statistically significant fall in blood pressure (BP, 127/83 to 115/70 and 123/68 mmHg), and the fall in BP correlated to the fall in ACR after 3 month ($r = 0.54$ – 0.57 , $p < 0.05$), but a significant relationship was lost after 12 months. There was no change in creatinine clearance, glycemic control or lipid levels during the observation period. A significant increase was seen in TNF- α after 3 and 12 months ($p < 0.05$), while a transient increase was also seen in VEGF after 3 months ($p < 0.05$), but lost after 12 months. A decrease in TGF- β 1 did not reach statistical significance. Neither von Willebrand factor, fibronectin or PAI-1 changed significantly.

Conclusion: In this pilot study, the consistent fall in ACR during a fixed irbesartan dose was associated with a fall in BP in normotensive, microalbuminuric patients.

Blood Pressure Control in Predialytic Chronic Renal Failure Patients

L.K. Prøtsch, M.G. Sælen, I. Os,

Department of Pharmacotherapeutics,
University of Oslo, Norway

Purpose of the Study: To assess blood pressure (BP) control in patients with chronic renal failure (CRF) attended ambulatory treatment in renal clinics.

Methods: A cross-sectional study based on patients records was undertaken at 6 different referral units in an area of Norway covering 1.8 million inhabitants. Predialytic patients with serum creatinine levels >200 μ mol/L who had never been transplanted or previously been treated with dialysis were included. Only those who attended regular control at least every third month at the renal unit could be included, and data from the last visit were recorded.

Results: Of the 365 patients that were included, 94% were classified as hypertensive based on BP or use of antihypertensive drugs (AHT). More men than women were hypertensive, and a substantial portion of the patients had macrovascular disease. Close to a ¼ of the patients were diabetics, and more than ¼ were classified as having nephrosclerotic kidney disease, indicating a substantial change in the etiological pattern in Norway. Furthermore, optimal BP control was only obtained in a minority of the patients despite extensive multipharmacy. Improved control would be expected with a more aggressive use of AHT. There seems in particular to be underuse of ACE inhibitors (I) or angiotensin receptor blockers (ARB) in this population. A slightly different pattern regarding use of AHT emerged among women compared to men as well as in diabetics compared to nondiabetics.

Conclusion: BP control is poor patients with CRF who are still predialytic, and there seems to be underuse of ARB and ACEI even in the diabetics.

Cyclosporin and Steroid Resistant Proteinuria

H.T. Khoroshahi, B.H. Asl, A. Nahali, A. Ghods

Imam Hospital, Tabriz, Iran

Cyclosporin is a lipophilic cyclic endecapeptid that inhibit interleukin 2 (IL2) production and has been used for prevention of allograft rejection in the past two decade. Recently it is also used for the treatment of proteinuria. The aim of this prospective study was evaluation of the efficacy of cyclosporin A in the treatment of steroid resistant proteinuria. 51 patients with massive proteinuria, resistant to steroid evaluated for at least 6 months on cyclosporin A 2–3 mg daily. Demographic parameter and also 24 h urine protein, creatinine, volume and renal function test was recorded. Then statistical analysis was performed.

In about 60% of our patients there was significant reduction proteinuria (less than 500 mg/24 h). In 20% of patients also there was reduction of proteinuria to less than 2 g/24 h. Only 20% of these patients were resistant to cyclosporin A. From the stand point of pathological pattern, more than 60% patients with minimal change disease, membranous glomerulonephritis, mesangio proliferative glomerulonephritis and focal segmental glomerulonephritis were responded to treatment with cyclosporin A. The lowest response was recorded in patients with membrano proliferative glomerulonephritis. There was not any complications related to cyclosporin A in the course of therapy, and renal fuction tests were stable in almost all of the patients.

In conclusion, cyclosporin appear to be safe and also effective agent in the treatment of massive proteinuria especially in steroid resistant and steroid dependent proteinuria.

Dialysis

159

The Effect of Substitution of Potassium Chloride Tablets with Potassium-Containing Salt Substitute in Peritoneal Dialysis Patients

S.L. Lim, H.C. Gan, S.H. Tan, J.C.E. Lee

National University Hospital, Singapore, Singapore

Aim: Peritoneal dialysis (PD) patients lose potassium via dialysate and usually have to be supplemented with potassium chloride (KCl) tablets to maintain normal serum potassium levels. The aim of this study is to determine whether substitution of KCl tablets with potassium-containing salt substitute (in cooking) would be able to maintain normal potassium levels and at the same time enhance the taste of food.

Methods: Nineteen patients who were on PD and KCl tablets were recruited for the study. During their first visit, serum potassium levels, 24h dietary recall, food frequency, and food-taste score on their current food intake were taken. They were then advised to stop KCl tablets and switch to potassium-containing salt substitute. The amount of salt substitute prescribed was calculated so that the potassium content would be almost equivalent to the KCl tablets taken previously. Subjects were advised to use this salt substitute in cooking to replace table salt. The patients were reassessed one week later.

Results: There was no difference in the mean serum potassium level before and after the substitution (4.3 ± 0.4 vs. 4.2 ± 0.5 mmol/L). 52% of patients reported improvement in the taste of food. 16% reported no change and 32% reported deterioration in taste of food.

Conclusions: We conclude that the use of potassium-containing salt substitute in cooking can replace the use of oral KCl tablets without affecting the serum potassium levels in PD patients. It also can improve the taste of food and reduce the number of medicines they need to consume.

160

A Prospective Randomised, Open-Label Study Comparing the Efficacy and Safety of Intraperitoneal Iron versus Intravenous Iron in Peritoneal Dialysis Patients

A.M. Khalid, S. Bhandari

Department of Renal Medicine, Hull and East Yorkshire Hospitals NHS Trust, Hull Royal Infirmary, Kingston upon Hull, East Yorkshire, UK

Purpose of Study: Anaemia in peritoneal dialysis (PD) is related to impaired erythropoiesis and/or iron deficiency. Iron deficiency may be either absolute (a reduction in total body iron stores) or functional. The latter occurring in subjects with adequate iron stores

who fail to supply adequate iron sufficiently rapidly to the erythroblasts. Oral iron is perhaps insufficient to supply adequate accessible iron to patients with end stage renal failure. Intermittent intravenous (IV) supplementation is effective but inconvenient in PD patients. Intraperitoneal (IP) iron may present a more convenient method of administration.

Methods: We examined the safety and efficacy of IP iron dextran in comparison to IV iron. Patients with a serum ferritin less than $200 \mu\text{g/L}$, stable on PD for ≥ 6 months, with no known drug allergy and had not received parenteral iron in the last 6 weeks were randomised to receive either IP or IV iron according to protocol (MCA and Ethical ELSYCHH321 approval). Patients given IP iron were then subsequently crossed over to receive IV to internal comparison.

Results: Interim analysis of 16 patients, 11 IP iron and 8 IV at a dose of 1.2 g given over 3 weeks in divided doses is detailed below. No adverse events occurred after a total of 72 doses of iron therapy administered. Two patients withdrew from the study, one because of transplantation and the other for no given reason. There were two episodes of peritonitis, one in each group due to staphylococci, which responded to standard therapy.

Conclusions: Intraperitoneal iron is safe but does not lead to an increase in storage or utilisable iron in peritoneal dialysis patients. Intravenous iron however remains safe and effective.

Patient group	Pre IP	Post IP	Pre IV	Post IV
n	11	11	8	8
Ferritin ($\mu\text{g/L} \pm \text{SEM}$)	139 ± 12.3	149 ± 19.1	$124.2 \pm 15.7^*$	$463.8 \pm 43.5^*$
Transferrin saturation, %	22.8 ± 1.4	22.3 ± 1.6	$24.2 \pm 1.6^*$	$52.7 \pm 7.3^*$
Hb, g/dL	11.8 ± 0.67	11.5 ± 0.89	10.6 ± 0.49	10.9 ± 0.68

*p < 0.001 (Mann-Whitney U-Test).

161

Tolerability and Efficacy of Parenteral Iron Therapy in Haemodialysis Patients

A.M. Khalid, S. Bhandari

Department of Renal Medicine, Hull and East Yorkshire Hospitals NHS Trust, Hull Royal Infirmary, Kingston upon Hull, East Yorkshire, UK

Purpose of Study: Haemodialysis patients continuously lose iron through blood letting, the dialysis circuit and gastrointestinal bleeding. This averages 2 g/year. Parenteral iron is therefore necessary to replenish and maintain sufficient iron stores this is essential for maximising the effects of erythropoietin (EPO) therapy. Several parenteral iron preparations are available, including iron dextran (Cosmofer) and iron sucrose (Venofer) and there have been many debates about the safety profiles of these preparations.

Methods: We performed a prospective crossover study in stable haemodialysis patients to examine the comparative safety and tolerability of these two iron preparations. Exclusion criteria consisted of a significant previous reaction to parenteral iron therapy. Side effects were monitored and recorded in detail, together with haemoglobin (Hb), ferritin and EPO dose.

Results: Thirty-nine stable patients (28 males and 11 females), mean age = 60.5 years, on fortnightly 100 mg of intravenous Venofer were converted to fortnightly 100 mg intravenous Cosmofer 100 mg for a period of six months. They were then subsequently converted back to Venofer. There was no difference in haemoglobin concentrations, EPO dose or ferritin levels throughout the study (Table). A total of 5 (2 diarrhoea, 3 headache) events and 7 (2 headache, 1 diarrhoea, 1 chest pain, 1 vomiting, 2 flushing/tingling) events occurred during therapy with Venofer (2,111 doses) and Cosmofer (2,287 doses) respectively with no major events or anaphylaxis. Those patients who reacted to Venofer also reacted to Cosmofer. Conversion to Cosmofer led to a cost saving of approximately £3,000.

Conclusions: Despite concerns regarding parenteral iron therapy in this study both forms of therapy were equally safe and effective. Examination of a larger cohort of patients is necessary to verify these findings.

Efficacy	Mean Hb	Mean ferritin	Mean EPO dose
On Venofer (before)	10.7 g/dl*	346.2 ng/ml*	6,600 units/week*
On Cosmofer	10.1 g/dl*	349.8 ng/ml*	6,500 units/week*
On Venofer (after)	10.5 g/dl*	415.7 ng/ml*	6,600 units/week*

*P value >0.05.

162

Anxiety and Depressive Symptoms Developing at Chronically Haemodialyzed Patients in Lower Silesia (Poland): Patients Quality of Life – Initial Data

B.J. Sapilak, A. Steciwko, D. Kurpas

Department of Family Medicine,
Wroclaw Medical University, Wroclaw, Poland

Purpose of these studies was estimation and recording of incidence and evolution of anxiety, depression and quality of life in chronically dialyzed patients in Poland (region of Lower Silesia). Members of research team were nephrologists, psychiatrists and general practitioners. 462 haemodialyzed patients from six haemodialysis centres were asked to participate in research. Every three months patients filled forms to reveal their quality of live (QOL), anxiety and depressive disorders. Forms were made up of nine psychological tools, personal data and medical history. Laboratory findings and progress report are also included. 281 HD patients successfully filed forms. According to patients scores initial diagnosis was made and appropriate treatment started. Observation is going to be continued for next two years. Thus we will be able to detect changes in patients' psychological condition and life satisfaction during long-term observation.

64.06% of 281 HD patients were depressive – 48.04% mild depression, 15.66% moderate one, 0.36% heavy one. 54.09% revealed anxiety. 36.30% mild anxiety and 17.79% exacerbated one. Average QOL score (51.51% of patients) fluctuated between 40–60% of maximum. Only 6.05% of HD patients have QOL above 80% maximum. 10.65% of our HD patients have admitted they have suicidal thoughts.

Collected data are well correlated with results found in literature, but they have shown polish HD patients are in worse mental state then similar ones from UE and USA. Majority of them were pleased with additional doctors' care, in particularly with possibility of regular meetings and conversation about their health and mental problems.

Our findings show urgent need of initiation of psychotherapy and proper medication in all HD centers in Poland. Problem should be the target of future investigations.

163

Critical Challenges to Exercise for Dialysis Patients

W.M. Low, S.C.J. Tay

National Kidney Foundation, Singapore, Singapore

With increasing recognition of the benefits of exercise for their patients, dialysis centres face challenges when implementing exercise programmes on a large scale. As NKF Singapore enters its 5th year of exercise initiatives, 21 dialysis centres are now integrated into a programme to promote physical activity and exercise to 2,000 patients. Five critical challenges were addressed by the NKFS Centre for Exercise Medicine in this programme:

1. **Physical Fitness Goals.** Given the patient medical and demographic situation, the programme was designed to develop functional fitness. This sought to improve individual and social management of patients' activities of daily living and quality of life.
2. **Type of Exercise.** In addition to improving joint range of motion, strengthening, and endurance enhancement, exercises focused on improving patients' balance and stability. This was to reduce the incidence of falls and improve self-confidence and mobility.
3. **Fitness Assessment.** The introduction of a functional fitness test battery enabled matching of progress to ADL and the setting of individual exercise goals related to life activities.
4. **Risk Management.** Given the medical condition, comorbidities and concerns of patients, staff and family, a medical fitness grading system was adopted. This facilitated medical review by nephrologists and the matching of appropriate exercise by CFEM professionals.
5. **Empowerment.** To maximize the acceptance of the exercise programme and to facilitate its implementation, all staff in the dialysis centres received training in exercise and fitness. Concerted efforts were made to communicate the programme to patients and their families.

On the Anaemia of Dialyzed Patients with Renal Disease from a Gastroenterology-Nephrology Perspective

G. Pák, M. Gál, L. Major

Vaszary Kolos Hospital Internal Medicine Department II, Gastroenterology, Fresenius MC Dialytic Centre, Esztergom, Hungary

In addition to EPO treatment, authors examined the ineffectiveness of EPO treatment and changes to EPO dosage in 101 dialyzed patients. In 2001, 48 patients received EPO treatment with a dosage of 73.8 ± 46.5 U/kg/week. The target haemoglobin level of 11 g/l was managed to be achieved in 53.7 and 49.1%. In order to research the background, 31 patients received gastroenterology examinations. 11 patients reported stomach and intestine complaints while 20 patients had no complaints. 31 patients received panendoscopy with histological sampling, and their *Helicobacter pylori* status was also established. Out of all patients, 5 were diagnosed with gastric ulcer, 3 with GERB and 3 with inflammation. 80% of patients were *Helicobacter pylori* positive. It was interesting to find that the examination of the blood content of excrement was positive at only 40% of patients. 80% of patients with complaints were also HP positive. In one case a malignant stomach tumor was detected while 6 patients had duodenitis with metaplasia complications as examinations revealed. In 45% of cases we saw a negative HP status although 55% of them were *Helicobacter pylori* positive.

The following can be recommended in case of EPO refracter anaemia or significant changes to EPO demand in chronic HD patients: examinations of excrement blood content of a period of several days, performance of panendoscopy, regional anticoagulation in the course of HD treatment (prostacyclin, mesilates citrate), use of minimum amount of heparin, protonpump inhibitor through the oral route, *Helicobacter pylori* filtering – test of exhalation of C14 – sensible drug prescription, especially NSAIDs, and putting coxib drugs in the forefront.

Endothelial Injury in Peritoneal Dialysis Patients with Ultrafiltration Failure

S.B. Kim, J.S. Heo, S.H. Kim, E.J. Park, E.K. Lee, J.W. Chang, J.S. Park

Department of Internal Medicine, Asan Medical Center, College of Medicine, University of Ulsan, Seoul, South Korea

Ultrafiltration failure (UFF) in peritoneal dialysis patients can cause fluid overload and hypertension which are associated with endothelial injury. To evaluate endothelial injury in peritoneal dialysis patients with UFF, we performed a modified peritoneal equilibration test utilizing 3.86% glucose in 41 patients who had been on peritoneal dialysis for longer than 4 years. Twelve patients whose net ultrafiltrate was less than 400 ml during a 4-hour exchange were assigned to the UFF group and another 29 patients to the control

group. The blood levels of vWF, a marker of endothelial injury, albumin, and lipid profile were measured.

The number of antihypertensive medications and amount of 3.86% solution used were higher in the UFF group than those used in the control group ($p < 0.05$, $p < 0.001$, respectively). The patients in the UFF group had a significantly higher vWF level than those in the control group ($164.8 \pm 23.1\%$ vs. $144.5 \pm 22.4\%$, $p < 0.05$). There were no differences in BUN, serum creatinine, Kt/V, normalized protein catabolic rate (nPCR), serum albumin and lipid profile. Distribution of small solute transport profile was different between the 2 groups ($p < 0.05$). Six out of 12 patients (50%) in the UFF group were high transporters and 4 patients (33%) were high average transporters.

These results showed that peritoneal dialysis patients with ultrafiltration failure had more severe endothelial injury than those without.

Karnofsky Performance Score is an Independent Predictor of Mortality in Hemodialysis Patients

S.-C. Yang, S.-P. Hsu, C.-K. Chiang, K.-Y. Hung

Department of Internal Medicine, Far Eastern Memorial Hospital, Taipei, Taiwan, ROC

Background: Karnofsky performance scoring system was well known as a powerful predictor of mortality in various disease categories. We tried to find its predictive power on mortality in HD patients.

Methods: We retrospectively analyzed the mortality rate of 183 chronic HD patients who had undergone HD three times per week through a full period of one year. The analyzed parameters at enrollment were: the demographic characteristics, etiology of end-stage renal disease, co-morbid conditions, the Karnofsky performance scores (KPS), duration and delivered dose of HD, serum albumin levels, and important laboratory parameters. A multivariate Cox proportional hazards model was applied to identify the predictive value of KPS on patient mortality, with adjustment of the aforementioned factors.

Results: By the Cox proportional hazards model, we confirmed that decreased serum albumin and lower KPS were both significant, independent predictors. The hazard ratios (HR) of death were: serum albumin (per 0.5 g/dL decrease), 1.72 (95% CI, 1.11–2.66, $P = 0.016$); and KPS (per 10 points lower), 1.50 (95% CI, 1.10–2.04, $P = 0.010$). Even KPS was treated as a rank variable instead of a continuous one, lower KPS (≤ 50) was still an independent predictor [vs. higher KPS (≥ 60), HR 2.75, 95% CI, 1.11–6.77, $P = 0.028$].

Conclusion: KPS is an independent predictor of mortality in HD patients.

Oral Alfacalcidol Therapy Twice a Week to Chronic Renal Failure with Secondary Hyperparathyroidism Undergoing Routine Hemodialysis

M. Sja'bani, B. Djarwoto, I. Kuswadi, D.A. Suhardi,
N. Pangesti

Department of Internal Medicine, Faculty of Medicine,
Gadjah Mada University, Dr. Sardjito General Hospital,
Yogyakarta, Indonesia

Purpose of Study: To know the oral alfacalcidol therapy effect, with 1 µg twice weekly dosage, for 12 weeks to chronic renal failure patients with secondary hyperparathyroidism undergoing routine hemodialysis. This consequence is to be therapied, done practically according to scheduled hemodialysis in Hemodialysis Center, twice a week, to prevent complication as manifestation in renal dystrophy.

Method: A double blind randomized clinical trial is done to 56 chronic renal failure patients undergoing routine hemodialysis with iPTH >200 pg/dl level, Ca serum <11 mg/dl level and multiplied result of CaXP <70. It is done in Renal Installation Unit from November until March 2003. After randomized in block system, oral alfacalcidol is administered with 1 µg twice weekly dosage immediately after hemodialysis for 12 weeks to therapy and placebo group.

Results: A study of 28 patients in placebo group and 28 in therapy group is done consisting of 32 males and 24 females, aged 46 ± 1.07 years. Subject underwent routine hemodialysis for 61.3 ± 46.6 months. Initial iPTH level was 485.8 ± 285.7 pg/dl with Ca serum level 5.8 ± 1.6 mg/dl and phosphate level 6.6 ± 1.6 mg/dl. There were no significant differences between the two groups (ratio male/female 16/12 vs. 17/11, aged 46 ± 14.07 years vs. 51.5 ± 13.35 years, 61 ± 46.62 months vs. 58.4 ± 44 months of dialysis, 448.84 ± 225 pg/dl vs. 435.0 ± 211.5 pg/dl of iPTH, 5.81 ± 1.6 mg/dl vs. 5.7 ± 1.5 mg/dl of calcium, 6.64 ± 1.6 mg/dl vs. 6.3 ± 1.3 mg/dl of phosphate and 71.4% vs. 64.3% of pain symptom. At the end of the study there was a significant decrease of iPTH level compared to placebo (248.25 ± 169 pg/dl vs. 386.9 ± 227.0 pg/dl of iPTH or $P < 0.05$), and significant pain improvement of symptom compared to placebo (35.7% vs. 57.1% or $P < 0.05$).

Conclusion: Oral alfacalcidol with 1 µg twice weekly dosage for 12 weeks can improve secondary hyperparathyroidism condition to chronic renal failure patients undergoing routine hemodialysis.

Acute Bioincompatibility Reactions in Hemodialysis with Different Membranes and Dialysate Composition: Effect of Reuse

H. El Kashef Essam, A. El Aggan Hayam,
M. El Gendy Wessam, H.A.G. Amal

University of Alexandria, Alexandria, Egypt

The aim of this work was to study of some of the acute bioincompatibility reactions and dialyser performance with the use of

different membranes; cuprophane, hemophan and polysulfone, in addition to the use of acetate and bicarbonate dialysate in the first use and reuse dialyser. The study was carried out on 20 patients with end stage renal disease (ESRD) on regular hemodialysis (HD) and 20 subjects as controls. They were subjected to the first use and reuse of the three different membranes and with acetate and bicarbonate dialysate, each for three consecutive sessions. Neutrophil count, platelet count, blood gases, serum complement 3 and 4 (C3, C4), S.tumor necrosis factor alpha (S.TNF-α), S.interleukin-Iβ (IL-Iβ) and plasma neutrophil elastase were estimated at the 0, 15 min and at the end of dialysis. Urea, creatinine and phosphate clearances were measured at 0, 60 min and at the end of dialysis. The neutrophil and platelet count and C3 were decreased after 15 min then increased gradually till the end of dialysis. IL-Iβ, TNF-α and granulocyte elastase were increased during dialysis and this was more with the cuprophane membrane and attenuated with the reuse. The dialysate type has no role. Although, IL-Iβ decreased with the use of the polysulfone and bicarbonate dialysis. Hypoxia was more with cuprophane membrane and less with bicarbonate dialysis and reused dialyser. There was insignificant difference in the urea and creatinine clearance with the use of the different membranes, with first use or reuse. Phosphate clearance increased with the use of the hemophan membrane. In conclusion, the production of cytokines and neutrophil activation in addition to the complement stimulation were responsible for the bioincompatibility during hemodialysis. The use of the modified or synthetic membranes as hemophan and polysulfone are more bio-compatible and less thrombogenic. Hemophan membrane can be used for patients with hyperphosphatemia. The reuse of the dialyser is safe, efficient and more biocompatible and can decrease the cost of the dialysis therapy if properly performed.

Long-Term Follow-Up of Vascular Access Grafts

T. Hiranaka, J. Nakamura

Shirasagi Hospital, Osaka, Japan

Purpose: The most common cause of A-V graft failure is thrombosis, and prophylactic treatments for stenotic lesions are recommended to improve graft survival. We reviewed our clinical experience on surveillance of A-V grafts by access flow and graft survival.

Methods: From January 1996 to December 2002, 590 patients who cannot create native A-V fistulas underwent prosthetic graft implantations for hemodialysis (mean age 63.0 years; 368 (62.4%) women; 199 (33.7%) diabetic). 466 grafts (79.0%) were ePTFE graft, 90 grafts (15.2%) were polyurethane graft, and 34 grafts (5.8%) were composite graft (ePTFE + polyurethane). 424 grafts (71.5%) were placed in the forearm, and 159 grafts (26.9%) were placed in the upper arm. Surveillance of A-V grafts for hemodynamically significant stenosis was initiated in January 2000. Access flow measurements were performed by dilution method using a Crit-Line Monitor every month or by Doppler ultrasound every two to three months. If access flow decreased below 600 ml/min, fistulography was scheduled, and stenotic lesions were treated by percutaneous transluminal angioplasty or surgical revision. Primary and secondary patencies were determined with Kaplan-Meier method.

Results: Primary patency rates at 1, 2, 3, and 4 years were 41.7%, 27.2%, 16.0%, and 10.9%, respectively. Secondary patency rates at 1, 2, 3, 4, 5, and 6 years were 87.6%, 82.7%, 75.0%, 67.2%, 65.9%, and 58.1%, respectively. Secondary patency rates at one year were 78.5% in 1999, 85.0% in 2000, 95.7% in 2001, and 97.5% in 2002.

Conclusion: Surveillance of A-V graft and prophylactic treatments for stenotic lesions seem to be effective to prolong A-V graft survival.

170

The Effect of Long-Term Peritoneal Dialysis (PD) on Adequacy, Nutrition and Quality of Life (QOL) of Chronic PD Patients

M. Lichodziejewska-Niemierko¹, Z. Afeltowicz²,
M. Majkowicz², B. Rutkowski¹

¹Department of Nephrology, Transplantology and Internal Medicine, ²First Department of Psychiatry, Medical University, Gdansk, Poland

New achievements in PD technology and technique appear to result in longer survival of patients on dialysis. There are a lot of controversies concerning the influence of long-term PD on adequacy, nutrition status and quality of life.

The aim of the study was the assessment of 20 PD patients in the beginning and after 3 years of dialysis. The group comprised of 13M, 7F age 25–69 (mean 51 ± 12). The adequacy was estimated with use of total, residual and peritoneal clearances. Anthropometrical, clinical and biochemical methods were used to assess the nutrition status. QOL was measured with QLQ-C30 questionnaire, PIL and negative emotions with help of HADS and aggression scale.

There was a significant drop in residual renal function with concomitant increase in peritoneal urea clearance and dialysate volume. Total weekly Kt/V and creatinine clearance remained unchanged. After 3 years on PD body weight and BMI have risen significantly while SGA, total protein, albumin and cholesterol levels were left unchanged. NPCR and total carnitine levels were lower after 3 years of PD. In the assessment of the QOL statistically worse results were obtained in general QOL and purpose in life test while patients' functioning as assessed on physical, role, cognitive, emotional, social and symptom scales were similar in the beginning and after 3 years of dialysis.

Conclusions: With time on dialysis a reduction in renal function can be replaced by the increased volume of dialysate to keep up with the optimal adequacy indices. Three years of PD did not result in malnutrition, although carnitine levels dropped significantly. QOL appears not to change dramatically. Providing optimal dose of dialysis and appropriate nutrition long-term PD may result in better survival in PD patients and relatively good QOL.

171

Infective Endocarditis in Maintenance Hemodialysis Patients

C.-C. Lin, C.-F. Chang, W.-C. Yang

Division of Nephrology, Department of Medicine, Taipei Veterans General Hospital and National Yang-Ming University, Taipei, Taiwan, ROC

Purpose: Infective endocarditis (IE) is one of the most serious infectious conditions, with high morbidity and mortality in hemodialysis (HD) patients, yet little is known about the risk factors of developing IE and mortality.

Method: We retrospectively reviewed 20 cases of IE on maintenance HD at our hospital over the past 25 years.

Results: There were 18 cases of definite diagnosis and 2 possible diagnoses according to the modified Duke criteria. There were 10 cases (50%) in the dual-lumen catheter group, 7 cases (35%) in the native arteriovenous fistula group, and 3 cases (15%) in the polytetrafluoroethylene graft group. The major pathogen was Gram-positive cocci in 85% (17 of 20) of cases, including methicillin-resistance *S. aureus* (MRSA, 40%), methicillin-susceptible *S. aureus* (MSSA, 20%), coagulase-negative staphylococci (15%), 5% each for group D non-enterococcus, viridian group streptococcus, besides 5% each for *E. coli*, mixed infection, and culture-negative. The overall mortality rate was 60% in this study. Significantly higher mortalities were associated with older age (68.5 ± 10.7 vs. 58.8 ± 14.5 years, $p < 0.05$), serum C-reactive protein (23.8 ± 8.8 vs. 12.9 ± 10.6 mg/dL, $p < 0.05$), pre-dialytic blood urea nitrogen (118.4 ± 49.5 vs. 69.5 ± 36.8 mg/dL, $p < 0.05$), and poorly glycemic control (176.0 ± 90.0 vs. 109.8 ± 14.0 mg/dL, $p < 0.05$). There were no significant differences in the prevalence of diabetes, use of dual-lumen catheter, serum albumin, pre-dialytic creatinine and blood white cell count between the expired and survived patients. As to the pathogens, MRSA was associated with higher mortality (100%, $p < 0.01$), but MSSA with lower mortality (0%, $p < 0.05$).

Conclusion: Since the increasing prevalence and higher mortality in MRSA endocarditis, vancomycin or teicoplanin should be given in patients with risk factors of higher mortality as soon as possible when blood culture results are available.

172

Seasonal Variations of Clinical Parameters in Chronic Hemodialysis

K. Vedran, K. Vinko

Hemodialysis Department,
Medical Center Trogir, Trogir, Croatia

Introduction: Seasonal variations in clinical variables occur commonly among chronic hemodialysis patients, but previous detailed investigations have been conducted mostly among the American chronic hemodialysis patients. In order to demonstrate seasonal differences, we prospectively compared biochemical and clinical parameters in a group of chronically hemodialyzed patients living in Europe, South Croatia; region with Mediterranean climate.

Methods: Data were processed on 135 single dialysis treatments involving a group of 34 chronic hemodialysis (HD) patients (18 males and 16 females). Outcomes were measured at 3-months intervals, in March, June, September, and in December. Differences between four groups were tested with one-way analysis of variances (ANOVA). Differences between two groups were calculated by Student's t-test for independent data.

Results: The seasonal differences were found in phosphorus ($p = 0.001$), creatinine before HD ($p < 0.001$), creatinine after HD ($p = 0.005$), alkaline phosphatase ($p = 0.012$), alanine aminotransferase ($p = 0.042$), urea before HD ($p = 0.039$), albumins ($p < 0.001$), total cholesterol ($p < 0.001$), low-density lipoprotein (LDL)-cholesterol ($p < 0.001$), high-density lipoprotein (HDL)-cholesterol ($p < 0.001$), glucose ($p = 0.033$), and ultrafiltration per HD ($p = 0.037$). When the data were grouped into cold (March and December) and mild (June and September) months; we found differences in phosphorus (1.48 ± 0.47 vs. 1.72 ± 0.51 , $p = 0.005$), alkaline phosphatase (119.46 ± 69.03 vs. 169.78 ± 107.98 , $p = 0.002$), urea before HD (27.13 ± 5.35 vs. 24.40 ± 5.99 , $p = 0.006$), albumins (37.92 ± 5.17 vs. 40.58 ± 5.69 , $p = 0.006$), total cholesterol (4.93 ± 0.93 vs. 5.30 ± 0.93 , $p = 0.023$), LDL-cholesterol (2.85 ± 1.04 vs. 3.23 ± 0.87 , $p = 0.046$), glucose (4.62 ± 1.15 vs. 5.57 ± 1.46 , $p = 0.004$), and ultrafiltration per HD (3.57 ± 1.18 vs. 2.97 ± 1.20 , $p = 0.004$).

Conclusions: In Mediterranean climate, seasonal differences in predialysis urea concentration and ultrafiltration rate per dialysis could be attributed to different food and water intake. The seasonal differences in blood concentration of phosphorus, alkaline phosphatase, total cholesterol, LDL-cholesterol, and glucose might be consequence of neurohormonal influences. This climate has not ability to impact hemoglobin and blood pressure.

173

Multiple Spontaneous Retroperitoneal Hemorrhage in a Hemodialysis Patient

K.-P. Lee¹, J.-M. Sung¹, T.-W. Tsai², C.-C. Tseng¹, M.-C. Wang¹, J.-J. Huang¹

¹Department of Internal Medicine, National Cheng Kung University Hospital, ²Li-Fu Clinic, Tainan, Taiwan, ROC

Spontaneous retroperitoneal bleeding is rare in hemodialysis (HD) patients. We hereby reported a HD patient who experienced three episodes of retroperitoneal bleeding.

A 67 years old male with diabetic nephropathy received chronic HD therapy and Nifedipine (Adalat oros®), Aspirin®, Gemfibrozil, and insulin therapy. On February 16, 2000, he had the lower abdominal pain, anemia (hemoglobin: 8.4 g/dl), and hypotension. He was treated with normal saline infusion and blood transfusion at our ER. Renal sonography and enhanced CT scan revealed right peri-renal hematoma. Angiography only showed multiple stenosis of bilateral renal arteries. He was discharged seven days later and discontinued aspirin and received LMWH (Fraxiparin). On November 3, 2001, left lower back pain attacked during HD, renal sonography and enhanced CT scan showed left perirenal hematoma. But he decided to discharge on the next day. In October 2002, severe right lower back pain occurred. Enhanced CT scan revealed right perirenal hematoma at our

ER. He received supportive therapy and was on heparin-free HD. Ten days later he was discharged smoothly.

The etiologies of spontaneous retroperitoneal hemorrhage include renal or adrenal tumor, AV malformation, polyarteritis nodosa, venous thrombosis, and anticoagulant therapy. Clinical presentations are variable, including: flank or back pain, local tenderness, mass, fever, shock, femoral neuropathy, and abdominal compartment syndrome, which can develop low cardiac output, ischemic bowel, and acute respiratory distress syndrome. Renal sonography, enhanced CT scan, and angiography are commonly used to evaluate retroperitoneal hematoma. Most of patients had well response to supportive therapy, including: discontinuing anticoagulant, bed rest, and blood transfusion. Surgical intervention is indicated for poor response to supportive therapy, persistent bleeding or abdominal compartment syndrome. In this case, the serial examinations did not show any abnormality except bilateral renal artery stenosis. So we concluded that unfractionated heparin or LMWH may be contributory to his repeated bleeding.

174

Cytotoxic Effect of Cyanate on ROS 17/2.8 Cells

K.C. Mun, E.J. Chang

Dong San Kidney Institute, Keimyung University School of Medicine, Daegu, Korea

Background: The factors contributing to uremic bone disease are still incompletely characterized. Variety factors appear to have ill-defined roles in this disease. Cyanate, which is derived spontaneously from urea at body temperature and pH, might also play a role in the renal osteodystrophy. We studied the effect of cyanate on the osteoblast-like osteosarcoma cells. The levels of hydrogen peroxide which is one of the reactive oxygen species, and malondialdehyde which is an indirect marker of lipid peroxidation were also measured.

Methods: ROS 17/2.8 cells, a cloned rat osteoblastic osteosarcoma cell line, were maintained and grown in DMEM containing 10% fetal bovine serum. ROS 17/2.8 cells were treated with various concentrations of sodium cyanate and then cells were incubated at 37°C for 48 h. The cytotoxicity was measured by MTT assay and cell growth was evaluated by cell counting. The production of hydrogen peroxide was determined by modified xylenol orange method and the amount of malondialdehyde was measured by the thiobarbituric acid assay.

Results: Cyanate inhibited cell growth and induced cytotoxicity on ROS 17/2.8 cell in dose-dependent manner. With cyanate, the levels of hydrogen peroxide and malondialdehyde were increased about 2- to 3-fold compared to that of without cyanate.

Conclusion: On the basis of these results, we suggest that cyanate is one of the contributing factors in uremic bone disease via oxygen free radicals.

The Use of the Limulus Amebocyte Lysate Test at Polish Haemodialysotherapy Stations

D. Kurpas¹, A. Steciwko²

¹Family Medicine Department of Wrocław Medical University, ²Haemodialysotherapy Station, State Hospital, Legnica, Poland

The LAL (limulus amebocyte lysate) test is the most sensitive and specific (more than the rabbit pyrogen test) means to detect and measure endotoxin (pyrogen). The basis of the test is that endotoxin produces an opacity and gelation in LAL.

The gel-clot LAL test method is a simple, reproducible, that is conducted by mixing LAL reagent and test specimen and promptly incubating the mixture undisturbed for 60 min at 37°C. A positive response on the gel-clot indicates there is an amount of endotoxin in the sample, which equals or exceeds the reagent labelled sensitivity.

We present the results from 5 haemodialysotherapy stations. We have made 86 tests (sensitivity 0.25 EU/ml) on the each stage of water purification system (including tap water) and 29 controls. We indicated that till the stage of reverse osmosis all tests were positive, after this stage – all tests were negative. We indicated that till the stage of reverse osmosis (RO) (29 tests) we detected pyrogens. 42 tests were negative and 15 – positive from the reverse osmosis stage. 56 tests were negative and 1 – positive, when it was changed formalin to dialin during the cleaning process. All controls were positive – in this way we excluded false negative results.

The simplicity and economy of the LAL test encourages the testing of in-process solution and raw materials as well as end product drugs, devices and biologics. The LAL test is also avail at control of vaccines, blood products (albumin, globulin), diagnosis of peritonitis, cholangitis, infections during chronic aggressive hepatitis, hepatocirrhosis, pancreatitis, hepatorenal syndrome, diagnosis of neonatal infections. The testing of pyrogen amount in serum and water enable very fast (after one hour) recognition, therapy and prevent the contamination of bacteria and endotoxin, in the future – even in the general practitioners' practices.

Early Failure of Radiocephalic Arteriovenous Fistula: Primary and Secondary Patency Rate of Angioplasty

Y.O. Kim, S.A. Yoon, Y.S. Kim, B.S. Kim, H.C. Song, Y.S. Chang, B.K. Bang, M.J. Shin, Y.S. Shin

Department of Internal Medicine, The Catholic University of Korea, Seoul, Korea

Purpose: To determine primary and secondary patency rate of angioplasty (PTA) in HD patients who had early failure of radiocephalic arteriovenous fistula (AVF).

Methods: This study enrolled 39 HD patients who had early failure of radiocephalic AVF. Early failure of AVF was defined as failure of AVF developed within 1 year after the AVF operation.

The lesions occurred at proximal vein of upper arm and central vein were excluded. The primary and secondary patency rate of PTA was evaluated using Kaplan-Meier method.

Results: The mean age of the patients was 54 ± 13 years and 24 patients (61.5%) had diabetes and among 39 lesions observed at venography, there were 33 cases of stenosis and 6 cases of complete occlusion due to thrombosis. The onset of AVF dysfunction after the operation was 5.3 ± 3.6 months and 11 cases developed before the first needling. Total PTAs were performed and initial success rate was 94.2% (n = 49). Primary patency rate at 6, 12, 24, and 48 months was 74.8%, 55.8%, 55.8%, and 55.8%, respectively. Secondary patency rate at 6, 12, 24, 48 months was 89.7%, 86.1%, 81.8%, 81.8%. Diabetes, age, sex, onset of AVF dysfunction after the operation, thrombosis did not influenced primary patency rate of PTA.

Conclusion: PTA is considered to be effective and safe treatment for early dysfunction of radiocephalic AVF in HD patients.

Lanthanum Carbonate versus Calcium Carbonate: Effect on Parathyroid Hormone Levels

A. Hutchison¹, F. Al-Baaj², I. Webster³, M. Gill³

¹Manchester Institute of Nephrology & Transplantation, University of Manchester, ²Hope Hospital Renal Unit, Salford, ³Shire Pharmaceutical Development Ltd, Basingstoke, UK, for the Lanthanum Study Group

Purpose of the Study: Recently, an increase in the prevalence of adynamic bone in patients with chronic kidney disease has been recognised. Over-suppression of parathyroid hormone (PTH) due to the use of calcium-based phosphate binders and calcitriol has been suggested as a cause. We assessed the effects of calcium carbonate (CC) and lanthanum carbonate (LC) on PTH levels to establish the risk of over-suppression of PTH.

Methods: After a screening visit and a 1- to 3-week washout period, patients with hyperphosphataemia (serum phosphorus >1.80 mmol/L [5.6 mg/dL]) were randomized (2:1) to receive either LC (lanthanum dose 375–3,000 mg/day, 533 patients) or CC (calcium 1,500–9,000 mg/day, 267 patients) during a 5-week dose-titration period. Thereafter, patients received maintenance treatment for 20 weeks, then all patients were invited to enter a 6 month extension period using LC only.

Results: Median (range) PTH levels at screening (i.e. with any previous phosphate binder) were 127 (0–2,018) ng/L and 163 (0–1,478) ng/L in the LC and CC groups, respectively. At the end of the titration period, median PTH levels in the CC group had fallen to 98 (0–1,203) ng/L; during the 20-week maintenance period, these recovered to 113.5 (6–1,560) ng/L. In comparison, LC was associated with an increase in PTH levels to 166 (3–1,250) ng/L by the end of the maintenance period. Whereas 83% of patients who had 'low' PTH levels (<100 ng/L) at screening remained low after 20 weeks of maintenance treatment with CC, 44% of patients in the LC group improved their PTH levels into the desired range of 101 to 300 ng/L over the same time period. When patients in the CC group were switched to LC, PTH levels increased to 197 (7–1,821) ng/L by the end of the 6-month extension treatment. PTH levels after 20 weeks of

maintenance plus 6 months of extension treatment in the LC group were 235 (0–2,300) ng/L. LC showed similar efficacy to CC with regard to phosphorus levels.

Conclusion: LC treatment was associated with PTH levels within acceptable limits, whereas CC was associated with levels indicative of an increased risk of low bone turnover.

178

High Volume Hemofiltration for Sepsis – An Early Experience in a Single Center

A.F. Fauzi, Z. Soehardy, V. Jeyabalan, A.G. Halim, M.K. Chua, N.N.C.T. Kong

National University of Malaysia, Kuala Lumpur, Malaysia

Introduction: Sepsis with multiorgan dysfunction has been a major cause of death. Other than activated protein C, high volume hemofiltration has been reported as a possible therapy targeting removal of inflammatory mediators based on the ‘peak concentration hypothesis’.

Methods: We chart reviewed our single center experience with high volume hemofiltration (HVHF) during the period of July–August 2003. HVHF was defined as hemofiltration ≥ 4 L/h. We used the Aquarius machine (Edwards) and bicarbonate replacement fluid with a potassium concentration of 2 mmol/L.

Results: A total of nine patients underwent HVHF. There were 7 male and 2 female patients with a mean age of 18.5 ± 2.5 years. 7 sessions were carried out in the intensive care unit (ICU) while one each in cardiothoracic ICU and Burns Unit. All the patients had evidence of severe sepsis. The femoral vein was accessed, using the Mahukar catheter (11.5F, 24 cm). Mean pre-hemofiltration blood urea was 47.7 ± 12.1 umol/L and serum creatinine was 336 ± 110 umol/L. Three patients had blood urea less than 20 mmol/L. All were able to tolerate $Q_b \geq 250$ ml/min. Eight sessions were completed for the prescribed 6 h and one was terminated due to a high transmembrane pressure. Post dilutional filtration fraction was $19.7 \pm 5.3\%$. The most common electrolyte imbalance noted was hypokalemia occurring in five patients. Four (44%) of the nine patients survived despite having multiorgan dysfunction.

Conclusion: HVHF is achievable with the use of current facilities in our center. It appears to complement existing best-care therapy in patients with severe sepsis and the multiorgan dysfunction syndrome who otherwise have a very high mortality.

179

Test of an Indirect Method to Quantify Free Water Transport (FWT) in Peritoneal Dialysis

R. Bengt, V. Daniele, R. Bert-Inge

Department of Nephrology, University Hospital of Lund, Lund, Sweden

Sodium (Na) sieving during peritoneal dialysis (PD) is postulated to occur due to the presence of aquaporin-1 (AQP-1) mediated water flow across the endothelial cells during glucose induced osmosis. Approximately 40% of the total osmotic ultrafiltration (UF) appears to be due to ‘free’ water transport. La Milia et al (NDT 2002;17:17–18) suggested a technique to assess sodium-associated water transport based on sodium removal (NaR) divided by plasma Na conc. during a ‘fast-fast’ (60 min) peritoneal equilibration test (PET) for 3.86% glucose, yielding an estimate of the UF passing through the small pores (UFSP). FWT was obtained by subtracting UFSP from the total UF. This technique will, however, slightly overestimate UFSP and underestimate FWT due to the presence of small pore Na diffusion.

In the present study we used the three-pore model of peritoneal transport to simulate the degree of overestimation of UFSP obtained with the technique presented by La Milia et al., during ordinary conditions and during UF failure (implying increases in small solute transport) for 3.86% glucose. The fractional UF coefficient accounted for by AQP-1 was set at 2%.

According to the computer simulations, there was an underestimation of the FWT throughout the dwell, which, however, was minimal between 40 and 80 min, amounting to $\sim 15\%$. The error was similar in relative terms during normal conditions and during UF failure. For dwell times shorter than 20 min or longer than 80 min, however, the error became unacceptably high.

It is concluded that estimated UFSP (based on plasma clearance of Na across small pores) yields only a moderate overestimation of small pore UF in a 60 min (‘fast-fast’) PET, during normal conditions and during UF failure. To convert the estimated UFSP into the ‘true’ UFSP during a 60 min PET, the present simulations indicate that the former quantity can be multiplied by the correction factor 0.91. Using that correction, the technique of La Milia et al. seems to work as a surprisingly adequate way of estimating the Na-free water transport in PD.

180

Hypokalemia in CAPD Patients: A Less Recognised Complication

M.M. Bahadur¹, L.R. Priti², G. Savita², K. Praveen², R.A. Anthony

¹Jaslok Hospital & Research Centre,

²Dr. BAM Hospital, Mumbai, India

Aim: To study the prevalence of hypokalemia in stable patients on CAPD belonging to lower to middle socioeconomic class.

Methods and Materials: Records of all CAPD patients registered from Jan 2000 to March 2003 and complete in clinical, renal biochemistry and anthropometry were reviewed. 44 CAPD patients

were selected and divided into two groups. Group A comprised of 20 patients having serum potassium of less than 3.5 mg/dL (at least 2 out of last 3 electrolyte readings). The remaining 24 patients having serum potassium of more than 3.5 mg/dL were labeled as Group B. The body mass index, serum albumin and hemoglobin were analyzed for both groups.

Result:

Parameter (average values)	Group A (n = 20)	Group B (n = 24)	Unpaired 't' value	Significant
Serum potassium	3.0	4.75	10.29	Yes
Body mass index	16.53	23.8	5.03	Yes
Serum albumin	2.9	3.2	1.69	No
Hemoglobin	9.44	8.9	0.87	No

Conclusions: CAPD fluid unlike dialysate used for hemodialysis does not contain any potassium. However patients from low socio-economic group having low BMI tend to become hypokalemic when put on CAPD. This problem is not encountered in patients with a higher BMI, and its prevalence has not been recognized earlier in the literature on such a large scale. These patients should be advised high potassium diet or supplementation or modified CAPD solutions to correct hypokalemia.

181

Sampling of Interstitial Fluid and Measurements of Colloid Osmotic Pressure after Peritoneal Dialysis in Rats

B.-I. Rosengren^{1,2}, B. Rippe¹, O. Tenstad², H. Wiig²

¹Department of Nephrology, Lund University, Lund, Sweden, ²Department of Physiology, University of Bergen, Bergen, Norway

The aims of this study were to develop a method to isolate interstitial fluid from the peritoneal membrane and to measure the interstitial colloid osmotic pressure (COP) in the normal peritoneum, and after peritoneal dialysis (PD).

Twelve female rats were anesthetized subcutaneously with fentanylmidazolam (1:1). Interstitial fluid was isolated using a method modified from that described for hindlimb muscle. Nylon wicks were implanted postmortem by means of a plastic catheter in the tissue just underneath the peritoneal membrane. The characteristics of this fluid was compared to that isolated from wicks implanted in intermuscular spaces in hindlimb muscle and back subcutis. All wicks were removed after 20 min and centrifuged in siliconized Eppendorff tubes. The wick fluid was collected and analyzed in a colloid osmometer constructed for submicroliter samples, and interstitial fluid COP was compared to that of plasma. All experiments were done in an infant incubator at 100% relative humidity. PD was done by injecting 20 ml of 3.86% Dianeal into the peritoneal cavity, with a dwell time of 4 h. Control rats were not dialyzed.

The ratios of each COP to that of plasma during control were 0.65 ± 0.05 in peritoneum, 0.53 ± 0.04 in muscle, and 0.59 ± 0.05 in skin. After PD, the ratios were 0.29 ± 0.03 in peritoneum, 0.54 ± 0.08 in muscle, and 0.41 ± 0.06 in skin. Thus, the COP ratio in the peritoneum decreased by 55% ($p = 0.014$), and in the skin by 30% ($p = 0.03$), while the COP ratio in muscle was unchanged.

The results imply that an acute PD dwell alters the COP in the peritoneal membrane, thereby shifting the Starling equilibrium towards an absorptive state. The effect was restricted to the peritoneal membrane, and to a lesser extent to the skin. We speculate that the increase in peritoneal hydrostatic pressure following PD cause an increase in the interstitial tissue volume, with dilution and/or washout of colloids. Further investigation of the COP in the peritoneal membrane is required to evaluate the effect of long-term PD in the peritoneal Starling fluid balance.

This study was supported by a Marie Curie Host Fellowship, contract no: QLK5-CT-2001-60039.

182

The Influence of B12 Therapy on Methylmalonic Acid Levels in Dialysis Patients and MTHFR Deficiency Phenotype

L. Svoboda, L. Stranik, J. Hyanek

Hospital Na Homolce, Prague, Czech Republic

Propionyl CoA is a common product of metabolism of essential AA (Val, Leu, Ile), fatty acids and cholesterol and is further metabolized to methyl-malonyl CoA, which is further isomerized to succinyl CoA. Because of common cofactor (cobalamin) can methylmalonic acid (MMA) serve as an early marker of B12 deficiency.

Purpose of Study: To evaluate possible hidden cobalamin deficiency and the effect of i.v. B12 treatment on MMA and total homocysteine (t-Hcy) levels in different MTHFR deficiency phenotypes among ESRD patients on HD treatment.

Patients and Methods: 48 HD treated patients (surprisingly 12% homozygotes, 45% heterozygotes for MTHFR deficiency and 43% normal e.g. without mutation C677T) in routine medication folic acid 5 mg/d, pyridoxin 20 mg/d were treated with B12 (cyanocobalamin 1 mg i.v.) after HD every week for 6 weeks, following 1 mg monthly for 6 months. Measurement of serum levels of MMA, folic acid, total Hcy, cobalamin, blood counts and healthy controls are given below.

Results:

1. Healthy controls MMA = 0.305 ± 0.005 umol/l (max. norm. 0.22).
2. MMA in HD patients before B12 treatment = 0.904 ± 0.389 .
3. MMA in HD patients after B12 treatment = 0.5538 ± 0.222 .
4. t-Hcy in HD patients before B12 treatment = 21.653 ± 6.851 (max. norm. 13.5 umol/l women, 14.5 umol/l men).
5. t-Hcy in HD patients after B12 treatment 16.055 ± 4.896 .

Conclusions: We did not find B12 deficiency in the group of our HD patients, but we confirm hidden B12 deficiency. Both MMA and t-Hcy levels were significantly ($p = 0.05$) improved/reduced after B12 treatment. Total homocysteine levels in the subset of patients with MTHFR deficiency phenotype (both C677T mutation heterozygotes and homozygotes) were not improved significantly.

Renal Replacement Therapy for End Stage Renal Disease Related to AA Amyloidosis

E. Abderrahim, L. Raies, K. Boubaker, H. Hedri, F. Ben Moussa, H. Kaaroud, F. Ben Hamida, R. Goucha, T. Ben Abdallah, K. Zouaghi, M. Ounissi, F. El Younsi, A. Kheder, H. Ben Maiz

Department of Nephrology and Internal Medicine,
Charles Nicolle Hospital, Tunis, Tunisia

We report our experience of providing RRT for 60 patients with ESRD related to AA amyloidosis on the aim to determine the clinical characteristics of such patients before and during RRT and to evaluate their morbidity and the factors influencing their mortality. Comparative analysis was performed using χ^2 test and t-test. Survival rates were calculated according to the actuarial method and Cox proportional hazards model was used to identify predictors of death. These 60 patients (M: 47, F: 13) represent 1.7% of all patients starting RRT in our centre between January 1990 and June 2002. Their age varied from 18 to 76 years at the onset of RRT. Chronic infections represent 70% of causes of RA which were attributed to tuberculosis in 47% of cases, FMF was observed in 4 cases and chronic rheumatism in 7 cases. At diagnosis of AA, 95% of patients had nephrotic syndrome, 30% were hypertensive and 80% presented with chronic renal failure which was at the end stage in 32 cases, the remaining 28 patients reached ESRD after a median period of 16.2 months. Thrombosis of vascular access was the main complication during haemodialysis so, 33% of patients needed more than one vascular access. Thirty-nine deaths were recorded during a cumulative follow-up of 126 years (32% per year), 38% of these deaths occurred within the first quarter of RRT and 30% were attributed to sepsis. Survival rates were 58.9%, 50.2%, 33.6% and 15.6% at 1, 2, 5 and 10 years, respectively. They are lower than those of two control-groups of patients with and without diabetes matched for gender, age and date of onset of RRT; the exclusion of early deaths make survival of patients with AA amyloidosis comparable to that of diabetics. Multivariate analysis revealed that age, urgent onset of RRT and hypoalbuminemia were independently correlated with survival time. We conclude that high mortality observed in dialysed patients suffering from AA amyloidosis could be explained by the delayed referral and the co-morbidities related to the causal disease and to the systemic character of amyloid process.

Long-Term Follow-Up of Uremic-Diabetics Receiving Renal Replacement Therapy

E. Abderrahim, K. Boubaker, K. Zouaghi, H. Hedri, A. Kheder, F. Ben Moussa, T. Ben Abdallah, M. Ounissi, F. El Younsi, F. Ben Hamida, H. Ben Maiz

Department of Nephrology and Internal Medicine,
Charles Nicolle Hospital, Tunis, Tunisia

The progression of diabetics among dialysed-patients is worldwide established but the long-term outcome of such patients is rarely

documented especially in developing countries. Our objectives were to determine the clinical characteristics of 299 diabetics starting renal replacement therapy (RRT) for end-stage renal failure and to identify the factors influencing their mortality during a cumulative follow-up period of 1103 years. This group represent all patients starting RRT for diabetic-ESRD (type 2: 238; type 1: 61) during the period 1990–1996 and was followed-up until December 31, 2002. Survival analysis was performed according to the actuarial method and Cox proportional model was used to identify the predictors of mortality. There were 207 men and 92 women aged from 23 to 80 years at the onset of RRT. Dialysis was started in urgent conditions in the third of cases using a temporary vascular access in 91% of patients. Complications related to diabetes were mostly aggravated during RRT period. At the date of point; 250 deaths were recorded representing an annual rate of 22%. The 1/4 of deaths occurred within the first quarter of start of RRT (early deaths) and 56% were attributed to infectious or cardiovascular complications. Actuarial survival rates, including early deaths, were 68.4, 59.4, 34.3 and 28.5% at 1, 2, 5 and 6 years, respectively. The predictors of mortality identified by multivariate analysis were: age (RR: 1.035/year; $p < 0.0001$), diabetes type 1 (RR: 1.97; $p < 0.009$), serum albumin < 30 g/l (RR: 1.51; $p < 0.004$) score comorbidities (RR: 1.53; $p < 0.005$) and urgent onset of RRT. We conclude that the late nephrology referral and coexistence of serious co-morbidities at the start of RRT were resulted in a high rate of early death in diabetics receiving RRT. Efforts should be increased toward improving the quality of medical care of diabetics during all stages of their disease.

Impact of Initial Blood Pressure on Mortality of Diabetics Undergoing Renal Replacement Therapy

E. Abderrahim, L. Raies, K. Boubaker, K. Zouaghi, H. Hedri, A. Kheder, F. Ben Moussa, T. Ben Abdallah, M. Ounissi, F. El Younsi, F. Ben Hamida, H. Ben Maiz

Department of Nephrology and Internal Medicine,
Charles Nicolle Hospital, Tunis, Tunisia

The aim of this study was to determine the impact of blood pressure indices (SBP, DBP, PP, MBP) on mortality in a cohort of uremic-diabetics treated by haemodialysis. There were 221 patients (M: 144; F: 77) aged from 37 to 78 years corresponding to all diabetics (type 2) starting haemodialysis in our centre during the period 1990–1996 followed-up until December 2002. Survival analysis was performed according to the actuarial method and Cox proportional model was used to identify predictors of deaths. 80.5% have hypertension (HT) at the start of HMD. The diagnosis was made before or at time of start of RRT in 37 patients (20.8%) and 16 (9%) did not receive any anti-hypertensive treatment. Our studied population was subdivided into four groups according to the levels of BP levels at the time of beginning of HMD: G1: Normal BP (SBP [90–140] and DBP [60–90]); G2: HT stage 1 (SBP [140–160] and/or DBP [90–100]); G3: HT stage 2 (SBP [160–180] and/or DBP [100–110]); G4: HT stage 3 (SBP [180–220] and/or DBP [110–120]).

	G1	G2	G3	G4	Total	P
Number	43	67	71	40	221	NS
Sex-ratio	1.7	1.9	3.2	0.9	1.87	0.025
Age (mean, year)	57	58.4	57.8	56.2	57.6	NS
Global mortality (%)	86	83.6	80.3	82.5	82.8	NS
<i>Survival</i>						
3 months	79.1	83.6	86	80	82.8	NS
5 years	32.6	37.4	33.8	40	35.7	NS
RR of death	1	0.77	0.94	0.55	—	NS

None of the BP-parameters seems to influence early or global mortality which was rather related to the urgent onset of RRT, age, serum albumin, and to the score of associated co-morbidities. We conclude that mortality of haemodialysed-diabetics did not influenced by the blood pressure parameters recorded at the start of HMD.

186

Unexpected Rise in GFR in a Patient of Chronic Kidney Disease with Single Functioning Kidney Following Keto-Diet: A Case Report

A.V. Ingale¹, F.A. Ingale², H.G. Kulkarni³

¹Department of Nephrology, MGM Group of Hospitals,

²Department of Medicine, NMMC Hospital, Navi Mumbai,

³Surya Hospital, Pune, India

Introduction: We report a case of an unexpected rise in glomerular filtration rate (GFR) in a patient of chronic kidney disease due to pyelonephritis with tubulointerstitial nephritis.

Case Report: Mr. S, a 60 year old male was referred to nephrology department after an accidental finding of high serum creatinine (2.6 mg%) in June 2002. After examination and investigations, a diagnosis of acute on chronic renal failure, secondary to pyelonephritis with tubulointerstitial nephritis with Lt ureteric calculi was made. Two weeks later, after proper (c and s) antibiotic therapy, patient's GFR (by DTPA scan) was 50.2 ml/min (left kidney only 1.6 ml/min). Patient was put on standard CKD treatment as per K-DOQI guidelines. Despite low protein diet (LPD: 0.6 g/kg/d) the GFR deteriorated to 37.6 ml/min in September 2002 and to 34.8 ml/min in February 2003. Ketoanalogues (Ketosteril® Fresenius Kabi, Germany) were added to the LPD at this juncture. In one month GFR improved to 44 ml/min and in July 2003 it was recorded 47.7 ml/min. By this time other renal parameters, including urea, creatinine and electrolytes were stabilized within normal limits. The left kidney was detected non-functional September 2002 onwards.

Conclusion: In this case of CKD with a single functioning kidney, GFR continued to deteriorate fast for 7 months under a LPD regimen but increased unexpectedly from 34 to 47.7 ml/min in 5 months once ketoanalogues were added to diet.

187

An Effective Way of Preventing Needle-Stick Injuries During Hemodialysis with a Safety Fistula Needle Set

M. Neo

Department of Product Development,
JMS Singapore Pte Ltd, Singapore

Purposes: Needle stick injury (NSI) has been a worldwide concern in hospitals and centers with steel needles. This is due to the risk of blood borne pathogens being transmitted through NSI. In hemodialysis (HD), there are >80% of HD patients who require fistula needles for vascular access. HD technicians are required to cannulate surgically created vascular access with 2 fistula needles three times per week for each patient. Use of these large gauge, hollow bore needles and high pressure accesses are unique factors for a hemodialysis setting, therefore HD technicians are exposed to a high risk of infection with blood borne pathogens such as hepatitis B, C and immunodeficiency virus should NSI occur. There are many safety devices with protection features to protect HD technician from NSI. However, most of the existing devices have pre-attached bulky guards, requiring HD technicians to re-position the guard close to the access site at the termination of hemodialysis, before activating the safety features. This causes inconvenience in use, and in some cases, unsuccessful activation of the safety protection, as well as discomfort to patients. In this study, by using the new guarded fistula needle set, we aim to enable HD technicians to follow conventional cannulation and gauze-holding procedures without having risk of vascular access damage due to lateral movement of the fistula needle set during removal. We also aim to eliminate NSI when engaging the safety mechanism.

Methods: Renal nurses (RN) of US based dialysis centers were given the new guarded fistula needle sets (AVF) for vascular access, to use concurrently with existing guarded devices. At termination of dialysis, RNs activated the safety features to guard the needle after retraction from the access.

Results: No NSI were reported after the trial. >95% RNs have agreed the new guarded AVF set is easy to use with integrated safety wing sheath. All features in the new guarded AVF set have given a safer feel, then existing safety devices due to incorporated audible click sound as well as additional final locking. Due to the smooth and easy needle retraction, >95% of HD patients do not feel any discomfort with the new guarded AVF set.

Conclusions: Overall, we have proven the new guarded AVF set is easy-to-use for RNs as the cannulation can be performed as per normal procedure. The new guarded AVF set is able to protect RNs from NSI, as well as eliminate complication or discomfort for HD patients. The safety features integrated into the new guarded AVF set have proven their effectiveness during the trial.

Continuous Venovenous Hemofiltration (CVVH) in Complex Therapy of the Patients with Hepatorenal Syndrome

I.V. Alexandrova, E.I. Pervakova, N.V. Vasina, L.V. Donova

N.V. Sklyfosovsky Scientific Research Institute for Emergency Medicine, Moscow, Russia

The aim of this study was the optimization of complex therapy of resistant ascites at the group of patients with hepatorenal syndrome. The indications for starting CVVH were the extension of hepar insufficiency, due to the diuretics therapy, hypercreatininemia, hypokalemia, hyponatremia. The algorithm of our treatment consisted of CVVH 3–5 times with the interval of 1.5–3 days and this interval depends on increasing such indexes as patient's body mass, creatininemia, electrolytes and the rate of diuresis. We used hemofilters HF-60 and HF-80 the determination of substitute solution volume was made according to the daily diuresis and the amount of liquid infusion. All procedure lasts from 5 to 10 hours (median time: 7.5 h). According to the results of ultrasound dopplerography after the treatment we determine the decreasing of renal parenchymatous layer edema, the improvement of hemodynamics and decreasing of Ri of renal arteries. We can also mention the improvement of biochemical status and increased clearance of creatinine with urea. There was a significant regression of encephalopathy right after the first CVVH.

CVVH improves renal bloodstream, glomerular filtration, increases creatinine clearance with urea, decreases the dose of diuretics, corrects acidosis and manifestation of encephalopathy.

Renal Replacement Therapy for the Patients with Acute Renal Failure in Postpartum Period

I.V. Alexandrova

N.V. Sklyfosovsky Institute for Emergency Medicine, Moscow, Russia

Purpose: The aim of this study was to estimate the efficacy of detoxication methods, such as: hemodiafiltration (HDF), continuous venovenous hemofiltration (CVVH), ultrafiltration (UF) on the group of the patients with acute renal failure (ARF), developed at the early postpartum period.

Materials and Methods: We analyzed the group of 114 women (age range 16–42 years). 62 patients (54.4%) underwent cesarean. The main reasons of ARF were hystosis (52%), massive bleeding and it's inadequate filling up (28%), accompanied renal diseases in anamnesis (14%), toxicallergical reaction on the antibiotics therapy (8%).

Results: Usually oligoanuria developed at the first 24h after the cesarean. We also observed significant hyperhydration up to wet-brain and wet-lungs, hyperkalemia, hypercreatininemia (430–1,100 mkmol/l), the concentration of urea was higher than 28 mkmol/l, anemia (Hb 58–38 g/l) and thrombocytopenia. In critical situations we started with HDF-blood speed – 250–300 ml/min, TMP 250–300 mmHg. The frequency of HDF depends on increasing the

level of hypercreatininemia and electrolyte disturbances. We used CVVH for 12–24 h at the group of the patients with unstable hemodynamic and with connection of septic complications. Standard poly-electrolite normo-osmolar solutions HF-41 (Fresenius) were used to compensate the waste of electrolytes and liquid gone with ultrafiltrate. Oligoanuria period lasted from 5 to 23 days, polyuria period – 5–12 days. Plasma absorption was used to stop the development of dissimulation intravascular coagulation syndrome and when the septic complications occurred.

Conclusion: Compensated chronic renal failure developed for 6 patients. 15 patients (13.2%) died.

The Impact of Early Vascular Access Failure on Cardiovascular Mortality in Hemodialysis Patients with Diabetes Mellitus

Y.O. Kim, S.A. Yoon, Y.S. Kim, B.S. Kim, H.C. Song, Y.S. Chang, B.K. Bang, E.J. Choi, S.Y. Kim

Department of Internal Medicine, The Catholic University of Korea, Seoul, Korea

Purpose: Early vascular access failure is considered to be associated with the poor quality of the vessel. Therefore, vascular access failure may be associated with cardiovascular mortality in the diabetic patients, but it is not reported yet.

Methods: This retrospective study enrolled 144 patients. We investigated vascular access failure within 1 year after the access operation and evaluated the cardiovascular death. We analyzed the cardiovascular mortality between early vascular failure group and patent group using Kaplan-Meier method and log rank test.

Results: Early vascular access failure developed in 68 patients (47.2%). During 32 ± 20 months of mean follow-up period, there was 62 cardiovascular deaths. The follow-up period tended to be shorter in the access failure group ($n = 68$) than the patent group ($n = 76$) (29 ± 17 vs. 35 ± 22 months, $p = 0.07$). But the access failure group had higher incidence of acute myocardial infarction (13.2% vs. 3.9%, $p = 0.044$), congestive heart failure (70.5% vs. 13.1%, $p < 0.001$), and peripheral arterial disease (20.5% vs. 3.9%, $p = 0.002$), compared to the patent group. The cardiovascular mortality of the access failure group was higher than that of the patent group (3 year; 54.6% vs. 24.6%, 5 year; 77.0% vs. 42.3%, $p = 0.005$).

Conclusion: This data suggest that early vascular access failure is associated with the cardiovascular morbidity and mortality in hemodialysis patients with diabetes mellitus.

Pulmonary Edema is a Sign for Presence of Significant Coronary Atherosclerosis in End-Stage Renal Disease Patients at the Initiation of Dialysis Therapy

N. Joki¹, H. Hase², T. Saijyo², Y. Tanaka², Y. Takahashi², H. Ishikawa², M. Fukazawa², Y. Inishi², Y. Imamura¹

¹Division of Dialysis and Nephrology, Nissan Tamagawa Hospital, Tokyo, ²Division of Nephrology, Toho University Ohashi Hospital, Tokyo, Japan

Background: In end-stage renal disease (ESRD) patients, the cause of pulmonary edema tends to be considered to be insufficiency of diuresis. We speculated that cardiac disease, especially severe coronary atherosclerosis, might be latency exist in ESRD patients with pulmonary edema.

Purpose: Our purpose is to clear the relationship between pulmonary edema and cardiac abnormalities, including coronary atherosclerosis, at the starting dialysis therapy in ESRD patients.

Methods: Eighty-nine ESRD patients (62 years, 19 females, 54 had diabetes), who were admitted to our hospital to initiate maintenance renal replacement therapy (RRT), were studied, and divided two groups, with pulmonary edema and without. All 89 patients received coronary angiography (CAG) within 3 months after starting RRT. The degree of coronary atherosclerosis was assessed by the results of CAG and changed numerically by Gensini scoring (GS) system. Clinical and cardiac parameters potentially relate to the presence of pulmonary edema at the initiation of RRT were examined by univariate and multivariate logistic regression analysis.

Results: The results of univariate analysis are shown below.

Variable	Odds ratio (95% CI)	P-value
Age (>65 yrs)	2.7 (1.1–6.8)	<0.05
Diabetes	2.5 (1.0–6.1)	<0.05
EF (per 1% ↓)	1.04 (1.01–1.07)	<0.05
EF (<40%)	4.7 (0.9–24)	0.062
GS (per 1 point ↑)	1.02 (1.01–1.04)	<0.005
GS (>22)	4.5 (1.8–11)	< 0.005
Albumin (>3.2 g/dl)	1.3 (0.6–3.1)	0.508

Moreover, by multivariate analysis, GS was closely associated with the presence of lung edema (OR: 3.2, $P < 0.05$) independent of age, diabetes, and EF.

Conclusion: These results suggest that as a cause of pulmonary edema in ESRD patients, not only insufficiency of diuresis but also cardiogenic factor should be considered, and that those patients should be performed screening for cardiac disease positively.

Pre-Dialysis Iron Profile in Patients Starting Hemodialysis at National Kidney Foundation, Singapore

V. Sreekrishna, N.S. Kulkarni, K.S. Prabhakar, S. Balasubramanian, K.S. Wong, M. Nandakumar

National Kidney Foundation, Singapore, Singapore

Purpose: Erythropoietin and iron supplementation is the main stay of management of anemia in ESRD patients. Adequate iron stores are required for optimum utilization of EPO and reflect the quality of care prior to starting hemodialysis. We studied the iron status in 2,431 patients beginning hemodialysis at NKF, Singapore over a 10-year period.

Methods: All the patients who have complete iron panel (hemoglobin, serum iron, ferritin and transferrin saturation (TS) %) at the initiation of dialysis were included in the study. Patients were sub classified into various groups to identify the factors associated with iron deficiency.

Results: Overall, 52.8% are males and 16.3% were over the age of 65 years at the initiation of dialysis. Mean hemoglobin was 9.03 ± 1.84 g/dl. Although the overall iron status for the entire group was noted to be adequate mean values for iron (70.6 ± 31.7 µg/ml), ferritin (356.3 ± 342.1 ng/ml) and TS% (28.6 ± 13.4), majority of patients (69%) were anemic (hemoglobin <10 g/dl) and only 15.7% of patients had Hb >11 g/dl. Variable number of patients had some form of iron deficiency with transferrin saturations <20% in 24.8% and ferritin <100 ng/ml in 19.5% of patients. However absolute iron deficiency (TS% <20 and ferritin <100) was noted in only 6.9% of them. Compared to males, female patients had less Hb (9.03 vs. 8.7) ($P < 0.001$), serum iron (70.6 vs. 68.9) ($P = 0.01$) and ferritin (356.29 vs. 340.45) ($P < 0.05$). Older patients (age >65 years) had higher ferritin (356.29 vs. 337.36) ($P < 0.001$) and higher TS% (30.68 vs. 28.25) ($P = 0.001$). Diabetic patients had less serum iron (67.83 vs. 71.83) ($P = 0.005$) and low TS% (27.67 vs. 29.06) ($P = 0.01$). There are no significant differences in iron status across all the races.

Conclusions: Majority of patients starting dialysis with NKF, Singapore are anaemic. Both functional and absolute iron deficiency is prevalent in the hemodialysis patient at the time of entry into our programme which may be contributory to the anaemia.

Effect of Dialyser Reuse on Small and High Molecular Weight Solute Clearance

M. Nandakumar, N.S. Kulkarni, V. Sreekrishna, S. Balasubramanian, K.S. Prabhakar, K.S. Wong

National Kidney Foundation, Singapore, Singapore

Reuse of dialysers is practiced in many dialysis centers around the world to make haemodialysis treatment more economical. But there is continuing controversy regarding the dialysis performance and dialysis outcome with reuse. We studied the effect of reuse on percentage of reduction of urea (PRU) and percentage of reduction of β_2 microglobulin (PRB2M).

15 patients on maintenance haemodialysis were randomly selected from 3 of NKFS dialysis centers for the study. All patients were on high flux polyamide dialysers. All dialysers were used up to 16 times unless failed to meet the criteria for continued use. Pre- and post-dialysis blood samples were collected on 1st, 5th, 10th and 16th use for measurement of urea and $\beta 2$ microglobulin. All dialysers were reprocessed with automated reprocessing machines using peracetic acid as sterilant. Dialysis prescription remained unchanged during the period of study. Paired T-test was used to assess significance.

There were 9 females and 6 males with a mean age of 46 (SD 9.6) years. Primary cause of renal failure was chronic GN in 7, unknown in 6 and diabetic nephropathy in 2. Mean body weight was 58 (SD 15) kg. Mean blood flow rate was 312 (SD 54) ml/min, 6 patients were on 500 ml/min and 9 patients on 800 ml/min dialysate flow rate. Average dialysis time was 236 (SD 28) min. Mean PRU achieved was 75.5 (SD 3.2) and mean PRB2M 49.3 (SD 12).

The difference between 1st use and 16th use PRB2M was 9.9 (SD 8.6). The difference between 1st use PRU and 16th use PRU was not significant ($p < 0.145$) but the difference between 1st and 5th, 10th and 16th use PRB2M was significant with P values of <0.006 , <0.001 and <0.001 respectively.

Our study shows that there is statistically significant drops of percentage of reduction $\beta 2$ microglobulin with reuse of polyamide high flux dialysers with peracetic acid as sterilant but is still able to achieve a mean PRB2M of forty-five percent with 16th use. There was no significant change in PRU.

194

Longevity of Permanent Vascular Access, Types of Interventions and their Outcomes

S. Balasubramanian, V. Sreekrishna, N.S. Kulkarni, K.S. Prabhakar, K.S. Wong, M. Nandakumar

National Kidney Foundation, Singapore, Singapore

The objective of this study was to analyze the longevity of various types of permanent vascular accesses, requirement of interventions and their outcomes.

We retrospectively analyzed the vascular access data obtained from the database of National Kidney Foundation, Singapore (NKFS) on the prevalent hemodialysis patient population from January 2002 to September 2003. The data included types and sites of all permanent accesses, dates of creation and failure, types of interventions performed and their final outcomes.

1,768 prevalent patients were included in the study. There were 2,058 permanent accesses. 1,429 (80.8%) patients had one access and the rest 339 (19.2%) had more than one. AV Fistulas (AVF) were 1,680 (81.6%) and AV Grafts (AVG) were 378 (18.4%). Among the AVF, Radiocephalic AVF (RCAVF) were 1,154 (68.7%), Brachiocephalic AVF (BCAVF) 447 (26.6%), Brachio basilic AVF (BBAVF) 73 (4.3%) and other sites were six. Among the AVG, Brachiocephalic Loop AVG (BCLAVG) were 216 (57.1%), Brachioaxillary AVG (BAX AVG) 73 (19.3%), Thigh AVG 33 (8.7%) and other sites 56 (14.8%). 336 interventions were performed, of which the type of intervention performed was available from our database for 318. These constituted percutaneous angioplasty 103 (32.4%), revision 97 (30.5%), surgical

thrombectomy 27 (8.5%), medical thrombolysis 18 (5.6%), others 73 (23%). 263 (80%) accesses could be successfully salvaged and 66 (20%) failed despite intervention (outcome not known in 32). AVG needed proportionately more interventions, 156 (52.67%) than AVF 180 (10.8%), the most being BAXAVG (61.6%) and the least being RCAVF (10.05%). The average lifespan of AVF in our population was 64.92 months (SD 46.44) and AVG was 27.57 months (SD 27.32). RCAVF (73.37 months, SD 48.12) and BCLAVG (29.08 months, SD 24.34) survived longer than other types of AVF and AVG respectively.

From our data, we found that AVF had a better longevity than AVG. AVG required more interventions than AVF, the maximum proportion needed on BAXAVG. We conclude that radiocephalic AVF is the ideal primary vascular access as it is likely to last longer and requires least number of interventions.

195

Survival of Chronic Dialyzed Patients in Romania

G. Mircescu, A. Covic, L. Gârneață, C. Bărbulescu, N. Constantinovici, M. Ardeleanu, I. Boca, V. Butnaru, D. Capsa, A. Ghenu, O. Golea, P. Kovari, R. Macavei, E. Mota, V.I. Patea, M. Pop, L. Rosu, C. Santimboreanu

Romanian Renal Registry, Bucharest, Romania

Survival is the ultimate outcome measure in renal replacement therapy (RRT). We evaluated the survival and factors that influenced it in chronic dialyzed patients in Romania.

A multicenter retrospective study was performed in 15 dialysis centers in Romania. Impact of gender, age, underlying renal disease, pre-dialysis monitoring, method of treatment, cardiovascular co-morbidity, diabetes mellitus, body mass index, anaemia, erythropoietin therapy, dialysate and dialysis membrane on patients survival was assessed.

We studied a cohort of 2,284 patients starting maintenance dialysis (82% on HD; 18% on PD) between 01.01.1995 and 31.12.2001 and survived at least 3 months on the initial method of treatment (mean age 46.9 ± 14.0 years; 56% males, 44% females). The etiology of CRF consisted of: glomerular nephropathies (primary 42.4%, secondary 12.2%), interstitial nephropathies (20.8%), hereditary and congenital disorders (9.2%), vascular nephropathies (6.3%), other renal diseases (9.1%). At the end of the study (15.06.2002) 73.3% of the enrolled patients were still alive. The main cause of death was cardiovascular disease (74.4%). The patients survival estimate is presented in the table.

Duration of RRT (years)	No. of deaths	Survival estimate (%)	95% confidence interval
1	203	90.6	89.4–91.8
3	477	74.5	72.4–76.6
5	593	62.2	59.4–65.0
7	633	51.6	47.1–56.1

Age, gender, etiology of CRF, cardiovascular co-morbidity (left ventricular hypertrophy, high blood pressure), diabetes mellitus, erythropoietin therapy, dialysate (bicarbonate/acetate) and dialysis membrane

(synthetic/cellulosic) but not the RRT method seems to influence the patients survival (Kaplan Meier analysis). Cox regression analysis revealed that age ($p < 0.001$), pre-dialysis monitoring ($p = 0.01$, OR = 0.8), erythropoietin treatment ($p < 0.001$, OR = 0.6), co-morbidity, eg. cardiovascular diseases ($p < 0.001$, OR = 1.8) and diabetes mellitus ($p < 0.001$, OR = 2.2) highly influenced survival.

196

Influence of Hemodiafiltration on Plasma Amino-thiol Redox Status

M. Nowicki^{1,2}, A. Czupryniak², E. Bald³, G. Chwatko³

¹Department of Nephrology, Medical University of Lodz, ²Department of Nephrology and Dialysis, Polish Mother's Memorial Hospital Research Institute, ³Department of Environmental Chemistry, University of Lodz, Poland

Hemodialysis (HD) has been recently shown to decrease plasma amino-thiol levels and the proportion of their oxidized to reduced forms, i.e. the redox status. Increasing use of convective dialysis methods, most notably hemodiafiltration (HDF), prompted us to investigate the effect of this technique on the plasma redox status of proatherogenic amino-thiols, i.e. homocysteine (HCSH) and cysteine (CSH) and antiatherogenic compounds: glutathione (GSH) and cysteinylglycine (CGSH).

Fourteen non-diabetic, long-term chronic dialysis patients (6M, 8F; mean age 28.2 ± 15.5 y) were included. Total plasma and reduced forms of amino-thiols, albumin, ferritin, vitamin B₁₂ and folate levels, hematocrit, residual renal function and dialysis adequacy parameters were measured in all subjects prior to and after a single mid-week hemodiafiltration session (predilution, with on-line production of the substitution fluid). The results were compared with those obtained before and after a standard hemodialysis session performed with modified cellulose membranes. Redox status of each of the amino-thiol compounds was calculated as a proportion of (total – reduced)/reduced concentration. Proatherogenic amino-thiol redox index (HCSH + CSH) and antiatherogenic index (GSH + CGSH) were calculated. Plasma amino-thiols were assessed with high-performance liquid chromatography. Oxidation of the reduced species was prevented in the collected blood by immediate adding of 2-chloro-1-methylquinolinium tetrafluoroborate.

Serum albumin, ferritin, vitamin B₁₂ and folate levels were within the normal range in all patients. Kt/V value calculated during the HDF session was 1.9 ± 0.4 . HDF induced a significant decrease of HCSH + CSH redox status (from 10.3 ± 3.9 to 7.0 ± 6.0 ; $p = 0.04$) but also of GSH + CGSH redox status (from 4.4 ± 2.5 to 2.1 ± 1.0 ; $p < 0.001$). Neither of these indexes was significantly influenced by the standard hemodialysis (11.7 ± 5.0 vs 9.8 ± 5.0 and 4.3 ± 1.8 vs 5.5 ± 2.6 , respectively).

We found that hemodiafiltration may decrease the proatherogenic amino-thiol redox status but it may be counteracted by the simultaneous decrease of the redox status of other thiol compounds which show antiatherogenic properties. Whether the net effect of HDF on plasma amino-thiol oxidation balance is more favorable than that of HD, remains to be proven in a long-term study.

197

Determining the Dosis for Blood Purification by Haemodialysis – New Software

M. Georgiev, Z. Kirjakov, K. Malakova, V.Ch. Ikonov¹

Clinic of Dialysis, Medical University, Sofia,

¹Clinic of Nephrology, Medical University, Varna, Bulgaria

Following the DOQI guidelines we developed software for estimation of the adequate dialysis dosis. At the beginning of the haemodialysis treatment we import the body weight, sex, age, ultrafiltration, blood flow, dialyzertype and diabetes mellitus yes or no. We determine the aimed dialysis dose according to the DOQI guidelines in URR% and/or Kt/V. The computer calculates and visualizes the time of the dialysis procedure and the blood volume passing the dialyzer. Using the change in the blood flow and in the type of the dialyzer we choose the optimal duration of the procedure. Before the start and after the haemodialysis procedure we analyze the plasma level of BUN and creatinine. Our results show 360 dialysis procedures with estimation of the dialysis dose.

Conclusion: The computer software for determination of the adequate dosis for blood purification is suitable for daily estimation of the dialysis treatment and for better rehabilitation of the patients with terminal renal failure.

198

Effect of Phonophoresis in the Kinesitherapy Programme for the Treatment of the Shoulder Joint Pain Syndrome in Chronic Dialysis Patients

M. Nikolova, Z. Kirjakov, V. Ch. Ikonov¹

Clinic of Dialysis, Medical University, Sofia,

¹Clinic of Nephrology, Medical University, Varna, Bulgaria

The dialysis related amyloidosis is one of the most important complications of the chronic dialysis treatment and one of the main reasons for the progression of periarticular shoulder joint pain syndrome. The reduced glomerular filtration rate is the reason for elevated plasma level of β_2 -microglobulins. These low molecular weight proteins impair the function in the soft tissue part of the joint. The objective of this study is to investigate the application of phonophoresis in the acute shoulder pain syndrome period to enable the start of kinesitherapy programme.

We investigated the application of phonophoresis on chronic dialysis patients aged between 8–23 years with shoulder pain syndrome – shoulderache, asthenia of the muscles, restriction of the joint movement. The pain becomes stronger during the night. Ultrasound wave make the diffusion process faster. To estimate the statement of the patients and the results of the ultrasound therapy we have used a system of routine functional dynamic parameters. For measuring the capacity of the joints' movement we used the SFTR method.

The ultraphonophoresis with antiinflammatory drugs is suitable procedure in the kinesitherapy programme of patients on chronic

dialysis treatment with shoulder joint pain syndrome. It improves the quality of life of dialysis patients on chronic dialysis treatment.

199

Test of the Permeability of High-Flux Dialysis Membranes for Beneficial Plasma Proteins using Microgel Electrophoresis

V.Ch. Ikonomov², I. Stefanidis¹, H. Melzer

Helmut Mann Medical Clinic II, RWTH Aachen, FRG, ¹Nephrology Division, University of Thessaly, Larissa, Greece, ²Clinic of Nephrology, Medical University, Varna, Bulgaria

In recent years hemodialysis therapy develops mainly from diffusion depending method to a contemporary method for convective removal of blood compounds with higher molecular weight. High-flux membranes were developed to eliminate low molecular weight compounds from the plasma of patient with renal failure. Their ability to remove uremic toxins should be similar to that of the human kidney. In order to investigate the permeability of different high-flux dialysers with membranes from modified cellulose and with synthetic membranes, the protein patterns in ultrafiltrate were analysed. Ultrafiltrate was obtained 2 times during routine hemodialysis therapy. Using our optimized by H. Melzer method of Sodium Dodecyl Sulfate gel electrophoresis and subsequent silver staining we verified the eliminated protein molecules. Documentation of the protein pattern is performed using laser densitometry.

The protein patterns of the ultrafiltrate corresponds to the protein permeability of the glomerular membrane containing IgG, transferrin, albumin, α -1-microglobulin, retinol-binding protein β -2-microglobulin. In high-flux membranes the permeability is modified by pore-size, charge, porosity and adsorption capacity giving typical cut-off and protein pattern for each type of membrane. In conclusion, protein permeability of high-flux membranes is similar to the glomerular membrane. This method is useful for testing of the balance between the removal of toxins with higher molecular weight and the minimal removal of beneficial plasma proteins.

200

Comparison of the Effect of Erythropoietin and Erythropoietin with Carnitine in Correction of Anemia in Patients on Chronic Dialysis

H.T. Khoroshahi, B.H. Asl, G. Saiidi

Dialysis Center, Imam Hospital, Tabriz, Iran

Introduction: Anemia is a major complication in patients on chronic dialysis. The availability of recombinant human erythropoietin from 1989, has been one of the most significant advance in the

care of anemia of patients with chronic renal failure (CRF). On the other hand, carnitine as a natural substance may be involved in the erythrocyte synthesis. We compared the effect of erythropoietin and carnitine separately and together in the correction of anemia in patients undergoing dialysis.

Methods: 42 patients with CRF on chronic dialysis were selected randomly in 3 groups.

- Group 1: rHu EPO was administered 6,000 IU weekly for 3 months in these patients.
- Group 2: Patients in these group were treated with carnitine 500 mg/day orally for 3 months.
- Group 3: These patients were treated with both erythropoietin 6,000 IU plus carnitine 500 mg daily for 3 months.

Then statistical analysis was performed with SPSS program.

Results: There was significant elevation of Hb and Hct in rHuEPO treated and carnitine treated group $P < 0.04$. There was also more significant improvement of anemia and elevation of Hb and Hct in patients who treated with rHuEPO plus carnitine $P < 0.002$.

It seem that carnitine is a safe and useful nutrient in CRF patients and may be used in combination with rhEPO for correction of anemia in dialysis patients.

201

Efficacy of Carnitine and Vitamin E Combination Therapy on Intradialysis Complication

H.T. Khoroshahi, B.H. Asl, A. Agazadeh, M. Mortazavi

Dialysis Center, Imam Hospital, Tabriz, Iran

Introduction: Patients with Chronic Renal Failure (CRF) in terminal stage need renal replacement therapy. Hemodialysis as one of these replacement therapy has many acute and chronic complications. The most common complications during dialysis are hypotension, muscle cramps, headache, nausea and vomiting, itching and anaphylactic reactions. There are many strategies for prevention and treatment of these complications. The aim of this study was evaluation of the efficacy of prophylactic vitamin E and carnitine supplementation on some intradialysis complications.

Methods: This study was performed prospectively on 20 patients with End Stage Renal Disease (ESRD) on chronic dialysis who had intradialysis complications such as hypotension, muscle cramp, nausea and vomiting and headache. These patients were evaluated without and with vitamin E and carnitine supplementation separately and intradialysis complications were recorded. Then statistical analysis was performed with Kruskal-Wallis test.

Results: There was not any significant improvement in intradialysis hypotension in treated groups. There was significant reduction of intradialysis muscle cramps in patients who were treated with vitamin E and carnitine and together. Other complications such as intradialysis nausea and vomiting and headache were also responded to these supplementation but statistically were not significant $P = 0.64$. Due to the safety and efficacy of these drugs in reduction of some intradialysis complications it seem that vitamin E and carnitine are useful in patients on chronic hemodialysis and we recommended both of them in these patients.

Transplantation

202

Anti-HLA Antibodies Production and Nitric Oxide Level in the Serum and Urine of Post Renal Transplant Patients in Relation to Graft Function and Survival

A. El Aggan Hayam, F.K. Amal, A.Z. Sherif, S.A.S. Mohamed

Faculty of Medicine, University of Alexandria, Alexandria, Egypt

The purpose of this work was to study the production of HLA antibodies (HLA-Abs) and nitric oxide level in serum and urine of post transplant patients, and their correlation to incidence of rejection, renal allograft function and survival. To achieve these goals, twenty patients with renal transplantation for the first time (GI) and twenty healthy control subjects (GII) were studied. Anti HLA-Abs class I and class II were detected by ELISA technique (Lambda antigen tray, LAT-M, One Lambda, Inc), serum and urinary nitrate and nitrite, and urinary N-acetyl- β -D-glucosaminidase (U.NAG) were detected. Using duplex Doppler ultrasonography, renal hemodynamics were studied by calculating the resistive and pulsatility indices (RI and PI). All patients before transplantation had a negative cross match. After transplantation anti HLA-Abs class I were detected in 7 patients (35%) and class II in 3 patients (15%), all the controls were negative for both anti HLA-Abs class I and II. Three patients (43%) with positive anti HLA-Abs class I and all the three patients (100%) with positive anti HLA-Abs class II had acute rejection episodes. In renal allograft recipients a significant increase of serum and urinary nitrite was found than the controls. Patients with rejection episodes had a significant increase in serum and urinary nitrate, serum nitrite, RI and PI and a significant decrease in U.NAG than transplant patients without rejection. In renal transplant patients the urinary nitrate was positively correlated with serum creatinine, nitrate, nitrite, RI and PI ($p < 0.05$). U.NAG was negatively correlated with serum creatinine, serum and urinary nitrate, RI and PI ($p < 0.05$). The RI and PI were positively correlated with serum creatinine, serum nitrite ($p < 0.05$). The presence of anti HLA-Abs of either class I or class II were correlated with the occurrence of graft rejection. From this study it can be concluded that anti HLA-Abs can be de novo appear in the post transplant period and can lead to acute and even chronic rejection. The detection of these antibodies, allows identification of high risk patients with poor outcome. The increase of urinary nitrate and the decrease in U.NAG can be a marker for detection of graft rejection episodes. Also, the increase in serum nitrate and nitrite during rejection episodes could be a compensatory mechanism for the renal hemodynamic changes.

203

Calcification of Failed Renal Allograft in a Maintenance Peritoneal Dialysis Patient

J.-J. Huang¹, Y.-M. Sue², W.-T. Lin¹, C.-C. Tseng¹

¹Department of Internal Medicine, National Cheng Kung University Hospital, Tainan,

²Department of Internal Medicine, Taipei Municipal Wan Fang Hospital, Taipei, Taiwan

Visceral metastatic calcification is an insidious complication in chronic patients dialysis. Block GA reported that hyperphosphatemia (>6.5 mg/dL) and high $\text{Ca} \times \text{P}$ product (>72 mg²/dL²) increased the mortality risk in dialysis patients. Calcification can be deposited in the renal cortex and medulla and is usually found incidentally. But renal calcification can develop when the serum calcium and phosphorus levels are normal. Diffuse cortical calcification has been reported in acute rejected renal allograft. Dystrophic renal calcification occurs in damaged or necrotic tissues, such as chronically rejected renal graft or tumors.

This 40 y/o chronic hemodialysis female received cadaveric renal transplantation in 1990. Because of chronic rejection, she started on continuous ambulatory peritoneal dialysis since 1994. Persistent hyperphosphatemia and hyperparathyroidism developed since 1996. The serum levels of intact-PTH, Ca, P, and $\text{Ca} \times \text{P}$ elevated (1,217 pg/mL, 11.6 mg/dL, 7.1 mg/dL, and 82.4 mg²/dL², respectively). Subtotal parathyroidectomy with auto-implantation in the left forearm was performed in 1998. In Dec 2002, one episode of gastric ulcer with abdominal pain developed. Plain film of abdomen incidentally revealed diffuse calcification of renal allograft, which did not show at the time of catheter implantation. Computed tomography of abdomen and pelvis confirmed calcification of cortex and medulla. However, Tc^{99m}-MDP whole body bone scan showed no increased uptake of tracer in end-stage rejected graft, native kidney, or other tissues and organs.

In this case, calcification of renal graft was not found at the time of catheter implantation but found after the development of secondary hyperparathyroidism. We suggested that chronic renal rejection might be the underlying cause of allograft calcification, which was further precipitated by high $\text{Ca} \times \text{P}$ product and secondary, or even tertiary, hyperparathyroidism, but without active uptake of radio-tracer. In addition, transplant nephrectomy is currently not performed following late allograft rejection unless clinical indications outweigh the risk involved.

204

Appropriate C₂ of Neoral® in Stable Renal Graft Recipient (Long-Term Follow-Up)

O. Alfurayh, A. Chaaban, N. Mutawa, N. Elkum, K. Al Meshari, A. Al Lehibi, Q. Nadri, I. Hamasni, K. Shaibani, I. Ahmadi, S. Raza, K. Mohan

King Faisal Specialist Hospital & Research Centre, Riyadh, KSA

Introduction: Cyclosporine nephrotoxicity influences chronic allograft nephropathy and long-term graft survival. CSA trough level

(C₀) does not reflect the desirable pharmacokinetic exposure. C₂ has been found to be more reliable in short-term follow up studies.

Aim: The purpose of our study is to determine the appropriate C₂ level in long term stable renal transplant patients with well functioning renal graft on Neoral®.

Methods: We studied 60 kidney transplant recipients (26 Cadaveric and 34 living donor kidneys). Male to female ratio was 36:24 mean age 42.7 ± 13 SD years with stable renal function, mean serum creatinine at entry data 127 ± 36 μmol/L and at the end 133.92 ± 38 over a mean duration time post transplantation of 92.2 ± 58 month (p value 0.7).

Results: Serum creatinine (over the study period) did not change significantly at mean (132.7 ± 38) indicates stable kidney function. Dose of cyclosporine was 2.3 mg/kg/Bwt/day, at mean daily dose (156.67 ± 47.36 mg). Mean C₀ was 126.25 ± 39 μg/L and C₂: 626.2 ± 229 μg/L using (FPIA Abbott assay). Twenty-two HCV+ patients with C₀: 129.77 ± 45, C₂: 709.46 ± 224 while in HCV negative patient C₀: 124 ± 35, C₂: 712 ± 95. The difference between the two groups was not significant. Mean ALT in both groups are similar 28.2 ± 31 IU/L. Diabetes was reported in 9 patients (15%) mean C₀ was 131.78 ± 37.3 C₂: 717.78 ± 300, the comparison to non-diabetic patients was not significant.

Conclusions: In long-term follow up C₂ monitoring appears to be reliable indicator of CSA exposure and relevant for clinical practice. In our study value of 626.2 ± 229 μmol/L represent an effective therapeutic range in long-term stable renal transplant patients.

AUC = Area Under Curve C₀ = CSA trough level
FPIA = Fluorescein Polaroid C₂ = 2 hour post dose
Immunoassay

205

Transplanted Rat Kidney Transfected with NFκB Decoy by Ultrasound and Microbubbles were Survived

N. Tomita¹, H. Azuma², H. Koike¹, Y. Taniyama¹,
T. Ogihara¹, R. Morishita¹

¹Clinical Gene Therapy, Osaka University, Suita,

²Urology, Osaka Medical College, Takatsuki, Japan

Purpose of the Study: NFκB plays a pivotal role in the coordinated transactivation of series of cytokine and adhesion molecule genes that are highly involved in the onset of acute rejection of transplantation. We hypothesized that synthetic double-stranded oligonucleotides (ODN) with high affinity for NFκB introduced in vivo as decoy cis elements bind to the transcription factor and block the activation of genes mediating acute allogenic response, thus providing the effective therapy for renal acute rejection.

Methods: To transfect ODN into the kidney, we employed a novel non-viral vector system using ultrasound irradiation with microbubbles, as safety issue using viral vector systems remains in relation to human gene therapy despite of high transfection efficiency.

Results: FITC-labeled decoy ODN could be successfully transfected into rat kidney using ultrasound with microbubbles in the kidney. Donor kidney transfected with NFκB decoy ODN orthotopically

transplanted into bilaterally nephrectomized Lewis recipients. In the control group, the marked destruction of renal tissue with the mononuclear cell infiltration occurred at day 4, accompanied by the increased cytokine production and adhesion molecule expression in the grafted kidneys. All animals died of renal failure by 10 days after operation. In contrast, the recipients of donor kidneys transfected with NFκB decoy ODN exhibited a significant prolongation in the death rate as compared to other groups (p < 0.01). Especially, graft function as well as histological appearance was well reserved in grafted kidney transfected with NFκB decoy ODN exhibited a significant prolongation in the death rate.

Conclusions: Using this new gene transfer method, transfection of NFκB decoy ODN significantly improved the survival rate of transplanted kidney associated with the inhibition of cytokine and adhesion molecule expressions in the kidney. This new approach may provide a novel therapeutic strategy for renal allograft.

206

Incisional Hernia in Renal Transplantation: Incidence and Predisposing Factors

S. Schmitz, A.D. Hoang, D.N. Mazi, M. Wissing,
F. Hut, L. De Pauw

Department of Nephrology Dialysis and Transplantation,
Erasmus University Hospital, Brussels, Belgium

Background: The incidence of incisional hernia after renal transplantation with vertical paramedian incision has been evaluated. Further on, we examined whether obesity, chronic steroid therapy, diabetes and advanced age were associated with an increased rate of incisional hernia.

Patients and Methods: We reviewed the records of 425 consecutive kidney transplants performed between January 1997 and December 2002. Among these 425 recipients, 31 patients (15 children, 10 lost for follow up, 4 explantations and 2 death) were excluded. All patients had vertical paramedian incision and fascia were closed with running no. 1 polyester nylon suture. Obese recipients proportionally got lower doses of steroids than non-obese. Mean doses of steroids were similar at 1, 2, 30, 60 and 365 days post transplant for all the patients.

Results: Among 394 recipients, 22 (5.58%) patients presented an incisional hernia at the transplant incision site. Hernia developed 5 to 770 days (mean 160.5 days) after transplant surgery and were significantly more common in obese recipients (BMI > 25). Incisional hernia occurred in 15.9% (7/44) of patients with BMI > 30 kg/m² and only in 2.97% (7/235) of patients with BMI < 25 kg/m². 41 patients had diabetes and only 2 of them presented incisional hernia. In this study, mean age of patients with incisional hernia was 47.7 years. During the postoperative period, incisional hernia was associated with lymphoceles (n = 9) and wound infection (n = 2). 4 patients were heavy smokers and another 4 patients had chronic respiratory disease.

Conclusions: The main risk factor for incisional hernia after renal transplantation is severe obesity. Diabetes and advanced age don't increase the incidence of incisional hernia. The use of steroids was similar in both groups. Incisional hernia was frequently associated with lymphoceles.

Flashback Case of the Patient with the Liver Abscess and Polycystic Degeneration of Kidneys, Liver and Pancreas

D. Kurpas¹, A. Steciwko¹, D. Patrzalek²

¹Family Medicine Department of Wroclaw Medical Academy, Poland Haemodialysisotherapy Station, State Hospital, Legnica, ²Surgery Department of Wroclaw Medical Academy, Poland

52 years old male patient after the right-side nephrectomy in 1992, left-side nephrectomy in 1997 (because of 'gigantic' cystic kidney with no sign of function) in course of the adult polycystic renal syndrome (with abscesses and feverish state), after kidney transplantation in 08.1997 and subsequent explantation in 09.1997 (because of the renal artery embolus) with the polycystic degeneration of liver and pancreas has been hospitalised because of a liver abscess.

The patient were during permanent dialysisotherapy from 1990 because of renal failure progression.

In 01.1998 it was observed a permanent feverish state in patient. After diagnostic process it has been recognized abscess of the liver and accomplished drainage (with evacuation of 400 ml of pus), rinsing with Betadine and leaving of Gentamicin sponges.

It had been observed pneumonia in the course of septicaemia because of the liver abscess.

After one month (02.1998) it had been accomplished the second drainage because of the residual liver abscess and in 05.1998 – it had been removed 3 drains. Antibioticotherapy with Vancomycin has been continued till 06.1998.

This second intervention was finally successful.

The patient in satisfactory general state has been haemodialysated till now at the Haemodialysisotherapy Station of State Hospital in Legnica (Poland).

High specialist, qualified and long standing care let the patient alive in quite high quality of life.

Our case study shows the possibility of treatment for patients with the similar course of the disease.

208

Review of Renal Transplants in Asian Population: A Single Centre Retrospective Study

B.K. Pandya, A.K. Asari, C.D. Short, H.N. Raid, T. Augustine

Renal Transplant Unit, Manchester Royal Infirmary, Manchester, UK

Purpose of the Study: Inter ethnic variation in pharmacokinetics of immunosuppressive agents after renal transplantation can cause either rejection or toxicity. African-Americans have lower cyclosporine bioavailability than Caucasians. Neoral clearance is higher in Latinos compared to Caucasians. We observed that cyclosporine monotherapy was effective immunosuppression in majority of Asian renal transplant

population. To evaluate this we retrospectively studied the immunosuppressive regime in our Asian renal transplant population.

Methods: Asian population transplanted between January 1973 and June 2001 was evaluated. The data was collected regarding immunosuppressive therapy, rejection rate, and graft survival.

Results: Between January 1973 and June 2001 about 211 kidneys were transplanted in Asian patients. 101 (47.8%) recipients had functioning graft with available relevant data. The average graft life of these kidneys was 81.4 months. Out of these, 40.5% (41 of 101) were on cyclosporine monotherapy, 17% (17 of 101) on cyclosporine and prednisolone, 11.8% (12 of 101) on tacrolimus monotherapy and 5% (5 of 101%) on tacrolimus and prednisolone, for maintenance immunosuppression. The mean serum creatinine for cyclosporine monotherapy was 152 $\mu\text{mol/l}$, with average graft life 80 months and for cyclosporine and prednisolone 216 $\mu\text{mol/l}$ and 105 months respectively. The mean cyclosporine dose on maintenance monotherapy was 3.6 mg/kg. The mean serum creatinine on tacrolimus monotherapy was 148 $\mu\text{mol/l}$ and average graft survival was 63.4. While for tacrolimus and prednisolone combination therapy mean serum creatinine and graft survival were 169 $\mu\text{mol/l}$ and 62.8 months respectively.

Conclusions: Cyclosporine monotherapy is the main form of maintenance immunosuppressive therapy among Asian population in our centre. Cyclosporine monotherapy can be used for Asian renal transplant recipients with cost benefit, without compromising graft survival in developing countries of Asia.

209

Renal Transplant in Hepatitis C ESRD Without Pre-Transplant Liver Biopsy

P. Namboodiri, D. Amarapurkar, U.G. Oza, H. Shah, S.D. Bichu, A.L. Kirpalani

Bombay Hospital Institute of Medical Sciences, Mumbai, India

72 Hep C patients of ESRD on MHD underwent Kidney Transplant (KTx) between 1990 and 2003. Patients (pts) with esophageal varices and/or nuclear scan showing bone marrow uptake and/or splenomegaly were excluded being defined as clinical cirrhosis (Cx). Liver Bx (LBx) was not performed pre-Tx because of its attendant morbidity. The data of 53 pts with Hep C (gp A) and 10 pts with Hep C+ B (gp B) is available.

Results:

Group	SGPT (%)		Liver survival (%)		Graft survival (%)		Patient survival (%)	
	A	B	A	B	A	B	A	B
At 1 yr	94	50	85	80	81	60	85	80
At 3 yrs	32	67	75	27	64	20	77	50
At 5 yrs	61	100	45	05	32	08	52	20
>5 yrs	64	100	42	1.8	26	05	48	15

Conclusion: Hep C pts free from esophageal varices and nuclear scan evidence of Cx may be offered KTx without pre-Tx Liver biopsy with acceptable outcomes except those with concomitant Hep B coinfection.

	A	B
Rejection (A/c/C/c)	11/15	2/1
Graft/pt loss	8/16	2/8
<i>Cause of death</i>		
Liver failure	4	6
Sepsis	15	7
Graft failure	4	2
Post LBx Hge	1	0

210

Clinical Recurrence of IgA Nephropathy after Renal Transplantation in the Allograft Transmitted Mesangial IgA Deposition from Related Donor

Y. Ito¹, K. Shimamoto¹, F. Gejyo²

¹Second Department of Internal Medicine, Sapporo Medical University School of Medicine,

²Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medicine and Dental Sciences, Japan

Objective: Recently, it has been shown that deteriorating renal function and substantial graft loss may occur in 13–60% of recipients with recurrent IgA nephropathy (IgAN) at long-term follow-up. The aim of our study is to investigate recurrence in recipients with primary IgAN.

Methods: We conducted a retrospective single-center study on 79 kidney transplant recipients over the period 1995–2001. Before transplantation, twenty of the 79 patients had biopsy-proven primary IgAN.

Results: After transplantation recurrent proteinuria and/or hematuria were observed in seven (35%) of the 20 patients. The recurrence occurred in four patients with mesangial IgA deposits in allograft at 0 h biopsy earlier than in three patients without deposits in allografts at 0 h biopsy (6 ± 2.6 vs 21 ± 7.0 months $P < 0.05$). There were no significant differences in age, sex, the duration of dialysis before transplantation, acute rejection, blood pressure, and immunosuppressant drugs between two groups. Serum IgA level was higher in the related donors of primary IgA nephropathy compared with those of other primary nephritis (331 ± 91 vs 239 ± 75 mg/dl, $P < 0.05$).

Conclusions: A clinical recurrence of IgAN may occur in recipients with mesangial IgA deposits in living-related donor grafts earlier compared with patients without such deposits. The related donors may have silent IgA deposition in their kidneys, especially when they show serum high IgA level. So it may be better to exercise great care in them at long-term follow-up.

211

Categorization of Transplanted Kidney Biopsies According to BANFF-97 Classification with Respect to Clinical Course

F. Norooznia, A. Ghafari, K. Makhdoomi, S. Salari, H.R. Taleb

Uromieh University of Medical Sciences, Emam Khomini Hospital, Uromieh, Iran

Introduction: Episodes of allograft dysfunction occur in 50–70% of kidney transplant recipients and biopsy is the gold standard to find its causes. If the severity of injury in pathologic reports defines as standard and semi-quantitative manner, the unification of these reports and their comparison will be achieved.

Methods: The specimens of three years (1999–2001) biopsies were classified according to BANFF-97 classification. And clinical data have taken from their medical reports treatment response based on decrease in creatine level, mean cyclosporine level of each groups, and induction and anti rejection therapy protocols were determined.

Results: From 62 biopsies taken from transplanted kidneys, 46 have the criteria for adequacy of specimen. The majority of cases (31) fall into no-rejection or borderline groups. The number of cases in other groups was from 2 to 9. There was no significant difference in respect to induction and anti rejection regimens between groups. There was significant difference in respect to treatment response within several BANFF grades.

Conclusions: It seems there is correlation between BANFF-97 classification of biopsies and clinical course of allograft dysfunction and response to treatment. So it seems helpful to categorize the biopsy specimens in such manner.

212

Is More Urine Better?

A. Ghafari, K. Makhdoomi

Uromieh University of Medical Sciences, Emam Khomini Hospital, Uromieh, Iran

Introduction: Acute rejection (AR) is one of the most important problem in renal transplant recipients. Early recognition and treatment of AR have significant effect on short and long term allograft survival. Identifying high risk patients for AR can help us to detect AR episodes timely. Is there any correlation between first 24 h post transplant urine volume (1st 24 h UV) and risk of AR.

Materials and Methods: In a prospective study we examined 115 consecutive renal transplant recipients in Uromieh Renal Transplant Center – Iran, 1st 24 h UV was recorded, and each patient was followed up for one year. Any AR that confirmed by biopsy was recorded. Patients were divided into two groups in respect to 1st 24 h UV. G1 consist of patients with 1st 24 h UV less than 12 l and G2 consist of patients with 1st 24 h UV more than 12 l. Two groups were compared in respect to AR episodes and need to dialysis in first year after transplantation.

Results: Of 115 patients 49 were males and 66 were females. Mean age at transplantation was 36.5 years there was no significant difference between two groups in respect to underlying renal diseases. There was significant difference between two groups in respect to AR episodes ($p = 0.008$). And there was significant difference between two groups in respect to need to dialysis ($p = 0.005$).

Conclusion: First 24 h post transplant urine volume may be used as a prognostic risk factor for AR and early graft loss in renal transplant recipients.

213

Impact of Hepatitis B and Hepatitis C Virus Infections on Patients and Allograft Outcomes in Iranian Renal Transplant Recipients

A. Ghafari, K. Makhdoomi

Uromieh University of Medical Sciences,
Emam Khomini Hospital, Uromieh, Iran

Introduction: HCV and HBV infection occurs frequently in ESRD patients. Concern has been risen as to whether these patients are at increased risks for mortality or allograft dysfunction after renal transplantation.

Materials and Methods: We examined 611 renal recipients from April 1995 through April 2002. All patients had been received allograft from living donors, and were treated with CSA, AZA, PRED, and had been followed until January 2003. Patients had been divided into four groups. G1: HBSAg positive (14 pts), G2: HCVAb positive (13 pts), G3: HBSAg and HCVAb positive (6 pts), and G4: HBSAg and HCVAb negative patients (578 pts). Four groups compared in respect to morbidity, mortality, and allograft function characteristics.

Results: Among 611 patients 347 were male and 264 were female. Mean age at transplantation time was 39.5 years, mean time of follow-up for G1 was 3.8 years for G2 was 1.8 years, for G3 was 1.2 years, and for G4 was 3.5 years. In respect to mean of creatinine there was significant difference between G1 and G4 ($p > 0.001$), and between G2 and G4 ($p = 0.028$), and no significant difference between G3 and G4. In respect to need for dialysis there was significant difference between G2 and G4 ($p = 0.034$) and between G3 and G4 ($p = 0.014$). There was no significant difference for mortality among groups.

Conclusions: HBV or (and) HCV infections is not a contraindication to kidney transplantation in Iranian patients and there was no effect on patient's survival. However allograft outcome may be worse in HBV or HCV infected patients.

214

Impact of Pregnancy on Transplanted Kidney and vice versa

A. Ghafari, K. Makhdoomi, R. Doosti

Uromieh University of Medical Sciences,
Emam Khomini Hospital, Uromieh, Iran

Introduction: Due to increasing number of renal transplant recipients in child bearing age, evaluation of morbidity and mortality in neonates and mothers, and renal function characteristics in pregnant renal transplant recipients are important.

Materials and Methods: In a retrospective study, 462 renal transplanted female have been evaluated from April 1995 until April 2002. All patients had been received kidney from living unrelated donors, immunosuppressive regimen consisted of CSA, AZA, PRED in all of them.

Results: 45 pregnancies accrued in 33 women, mean age at pregnancy was 28.45 yrs, mean interval between transplantation and pregnancy was 33.24 months. 75% of pregnancies were successful. 97% neonates had desirable appars, and their average weight was 2,198 g. Two anomalies was seen, one facial hemangioma and one club-foot. Complications in order to frequency were; Proteinuria 27.5%, hypertension 21.4%, urinary tract infection 19%. One patient died from sepsis. Allograft dysfunction did not occur in any patients.

Conclusions: Pregnancy after renal transplantation may be safe, however some complications may occur more frequently.

215

Homocysteine (H), Interleukins (IL-2, IL-6) and Serum Amyloid (SA) in Renal Transplantation 'de novo'

J.M. Gago¹, D.M. García¹, A. Mendiluce¹,
R. Gordillo¹, J. Bustamente¹, R. Bustamente²,
I. Ramirez², A. Antelo², F. García²

¹Nephrology Department, ²Central Laboratory
Department, University Hospital, Valladolid, Spain

Background: Immunosuppressant therapy produces diverse modifications in the system immunity. There are cytokines (IL-2 and IL-6) and other substances like the homocysteine and the serum amyloid that play a fundamental role in the regulation of the immunity system.

Objective: Our study makes reference to the modifications that experience the homocysteine, IL-2, IL-6 and serum amyloid in connection with the immunosuppressive medications, during the first month of kidney transplant; we will value their interest like markers of acute rejection.

Methods: 19 patients were studied during the first month kidney post-transplant, determining the serum levels of homocysteine, IL-2, IL-6 and SA, in four moments different (the day before to kidney transplant, 7th day, 15th day and 30th day), elected in a random way. The immunosuppressive treatment that all the patients received was: Corticoides + Tacrolimus + Basiliximab.

Results: The half value of homocysteine in the four carried out determinations doesn't present significant variations. The half values means of IL-2, IL-6 and SA presented significant variations, in the carried out determinations.

Conclusions: The half value of homocysteine did not suffer significant modifications ($p = 0.512$) along the study. For what a relationship cannot settle down between the immunosuppressive therapy and this substance in the period of studied time. The half values of IL-2 and IL-6 presented significant modifications ($p = 0.019$ and $p = 0.05$ respectively). IL-2 suffered a significant decrease on 7th day post-transplant. Corticosteroids, tacrolimus and basiliximab inhibit the secretion and action of IL-2 or block its action. The half value of SA, as marker of immunologic answer in front of the injection, suffered a significant increase in the 7th day post-transplant with a grade of significance of $p < 0.0001$, paradoxically any acute rejection didn't take place, that's why we cannot know which are the values of SA that will be possible considered significant as indicator of acute rejection, on the other hand this ascent of SA to the 7 days of the transplant could be very justified for any process infectious at the same time.

216

De novo-Adenocarcinoma of the Renal-Transplant: Report of a Case

M. Mahfoudhi¹, M. Cherif¹, E. Abderrahim¹,
T. Ben Abdallah¹, H. Hedri¹, F. Ben Moussa¹,
A. Kheder¹, H. Ben Maiz¹

¹Department of Nephrology and Internal Medicine,

²Department of Urology, ³Department of Radiology,
Charles Nicolle Hospital, Tunis, Tunisia

Malignancies observed after solid organ transplantation were often related to over-immunosuppression and oncogenic virus. The Lympho-proliferative disorders and skin tumors remain prevalent whereas de novo and graft-transmitted cancers were rarely described.

We report the case of a 27-years-old renal recipient who developed an adenocarcinoma of the transplanted kidney.

The transplantation was performed in June 1992 using the left kidney of his mother aged of 50 years. The donor's blood tests were normal as was her renal arteriography. During the first year after transplantation, the recipient was regularly followed on normal biologic tests and ultrasonographic exams. A routine Doppler ultrasonography performed on July 1997 showed a vascularized solid mass of the lower pole of the renal graft. CT scan confirmed the diagnosis of graft tumor and didn't revealed features for venous invading nor metastases. Extra-capsular detransplantation of the functional renal graft was realized and hemodialysis was restarted. Five years later, both donor and recipient didn't developed local recurrence of metastases. We conclude that preventive measures before, during and after renal transplantation should be done to avoid the risk of graft-transmitted de novo tumors and must include meticulous screening of potential donors, careful exploration of the kidney before its removal, biopsy of suspected or precursor lesions and regular ultrasonographic exam of the graft.

217

Reversal of Renal Dysfunction after Strong Reduction in Calcineurin Inhibitors (Cyclosporine or Tacrolimus) and Introduction of Mycophenolate Mofetil in Liver Transplant Patients with Acute or Chronic Renal Failure

A.W. Avolio, S. Agnes, E. Nure, G. Pepe, M. Castagneto

Department of Organ's Transplantation,
'A. Gemelli' Catholic University of Rome, Rome, Italy

Background: Calcineurin inhibitors (CNIs) may present acute and chronic nephrotoxicity. Mycophenolate Mofetil (MMF) is not nephrotoxic. MMF has been used here as main rescue immunosuppressive agent associated with minimal levels of CNIs, after liver transplantation (LTx).

Patients and Methods: Immunosuppressive therapy in 27 LTx patients (pts) with renal impairment was switched from CNIs to MMF and small doses of CNIs. MMF was administered at 25–30 mg/kg/day. Target cyclosporine and tacrolimus through-levels (whole blood assay) were maintained between 25 and 50 ng/ml and between 4 and 7 ng/ml, respectively.

Results: *Group 1:* 7 patients with acute toxicity (early conversion, median = 2.6 weeks after LTx). Kidney function improved in all: creatinine values decreased at 1, 3, 6 and 12 months ($p < 0.05$). Rejection rate was 14.3%. Gastrointestinal side-effects occurred in 1 pt. *Group 2:* 20 pts with chronic toxicity (late conversion, median = 56 months after LTx). Improvement in renal function occurred in 90%. In the remaining patients a further deterioration occurred leading to hemodialysis. Rejection rate was 15%. Minor side-effects were observed in 35%.

Conclusion: Conversion to MMF + small doses of CNIs seems to be safe and leads to improvement in renal function in early/long-term LTx patients.

218

Tacrolimus-Basiliximab vs. Cyclosporine (CsA)-Basiliximab in Renal Transplantation 'de novo': Acute Rejection and Other Complications

D.M. García, J.M. Gago, A. Mendiluce, R. Gordillo,
J. Bustamante

Nephrology Department, University Hospital,
Valladolid, Spain

Background: A best immunosuppressant drugs is essential to maintain the viability in kidney allograft. Minimizing their toxicity of this immunosuppressant drugs is fundamental too.

Objective: Our study is referring to different types of immunosuppressant drugs (corticosteroids, cyclosporine, tacrolimus and basiliximab) which are used in the primary renal transplantation, comparing them and valuing the effectiveness to prevent the incidence of acute rejection and the appearance other complications, mainly infections disease complications.

Methods: 95 patients during the first year of its primary renal transplantation. They were included, in a random way, in 3 different groups, in accordance with the immunosuppressant drug therapy that we had been administered. Group I (35 patients) 44 ± 12 year-old half age: Corticosteroids 0.5 mg/kg/day and later descending dose was continued until reaching a 10 mg/day to the 6th month of the transplant, maintenance dose, and CsA 8 mg/kg/day and later we left adjusting according to levels; Group II (35 patients) 58 ± 10 years: Corticosteroids and CsA with the same dose that the group I and Basiliximab was administered in two intravenous doses of 20 mg each the first dose before the renal transplant and the second dose, 4 days after the transplant. Group III (25 patients) 53 ± 13 years old half age: Corticosteroids 0.3 mg/kg/day and later a descending dose was

continued until reaching a 5 mg/day to the third month of the transplant, maintenance dose, with Tacrolimus 0.2 mg/kg/day and later according to levels and with Basiliximab to same dose that it was administered in the group II.

Results: Of the 95 valued patients, 9 presented a acute rejection, concerning to the group I. In the groups II and III, there was just a case. Referring to the infectious disease complications, the incidence of lip herpes was valued, appearing 6 cases in the groups II and III, in front of a case in the group I.

Conclusions: The treatment with Basiliximab (associated with other immunosuppressant drugs) produces a significative descent in acute rejection cases and an increase of infectious disease complications, as the lip herpes.

Nursing – Advanced Practice Stream

219

The Survey of Nursing Documentation for Outpatient Hemodialysis Patients in Japan

C. Kamiya, I. Honda, M. Daitoku, K. Shintani,
A. Misima, T. Egawa

Akita University, Akita city, Osaka University,
Suita City, Japan

Purpose: To obtain knowledge of the state of nursing records for outpatient dialysis patients in Japan.

Methods: We conducted a survey by mail of 1,000 outpatient dialysis facilities all over Japan. The survey asked about the state of nursing records on the functioning in daily life of outpatient dialysis patients. The survey was based on the International Classification of Functioning, Disability and Health (ICF) from WHO and was made up of 57 items, including a description of the facility.

Results: Eligible replies were obtained from 566 facilities (56.6%). The items most often recorded were on physiological function, such as heart function and laboratory test data. The least reported items were on sources of information under personal factors, and muscle power under movement function. 19 facilities (3.4%) made regular records of items related to activity, such as Activities of Daily Living (ADL) and other items that are considered areas of nursing problem. 188 facilities (33.2%) made regular records of items related to restriction of water intake, 150 (26.5%) on restrictions of food intake, and 167 (29.5%) on self-management of the shunt, under the category of participation. The number of institutions that used disability rating scale in activities of daily living was 123 (21.7%) and those that used degree of independence was 173 (30.6%). Most institutions used clinical data or the speech and behavior of the patients to evaluate self-management, with 45 facilities (8.0%) using the Food Self-care Index. The items that nurses felt they needed to track the most to understand patient problems (multiple answers allowed) were mostly related to food and water intake restrictions, with the patient's family situation being next in importance. The item that was listed as least needed to track was muscle power.

Conclusions: Records on muscle power, a factor affecting daily life and the ease and ability to make visits to the hospital, were rarely being taken and were not even considered important. We believe it is important, for improving the quality of life in hemodialysis patients the state of nursing records about a movement function be examined.

220

The Evolving Role and Diversity of Renal Anaemia Co-ordinators: Achievements the Australian Way!

L. Basham¹, P. Byrne², J. Chow³, A. Lee⁴, V. Owens⁵

¹Geelong Hospital, Victoria,

²Illawarra Health Service,

³South West Sydney Area Health Service,

⁴Prince of Wales and Sydney Children's Hospital,

⁵Lismore Hospital, NSW, Australia

The role of the registered nurse is moulded by traditions and rigid boundaries which provide structure and role specificity. Within the field of renal nursing, a specialised role of Renal Anaemia Co-ordinator has been developed. Through the support of the individual hospital nephrologists and sponsorship of Janssen-Cilag this new role has challenged nursing tradition.

This presentation will demonstrate:

- How the impact of individual co-ordinators has resulted in a change of practice in anaemia management within their renal units.
- How proactive intervention by staff at a clinical level leads to improved overall patient management and outcomes.
- Where the successful development, and maintenance of a new role can evolve into the foundation for the creation of other autonomous positions.

Achievements within the role include:

- Development of an expert person in renal anaemia management.
- Establishment of pre-dialysis co-ordinated care and clinical pathways.
- National exchange of information for the optimal management of the overall health of the renal population both haematological and biochemical data.
- Career path incentives and motivation for nurses-building confidence in the overall professional development of nurses, working toward the path of nurse practitioner.

The role of the Renal Anaemia Co-ordinators is an ever-evolving process. Each Renal Anaemia Co-ordinator is bound by their parent hospital and associated peripheral units, positive support from within a collaborative team framework has allowed for Renal Anaemia Co-ordinators to strive for common goals in a diverse and flexible approach.

221

The Effectiveness of Videoconferencing in the Learning Experience of Rural and Remote Postgraduate Nephrology Nurses

D.C. Ind

The Queen Elizabeth Hospital, Adelaide, South Australia

Purpose of the Study: To assess the effectiveness of videoconferencing in the learning experience of rural and remote postgraduate nephrology nurses.

Methods: The study used qualitative methods in order to focus on understanding the meaning and importance of the videoconferencing and associated contextual effects in students of the nephrology nursing program (NNP).

Study Participants – The participants were drawn from past students of the NNP who had completed the program at least two years previously.

Data Collection – The data were collected from four Focus Group discussions. The discussions were conducted via videoconferencing with the participants in their own unit.

Results: Following analysis of the data 3 key issues appeared to have influence on the students' learning experience:

- i) the effects of prior experience in study and videoconferencing;
- ii) the 'costs', both social and financial as it effects the potential students' choice whether to commence studying, the 'difficulties associated with remote learning';
- iii) the 'effects of education on the individual' – their past experience and socio-cultural expectations.

Conclusion: Videoconferencing was seen as a powerful 'tool' in assisting students to study a distance program. However there are many other factors that can affect student 'success'.

222

Nephrology Nursing as a Specialization: The Current State of Development in Japan

I. Terada, C. Hyde

Tottori University, Yonago, Tottori, Japan

The end-stage renal disease (ESRD) population is estimated to be increasing rapidly not only in Japan, but also internationally. This trend produces many dilemmas for the providers of health care as well as for the general public. In this presentation, the current situation regarding the provision of renal services to patients with ESRD in Japan is explored. The statistical data reveal that Japan is in a predicament

regarding the current rate of incidence of ESRD in the population. In order to improve the situation of the health care system for patients with ESRD, development of Japanese nephrology nursing as a speciality in its own right is crucial. Unfortunately the development of nephrology nursing is far behind that of the other developed countries. Therefore Japanese nurses who work in the field of nephrology are still struggling to establish their own professional identity and to improve the professional level of their practice. This situation persists in Japan despite support from the literature which confirms that appropriately qualified nephrology nurses are well equipped to provide specialized care. The recent decision by the Japanese Association of Nephrology Nurses is to establish the position of the specialized dialysis nurse, which does not cover the area of kidney transplantation and will start in 2004. It is expected that it will be an important challenge to improve professional skills and nephrology nursing status in Japan.

223

Physical Activity and Sedentary Behaviour in End Stage Renal Disease

Y. White

Department of Nursing, University of Wollongong, Wollongong, NSW, Australia

The Purpose of the Study: End stage renal disease is a complex medical condition that has major metabolic effects on all body systems. Recent research has found that increasing a dialysis patient's level of physical activity has positive effects on both psychological and physiological parameters (Painter 1994). These reported improvements increase the individual's perception of their quality of life. However, the baseline physical activity and sedentary behaviour levels of these individuals, and the relationship between these and severity of renal disease, nutrition and dialysis adequacy have not been established. This paper will present a study, which is part of a doctoral research project. The main aim of this study was to investigate baseline levels of physical activity in those people with end stage renal disease and to further investigate the relationship between the found level of physical activity and psychological well being.

Methodology: A total of 100 adults with end stage renal disease were recruited to participate in this study. All participants were on renal replacement therapy. This was a cross sectional study. Assessment included physical activity and sedentary behaviour levels, mental health, severity of renal disease, and demographic data. The project survey consisted of self-report questionnaires.

Results: This paper will present the results of the cross sectional study. Results indicate that there is a very low level of physical activity undertaken by the study participants.

Conclusions: Results have also provided baseline information on physical activity in the end stage renal disease population and have provided insights for future research.

224

The Effectiveness of Self-Care Educational Program to Decrease the Hemodialysis Patients' Problems

O. Khodayar

Hamedan Medical Science University, Tabriz, Iran

Purpose of Study: The purpose of this study was to examine the effectiveness of self-care educational program to decrease the hemodialysis patients' problems.

Method: This study was a Quasi-Experimental design, which carried out on thirty-six patients who are admitted for hemodialysis. Patients were assessed by questionnaire and check list before weekly dialysis treatment, before and after the intervention of educational program and data were collected.

Results: During the first five weeks of intervention the results indicated that there were a significant decrease in serum urea, serum uric acid, serum potassium, serum phosphate, weight gain, systolic blood pressure, edema, local vascular access problems and a significant increase in knowledge about vascular access care. But there were no significant change in serum calcium, serum sodium, serum albumin, serum total protein and diastolic blood pressure.

Conclusion: According to these results, the designed self-care educational program, was significantly effective on decrease in most hemodialysis patients' problems and did not cause hypoproteinemia.

225

The Study of Depression in Renal Dialysis Patients

F. Shamsaei

Faculty of Nursing, Medical University, Hamedan, Iran

Purpose of Study: The purpose of this study was determination of depression in dialysis patients. The study setting was a dialysis ward, from a Akbatan hospital in the Hamedan city.

Method: This study was descriptive-cross sectional design the data was collected by beck depression test.

Participation: A total of 76 patients participated in the study that included 37 men, 39 women, with a mean age of 45 years. Sample consists of all patients.

Results: Out comes showed that 46% of subjects had mild depression, and 38.16% had depression, and 6.58% had severd depression. There were significant relationships between age, sex, level education and depression.

Conclusions: Quality of life and the psychosocial impact of chronic diseases (renal dialysis) are receiving more attention in the literature. Plough (1981) points out that some clients are unable to work because they cannot deal with additional stresses beyond dialysis, and because the time spent on the machines and in commuting blocks many job opportunities.

226

Renal Enrolled Nurse Course

M.-J. Arnold

The Queen Elizabeth Hospital, Adelaide, South Australia

Enrolled Nurses first started working in the Haemodialysis Unit in 2001, after consultation the ENs from the ward area and the haemodialysis unit were offered the opportunity to undertake an education program. The course was implemented to assist with appropriately educated staff and provide recognition of the enrolled nurses' contribution within the renal unit.

The students learnt about haemodialysis, transplantation, chronic renal failure and peritoneal dialysis. They've had clinical exposure in both the renal ward and haemodialysis and the course has facilitated this transition.

The course provide the nurses with opportunity to gain specialist clinical skills and theoretical knowledge to assist in the provision of holistic and quality care for patients with renal dysfunction.

Areas Covered:

- physical assessment and observation taking
- anatomy and physiology of the renal system (normal and altered)
- acute renal failure
- chronic renal failure
- end stage renal failure
- principles of dialysis
- care of the person with chronic renal failure
- care of the transplant patient
- care of the dialysis patient (haemodialysis and peritoneal dialysis)
- pharmacological and nutritional management of the patient with renal dysfunction
- role of the EN in the renal unit
- psycho-social aspects of nephrology nursing
- equipment/technology used in renal nursing

Nephrology Practice Stream

227

Efficacy of Intravenous Epoietin Alpha in Patients with Renal Anemia

T. Thiruvethiran

National Kidney Foundation of Malaysia, Malaysia

The use of human recombinant erythropoietin is now widespread amongst dialysis patients. The dialysis outcomes quality initiative by the National Kidney Foundation of United States recommends subcutaneous administration of erythropoietin to optimize efficacy of the drug. However due to the adverse effect of pure red cell aplasia (PRCA), the company marketing epoietin alpha has issued a recommendation that epoietin alpha should only be administered

intravenously. This may have cost implications, as the required dose may be higher.

The National Kidney Foundation of Malaysia (NKFM) undertook to determine the efficacy of epoetin alpha when administered in the intravenous route. All patients dialyzing at NKFM who were receiving subcutaneous erythropoietin and had stable hemoglobin levels prior to conversion were recruited into the study. Patients with evidence of bleeding, active or chronic infections, blood transfusions three months before the study, ferritin <200 ug/l and transferrin saturation <20% were excluded. Patient's hemoglobin levels were monitored pre-conversion, one-month post conversion and two months post conversion to determine changes in hemoglobin levels. The dose of epoetin alpha were maintained the same throughout the study period. Patients in whom the hemoglobin dropped more than 0.5 g/l of baseline were deemed to have loss of efficacy of intravenous epoetin alpha.

A total of 96 patients were recruited, the minimum hemoglobin pre-conversion was 97.1 g/l and this was maintained at one-month post conversion, however at two months post conversion it was 96.4 g/l, a drop of 0.7 g/l. In addition 23.9% of patients experienced a drop in hemoglobin at one month and this increased to 33.3% at two months.

A significant number of patients experienced a drop in hemoglobin post conversion and this may have important cost implications, as higher doses will be required to maintain hemoglobin levels.

228

Korean Health Professionals' Attitudes and Knowledge Toward Organ Donation and Transplantation

J.R. (Theresa) Kim, D. Elliott, C. Hyde

The University of Sydney, Sydney, Australia

Purpose of the Study: As social interest in, and demand for, organ donation and transplantation has increased, the role of health care professionals in the organ procurement process has also been emphasised. Previous studies found that health care professionals' attitudes, and knowledge of, organ donation and transplantation, and their willingness to approach family significantly influenced the bereaved family's decision-making process. It was also identified that nurses with a high knowledge level have more positive attitudes toward organ donation of their own organs. The purpose of this study is to identify and analyse Korean health professionals' attitudes towards, and knowledge of, organ donation and transplantation.

Methods: An exploratory study using semi-structured interviews with nine key informants was conducted to provide a description and critical analysis of Korean health care professionals' attitudes towards and knowledge of organ donation and transplantation. Three major hospitals which provide transplant services in Seoul, Korea, were selected to conduct the key informant interviews with health professionals: Chief of an organ transplant team; a surgeon; three organ transplant nurse coordinators; two ICU nursing unit managers; and two ICU nurses.

Results: Analysis of the concepts expressed in the respondents' discussions led to identification of issues related to social environment, medical and nursing professional practices. Overall, there was a lack of knowledge by Korean health professionals surrounding the

organ procurement process. It was also found that their attitudes were mixed and somewhat negative, as they did not regard brain death as true death. In addition, a majority of key informants demonstrated a contradiction when it became a more personal issue.

Conclusions: There is a lack of knowledge related to the organ procurement process amongst health professionals. Their attitudes are mixed. Based on these findings, and through the analysis of current questionnaires from other studies, a new questionnaire will be developed to conduct a survey.

229

Haemodialysis Patients and Responsiveness to Epoetin Alfa

W. Purcell

Royal Melbourne Hospital, Victoria, Australia

Purpose of the Study: To examine possible patient characteristics that may be responsible for differing patient responsiveness to recombinant human erythropoietin (Epoetin alfa (Epo)).

Methods: The Renal Anaemia Management (RAM) database is a software program provided by Janssen-Cilag for use in 16 major renal units in Australia, with point-of-care data entered and monitored by 18 Renal Anaemia Coordinators. The RAM database contains data on approximately 40% of Australia's haemodialysis population. The database was searched to identify all haemodialysis patients on Epo therapy between 1/7/2002 and 1/10/2002. A total of 1,638 patients were included in the study.

An erythropoietin response index (ERI) was calculated by dividing each patient's haemoglobin (Hb) (g/dL) by the Epo dose (u/kg/week) then multiplying the result by 1,000 ((Hb/Epo dose) × 1,000). The range of scores was 10.3 to 1,239 with a low ERI indicating a decreased responsiveness to Epo. ERI values were split into quartiles (≤ 57 , 58–91, 92–156 and > 156) and their association with serum ferritin, transferrin, transferrin saturation, serum albumin, and C-reactive protein was determined.

The results were analysed by the Kruskal-Wallis test.

Results: ERI was associated with serum albumin, transferrin, transferrin saturations and C-reactive protein ($P < 0.001$). There was no association between ERI and serum ferritin ($P = 0.10$).

Conclusions: Better responsiveness to Epo appears to be associated with a higher serum albumin, transferrin, and transferrin saturation and with a lower C-reactive protein. Interestingly there was no association between better Epo responsiveness and a higher serum ferritin. Further evaluation with multivariate analysis is required to understand if and how the interaction of these variables affects responsiveness to Epo therapy.

Continuous Ambulatory Peritoneal Dialysis (CAPD): Coming of Age

A.R. Fauzi, E. Saeyah, C.A. Junaidah, M. Azlina, M. Menah, A.G. Halim, C.T.N. Kong

National University of Malaysia, Kuala Lumpur, Malaysia

Introduction: Our CAPD programme was inaugurated in October 2000 using the Andy-plus double bag system and later converted to Andy-disc system in 2001. Younger, gainfully, employed, 'educated', motivated patients with no multiorgan dysfunction were preferentially selected.

Objective: To review our 3-year CAPD experience with CAPD using the Fresenius double-bag non-spike system.

Results: A total of 50 patients were started on CAPD from Oct 2001–Sep 2003. There were 21 females (42%) and 29 males (58%). 24 (48%) of them were Malay, 20 (40%) Chinese, four Indian and two others. Mean age was 40.0 ± 10.9 years (range 21–64 years). 35 maintained their occupations (7 professionals and 28 non-professionals). 12 of the latter were house-managers while three are currently unemployed. 4 patients died of sepsis, one of extensive myocardial infarction and one of a massive stroke. Thus patient survival was 92%. 21 patients dropped out – two underwent transplantation, one recovered renal function, three transferred to other centres and one was terminated due to relapse of schizophrenia. A total of 28 patients have remained in the program giving a technique survival of 65%. In the current patient group, serum haemoglobin is 10.2 ± 1.7 gm/dl and serum albumin is 37.1 ± 5.6 gm/L. Calculated kt/V is 2.18 ± 0.4 . Peritonitis rate for the past 9 months is 1:32 patient-month compared with 1:22 in our first year experience.

Conclusions: CAPD is an excellent CRRT modality, which allows maintenance of an active lifestyle in younger and productive patients. As our CAPD team matures the years, better results are obtained.

First Cannulation of Permanent Vascular Access for Chronic Haemodialysis

M.K. Chua, A.L. Lim, C.T.N. Kong, B.K. Lim, A.R. Fauzi, et al.

Renal Unit, Hospital UKM, Kuala Lumpur, Malaysia

Introduction: Permanent vascular access is a lifeline for chronic haemodialysis patients. Complications of these vascular accesses are a major cause of morbidity, prolonged hospitalization and increased costs. In particular, proper needling technique can greatly reduce loss of the said accesses.

Objective: To evaluate the success rate of first cannulation of permanent vascular accesses in haemodialysis patients by our staff.

Design and Method: Prospective study of consecutive patients.

Results: From April 2001 to April 2002, a total of 63 patients underwent first cannulation of their permanent vascular accesses. There were 49% (n = 31) Malays, 37% (n = 23) Chinese and 14% (n = 9) Indians. There were 59% (n = 37) female patients and 41%

(n = 26) male with a mean age of 55 ± 26 years (range 30–77). Among these patients 63% (n = 40) had AV fistulae, 22% (n = 14) BC fistulae and 14% (n = 9) AV Grafts. There were 46% (n = 29) diabetics and 54% (n = 34) non-diabetics. Maturity of these vascular accesses ranged from one week (post thrombectomy) to 1.5 years (mean 12 weeks). Among these patients, 11% (n = 7) have had their AV fistulae created 6 months pre-dialysis as per DOQI Guideline 9. Upon maturity, these accesses were first cannulated by staff with different levels of working experience (range one to six years) with and without post basic training. Despite this we achieved a success rate of 87% (n = 55) was achieved at first attempt. 11% (n = 7) of patients underwent 2–3 attempts in which case we managed to prick the supply but returned the blood using a vein on the other arm. Failure occurred in only one diabetic patient (2%).

Conclusions: The success rate of first vascular access cannulation depended on both the levels of skill of the staff as well as the maturity of the vessels. Nevertheless the success rate of first cannulation of 87% is highly gratifying.

Iron Status of Chronic Dialysis Patients and Action Plan to Optimize Anaemia Therapy

A. Suriani, M.K. Chua, T. Rizal, S. Surani, E. Saeyah, A. Azlina, K.N. Kay, A.R. Fauzi, C.T.N. Kong

Hospital Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Objective: To ascertain the current iron status of our chronic dialysis patients on oral FeSO_4 and SC erythropoietin protocol prior to optimizing iron status with IV iron ('Venofer') before conversion from SC to IV erythropoietin (EPO).

Design and Methods: This is a prospective interventional study to first optimize patients' iron status with IV iron ('Venofer') prior to converting them from SC to IV EPO.

Results: 52 patients – 24 on chronic haemodialysis and 28 on CAPD ('Stay Safe', Fresenius) had their iron status screened in early Dec 2002. There were 33 males and 19 females with a mean age of 45.3 ± 11.2 years (range 21–65). There were 34 Malays, 15 Chinese and 3 Indians. The mean duration of dialysis was 24 ± 21 months. 34 patients were on SC EPO with a mean dose of $3,853 \pm 1,351$ IU. Serum albumin was 40 ± 5 g/l. Mean serum Hb was 10.2 ± 1.8 gm/dl. Serum folate and vitamin B_{12} levels were in the upper normal ranges. Mean serum transferrin saturation was $41 \pm 5\%$ and mean serum ferritin was 333 ± 241 ng/ml (optimal 300–500).

Conclusion: Based mainly on the serum ferritin levels, our action plan is as summarized in the table below:

Serum ferritin (ng/ml)	No. of patients (%)	IV Venofer
(<100)	6 (12%)	Weekly $\times$ 4 (review)
(>100–<300)	25 (48%)	Weekly $\times$ 4
(300–500 ng/ml)	8 (15%)	Monthly
(>500)	13 (25%)	Observe

Continued EPO Therapy during EPO Antibody Induced PRCA – A Case Study

A. Flynn, A. Linton

Bendigo Health Care Group, Bendigo, Australia

In recent years the emergence of anti-EPO (erythropoietin) antibodies in the renal population, causing pure red cell aplasia (PRCA), has created much concern. In January 2002, anti-EPO antibodies were detected in the serum of one of the haemodialysis clients at the Bendigo Health Care Group. This presentation will follow a case study of Victor and his journey with PRCA and anti-EPO antibodies.

Despite the recommendations at the time to cease EPO therapy in the treatment of PRCA, Victor remained on EPO. The therapies selected for Victor's management were immunosuppression therapy, prednisolone and EPO. EPO therapy continued with doses reaching 50,000 u/s per week. Victor required multiple blood transfusions during the eleven months prior to commencing cyclophosphamide. Within nineteen days of commencing this therapy he became transfusion independent and has remained this way. Frequent monitoring of haemoglobin (Hb) and reticulocytes was paramount in order to observe the effectiveness of this regime.

Victor, to date, has successfully decreased his EPO requirements while maintaining an adequate Hb and reticulocyte count. He is now EPO antibody negative and has ceased all immunosuppression therapy and prednisolone.

The purpose of this presentation is to highlight PRCA due to anti-EPO antibodies and to describe Victor's case. Bendigo Health Care Groups successful management of this condition with continued EPO therapy is thought to be a unique world first.

Influence of Time to Process (TTP) on Iron Deficiency Parameters in Dialysis Dependent Patients

F.S. Doss, J.B. Rosman

Department of Nephrology, Auckland Hospital, Auckland, New Zealand

The ideal parameter reflecting iron stores in dialysis patients is yet to be found. Commonly used are reticulocyte haemoglobin content (CHR), percentage of hypochromic red blood cells (HYPO), total iron binding capacity, serum ferritin and transferrin saturation index. CHR and HYPO are preferably used because of the shortcomings of the other parameters.

This study addresses whether validity of CHR and HYPO is influenced by the time it takes to start processing of the sample after being obtained (TTP). We analysed 57 haemodialysis patients (19 in a hospital-based dialysis centre and 38 from a satellite). Their median TTP was 156 min (range 46–267).

	Lab testing	3 h later	6 h later
Median CHR (range)	32.4 (23.1–39.2)	32.4 (23.2–38.9)	32.5 (22.3–38.7)
Median % Hypo (range)	2.5 (0.2–30.9)	2.7 (0.3–32.0)	3 (0.4–36.4)

The scattering in the HYPO group was important ($p < 0.001$) in contrast to the CHR group (NS).

TTP was plotted against % change in HYPO and CHR over 6 h. Percentage change in HYPO is high if related to TTP (variance 21%, $p < 0.001$), whereas CHR remains unchanged (variance 0.6%, NS). We conclude that HYPO is only to be considered if the TTP is very short (lab onsite). For satellite care/home haemo however, CHR will be a more reliable indicator as in those patients TTP is longer.

Perception and Performance of Health Care Providers about Prevention Methods of Urinary Tract Infection

A.A. Sarjou, A.A. Moammad, A. Navidian, N.M. Negad

Zahedan University of Medical Sciences, Balouchestan, Iran

Introduction and Aims: Urinary tract infections (UTIs) are one-third of nosocomial infectious diseases, which are a significant source of morbidity and mortality in modern medicine, despite the wide-spread use of antibiotics. The important teaching role of health care providers, they are not only responsible for teaching needs of clients about diseases signs and symptoms, prevention and transmission, but also they should have optimum performance in self ADLs. This survey carried out to determine perception and performance of health care providers of UTIs prevention methods.

Materials and Methods: This descriptive-comparative survey carried out in Iranshahr health and cure network (hospitals and urban health centers).

Research population included all of health care providers except physicians. The sampling is convenience. Data gathering carried out by questionnaire and analyzed by SPSS software.

Results: Findings clarified 59.5% of health care providers has good perception and 53.2% moderate performance about the UTIs prevention methods and maximum of them (39%) has less perception about the UTIs signs and symptoms too. The findings showed significant correlation between performance and gender ($r = 0.32$, $p \leq 0.05$), gravidity ($r = 0.42$, $p = 0.01$) and UTIs signs and symptoms perception with past illness ($r = 0.36$, $p = 0.001$).

Conclusion: Continuing and in-service education about recognition of complications, prevention methods and ways of transmission diseases are emphasized for health care providers.

Technology – Technology/ Bioengineering

236

Measures in Dialysate Purification for High-Flux Dialyzers: A Review Over Peracetic Acid Based Disinfectants

N. Ono, I. Matsuyama

Medical Corporation Seiikai Matsuyama Clinic,
Kazuhiro Matsuyama, Masashi Tomo, 2nd School
of Internal Medicine, Medical College of Oita, Japan

Objective: In 1985 when the role of β_2 -microglobulin in amyloidosis was first reported, the use of high-flux dialyzers started. At present, over 80% of the hemodialysis patients are treated with high-flux dialyzers. Clinical benefits are also well documented.

However, with high-flux dialyzers, there is a fear that endotoxins in the dialysate can in the long-term lead to chronic inflammation responses and other serious complications. Therefore suggesting that the dialysate needs further purification.

Methods: With this in mind we have been trying different methods of increasing the purification, using endotoxin level reductions as an index. We have been examining the peracetic acid based disinfectant hemoclean, 2% dilution, in the dialysate distribution pipes closed circuit. A 5% dilution in the cleaning of the RO membrane and 2% dilution in the tank.

Result: After about 17 months the average endotoxin level of the RO water was 1.7 ± 0.6 IU/l and in the dialysate 1.1 ± 0.9 IU/l.

Conclusion: We believe that this peracetic acid based disinfectant is effective in removing biofilm which releases endotoxins and that the disinfectant is suitable for the purification required for the hemodialysis treatment of today.

237

DIAFIL – New Membrane for Dialysis Therapy

G. Hausbrand, J. Osterloh

RenaSelect GmbH & Co, KG Pirna, Germany

DIAFIL is a new hollow fiber membrane especially designed for application in dialysis therapy. Due to its unique properties the membrane is currently under investigation for applications for other medical purposes. DIAFIL consists of viscose which is obtained from spruce wood. The membrane is produced employing air spinning technology. High ultrafiltration rates are achieved by a patented mixture of additives, added during the spinning process. In the following table the key differences between the DIAFIL production and standard cellulose membranes are listed.

In several parts of the world, low flux dialysis is still the dominating mode of dialysis therapy. Due to the superior ultrafiltration DIAFIL dialysers might contribute to more effective therapy in those regions. NOUVELLE dialysers containing DIAFIL membranes have just recently been introduced to the dialysis market. An overview of the recent studies and investigations on both dialysers and membrane will be presented. Additionally, detailed information on the spinning process will be given.

	DIAFIL	Cellulose
Raw material	Spruce wood	Cotton linters
Dissolving	NaOH/CS ₂	NH ₃ /Cu ²⁺
Bore solution	No; highly purified air	Yes; e.g. i-propylmyristate
Pore structure	Governed by additives	No additives

238

Analysis of Risk Based Maintenance Practices in Dialysis Units

V. Singhal, N. Venkataraman

Bio-Medical Engineering Department, National Kidney
Foundation Singapore, Singapore

Effective maintenance of modern medical devices is necessary for minimizing operational costs, enhancing patient care and has a direct

impact on process efficiency. Risk based inspection and maintenance protocol provides a measurable response by reducing medical device maintenance time through optimizing inspection and testing strategies. A risk based process includes risk identification, evaluation of the potential impact and likelihood of the risk, analysis and determination of risk treatment measures. Because risk cannot be completely eliminated, the residual risk must be managed, inline with the organization's risk appetite.

The risk assessment approach to medical device maintenance undertaken at 22 dialysis centers and prevention clinics, incorporated a structured methodology wherein firstly, a comprehensive medical device inventory was established, risk of failure for each device determined, its impact and likelihood were ranked. Risk acceptability was determined by plotting on a risk matrix. Finally, treatment measures were determined for implementation.

Such an exercise enabled us to optimize maintenance time and associated costs, like reduced manhours spent and parts replacement.

239

Preventive Maintenance Practices for Ensuring Ultra-Purity of Water in Haemodialysis

N. Venkataraman, M. Nandakumar, R.M. Babu

Bio-Medical Engineering Department, National Kidney Foundation Singapore, Singapore

Risks posed by contaminants and toxins in water used for haemodialysis have been well documented. Adverse events have continued to occur globally inspite of new technologies and improved design by manufacturers. Modern water purification systems are complex with many components including pre-treatment modules, reverse osmosis membranes, pumps, micro and nano filtration modules and distribution loop systems. This underlines the need for periodic maintenance and monitoring of water quality and technical parameters by trained technicians and clinical staff.

The maintenance activities should include daily monitoring of hardness, chloramine, pressure, conductivity and RO parameters. Weekly checks of system hardware and distribution loop is also a recommended practice. Monthly monitoring of bacterial counts and endotoxin levels in water and dialysis fluid, is a quality control activity and gives vital information for corrective actions. Systematic replacement of key components like endotoxin filters, micro-filters and machine connectors is essential. Half-yearly maintenance of hydraulic parts, pumps and membranes assists in prolonged performance. Our results over the past 6 years highlight the benefits of this program.

The key to long-term benefits, however, is to follow a proactive strategy to prevent bio-film formation at any point of the fluid pathway. This may include using an integrated heat disinfection process or periodic chemical disinfection of the whole system. Hence, to salvage the full advantages of a well designed water purification system, a planned preventive maintenance program is mandatory and is, beyond doubt, a responsibility of the dialysis service provider.

240

Systematic Heat Disinfection of Haemodialysis Machines between Shifts Increases Failure Rates

N. Venkataraman, J.A. Raj, J. Rajmohan

Bio-Medical Engineering Department, National Kidney Foundation Singapore, Singapore

Heat disinfection of dialysis machines has been recommended by most manufacturers to be performed on a daily basis. International standards, guidelines and practices vary across countries. There is little documented evidence showing any adverse effect of frequent heat or chemical disinfection between shifts on machine performance and failure rates. Frequent heat cleaning programs are recommended for infection control and as a patient safety measure.

A study was carried out across 20 dialysis centers to investigate the relationship between component failures and frequency of heat disinfection. The study included different models from three leading manufacturers and disinfection protocols were standardized. The conventional protocol of 2 heat cleaning cycles at the beginning and end of the day was modified as per the recommendations under the SARS preventive measures.

Machines with 4 heat cleaning programs daily for 3 patient shifts were identified and monitored daily. Machine failure rates, component failures and frequent alarms were analyzed and tabulated. There was a significant increase in failure rate of specific components when heat disinfection was performed between every shift and incidence increased with time from date of implementation. This trend was observed in all models of dialysis machines (different incident rates) and had high correlation with device runtime. It can be inferred that frequent heat cleaning programs increases operational costs, downtime and, under these circumstances, performance of machine hydraulics needs to be monitored carefully.

- Abderrahim, E. 216, 183–185
 Adiku, W. 115
 Adu, D. 1, 2
 Afeltowicz, Z. 170
 Agazadeh, A. 201
 Agnes, S. 217
 Ahmadi, I. 204
 Ahmed, S. 148
 Ahmed, T. 148
 Al Lehibi, A. 204
 Al Meshari, K. 204
 Al-Baaj, F. 177
 Alexandrova, I.V. 188, 189
 Alfurayh, O. 204
 Al-Shamran, A. 115
 Amal, F.K. 202, 127
 Amal, H.A.G. 168
 Amarapurkar, D. 209
 Amir, A.R.A. 149
 Anderson, J. 139
 Ando, D. 130
 Angelova, P. 131
 Antelo, A. 215
 Anthony, R.A. 180
 Anunciada, A.I. 125
 Ardalan, M.R. 150–152
 Ardeleanu, M. 195
 Arnold, M.-J. 226
 Asari, A.K. 208
 Aseem, T. 145
 Asl, B.H. 158, 200, 201
 Atef, A.H. 168
 Augustine, T. 208
 Avolio, A.W. 217
 Azlina, A. 232
 Azlina, M. 230
 Azuma, H. 205

 Babu, R.M. 239
 Bahadur, M.M. 145, 146, 180
 Bakker, W.W. 112
 Balasubramanian, S. 192–194
 Bald, E. 196
 Bang, B.K. 133, 134, 176, 190
 Bankova, M. 132
 Băbulescu, C. 195
 Basham, L. 220
 Bayrakdar, A. 115
 Bellomo, R. 4
 Ben Abdallah, T. 183–185, 216
 Ben Hamid, F. 183–185
 Ben Maiz, H.B. 183–185, 216
 Ben Moussa, F. 216, 183–185
 Bengt, R. 179
 Bert-Inge, R. 179
 Bhandari, S. 160, 161
 Bichu, S.D. 209
 Blake, P. 5
 Boca, I. 195
 Bosetto, A. 6, 7
 Boubaker, K. 183–185
 Bounatiro, I. 115
 Bounatiro, Y. 115
 Brenner, B.M. 155
 Brown, E.A. 8–10
 Brunkhorst, R. 124
 Bryant, R. 11
 Bustamente, J. 215, 218
 Bustamente, R. 215
 Butnaru, V. 195
 Byrne, P. 220

 Capsa, D. 195
 Carides, G. 155
 Carlson, W. 12
 Carrera, F. 125
 Castagneto, M. 217
 Chaaban, A. 204
 Chan, C.-M. 154
 Chan, J.C.N. 155
 Chan, J.S.D. 117
 Chang, C.-F. 171
 Chang, E.J. 174
 Chang, J.W. 165
 Chang, Y.S. 133, 134, 176, 190
 Chapman, J. 13
 Chee, S.S.S.W. 14
 Chen, F.-F. 128
 Chen, J.-B. 136
 Cherif, M. 216
 Cheung, A.K. 15
 Cheung, M. 139
 Cheung, R. 139
 Chiang, C.-K. 166
 Chiang, S.-S. 136
 Choi, E.J. 134, 190
 Choong, L.H.L. 120
 Choroszy-Król, I. 135
 Chow, J. 220
 Chow, J.S.F. 16, 17
 Chua, M.K. 178, 231, 232
 Chwatko, G. 196
 Constantinovici, N. 195
 Couser, W. 18, 19
 Covic, A. 195
 Curhan, G.C. 20
 Czupryniak, A. 196

 d'Apice, A.J.F. 3
 D'Haese, P.C. 138
 Daitoku, M. 219
 Damment, S. 140–143
 Daniele, V. 179
 De Broe, M.E. 138
 De Pauw, L. 206
 Deliyiska, B. 131, 132
 Dham, R. 123
 Dita, K. 144
 Djarwoto, B. 167
 Djurovic, S. 156
 Donova, L.V. 188
 Doosti, R. 214
 Doss, F.S. 234
 Downes, N. 142
 Draganov, B. 156

 Edwards, K. 21, 22
 Egawa, T. 219
 El Aggan Hayam, A. 127, 168, 202
 El Batet Kamel, M. 127
 El Gendy Wessam, M. 168
 El Kashef Essam, H. 168, 127
 El Tayeb Abbas, E. 123
 El Younsi, F. 183–185
 Elkum, N. 204
 Elliott, D. 228
 Enzan, H. 114

 Fauzi, A.F. 178
 Fauzi, A.R. 230–232
 Feehally, J. 23
 Fiddler, G. 143
 Finn, W. 137
 Fischbach, L. 24, 25
 Flynn, A. 233
 Foley, R. 26, 27
 Fook-Chong, S. 120
 Fouque, D. 28
 Fukazawa, M. 191

 Gago, J.M. 215, 218
 Gál, M. 164
 Gan, H.C. 159
 Gandhi, B.V. 145
 García, D.M. 215, 218
 García, F. 215
 Gârnetă, L. 195
 Garvan, K.C. 144
 Gejyo, F. 210
 Georgiev, M. 197
 Gerth, W. 155
 Ghafari, A. 150, 211–214
 Ghenu, A. 195
 Ghods, A. 158
 Gill, M. 136, 137, 139, 141, 143, 177
 Glasscock, R.J. 29–31
 Gokal, R. 32–36
 Golea, O. 195
 Goovaerts, T. 37, 38
 Gordillo, R. 215, 218
 Gotch, F. 63
 Goucha, R. 183
 Greaves, P. 142

 Ha, H. 116
 Hahn, K. 153
 Halim, A.G. 178, 230
 Hamasni, I. 204
 Hase, H. 191
 Hashemi, Gh. 122
 Hassan, M.S. 148
 Hausbrand, G. 237
 Hedri, H. 183–185, 216
 Heo, J.S. 165
 Hiranaka, T. 169
 Hirasaka, N. 113
 Hiroi, M. 114
 Hoang, A.D. 206
 Honda, I. 219
 Horiuchi, S. 116
 Hostetter, T.H. 39, 40
 Hruska, K.A. 41
 Hsieh, C.-C. 128
 Hsieh, T.-J. 117
 Hsu, S.I.-H. 42
 Hsu, S.-P. 166
 Huang, J.-J. 128, 173, 203
 Hudson, M.V. 43
 Hung, K.-Y. 166
 Hut, F. 206
 Hutchison, A. 137, 138, 177
 Hyaneck, J. 182
 Hyde, C. 222, 228
 Hyde, C.D. 44, 45

 Ikononov, V. Ch. 197–199
 Imamura, Y. 191

- Ind, D.C. 221
Ingale, A.V. 186
Ingale, F.A. 186
Inishi, Y. 191
Iqbal, M. 148
Ishikawa, H. 191
Islam, M.S. 148
Islam, N. 148
Ito, Y. 210
- Jamal, H. 121
Jayakumar, K.P. 129
Jeyabalan, V. 178
Joki, N. 191
Jones, C. 138
Junaidah, C.A. 230
- Kaaroud, H. 183
Kalhid, A.M. 160
Kalra, P.A. 47
Kamiya, C. 219
Kaplan, B. 46
Karupaiah, T. 48
Kay, K.N. 232
Kessler, M. 126
Khalid, A.M. 161
Kheder, A. 183–185, 216
Khodayar, O. 224
Khoroshahi, H.T. 158, 200, 201
Kim, B.S. 133, 134, 176, 190
Kim, J.R. (Theresa) 228
Kim, S.B. 165
Kim, S.H. 165
Kim, S.Y. 134, 190
Kim, Y.O. 133, 134, 176, 190
Kim, Y.S. 176, 190, 133, 134
Kirjakov, Z. 197, 198
Kirpalani, A.L. 209
Koike, H. 205
Kong, C.T.N. 230–232
Kong, N.N.C.T. 178
Kong, S. 49
Konner, K. 50–52
Kovari, P. 195
Krietemeyer, S. 53
Krivitski, N. 54
Kriz, W. 55, 56
Kulkarni, H.G. 186
Kulkarni, N.S. 192–194
Kuroda, N. 114
Kurokawa, K. 155
Kurpas, D. 135, 162, 175, 207
Kuswadi, I. 167
Kwon, M.K. 116
- Lai, K.N. 57, 58
Lau, Y.-K. 120, 154
Lee, A. 220
- Lee, E.K. 165
Lee, H.B. 59, 116
Lee, J.C.E. 159
Lee, K.H. 60, 61
Lee, K.-P. 173
Levin, N. 62, 63
Liang, X.M. 113
Lichodziejewska-Niemierko, M. 170
Lim, A.L. 231
Lim, B.K. 231
Lim, S.L. 159
Lin, C.-C. 171
Lin, S.Y. 64, 65
Lin, W.-T. 203
Lindholm, B. 66–69
Lindley, E. 70
Linton, A. 233
Liu, F.-E. 120
Liu, H.-L. 128
Locatelli, F. 71, 72
Lopot, F. 73, 74
Low, W.M. 75, 163
- Macavei, R. 195
Macdougall, I. 76, 77
Maha, M.E. 127
Mahfoudhi, M. 216
Maiz, H.B. 216
Maiz, H.B. 183–185
Majkiewicz, M. 170
Major, L. 164
Makhdoomi, K. 211–214
Malakova, K. 197
Mani, M.K. 78
Mansur, M.A. 148
Marseiler, R.L. 53
Massy, Z.A. 79, 80
Mastalerz-Migas, A. 135
Matsuyama, I. 236
Mazi, D.N. 206
Melzer, H. 199
Menah, M. 230
Menawy, L. 115
Mendiluce, A. 215, 218
Mircescu, G. 195
Misima, A. 219
Moammad, A.A. 235
Mohamed, S.A.S. 202
Mohan, K. 204
Mondry, A. 153
Morishita, R. 205
Mortazavi, M. 201
Motellon, J.L. 147
Mota, E. 195
Moussa, F.B. 183–185, 216
Mujais, S.K. 81
Mun, K.C. 174
Mune, M. 113
Mutawa, N. 204
- Nadri, Q. 204
Nagai, R. 116
Nahali, A. 158
Nahed, M.B. 127
Nakamura, J. 169
Nakayama, M. 82
Namboodiri, P. 209
Nandakumar, M. 192–194, 239
Navidian, A. 235
Nedialkov, A. 131
Negad, N.M. 235
Nelson, R.G. 83
Neo, M. 187
Nikolova, M. 198
Nogueira, C. 125
Norooznia, F. 211
Nowicki, M. 196
Nure, E. 217
Nystrand, R. 84
- Obeid, M. 115
Ogawa, N. 130
Ogihara, T. 205
Ono, N. 236
Os, I. 156, 157
Osterloh, J. 237
Otani, H. 113
Ounissi, M. 183–185
Owens, V. 220
Oza, U.G. 209
- Painter, P. 85
Pák, G. 164
Pandya, B.K. 208
Pangesti, N. 167
Park, E.J. 165
Park, J.S. 165
Parving, H.-H. 86
Patea, V.I. 195
Patrzkaek, D. 207
Pennick, M. 140, 141, 143
Pepe, G. 217
Pervakova, E.I. 188
Pirogowicz, I. 135
Polaschegg, H.-D. 87–89
Pop, M. 195
Prabhakar, K.S. 192–194
Praveen, K. 180
Priti, L.R. 180
Prötsch, L.K. 157
Purcell, W. 229
- Rahman, M. 90
Raid, H.N. 208
Raies, L. 183, 185
Raj, J.A. 240
Rajmohan, J. 240
Ramírez, I. 215
Ramirez, S. 91
- Rapondjieva, A. 132
Rapondzhieva, A. 131
Rashid, H.U. 148
Raza, S. 204
Rippe, B. 181
Rizal, T. 232
Rosengren, B.-I. 181
Rosman, J.B. 234
Rosu, L. 195
Russ, G. 92
Rutkowski, B. 93, 170
- Sælen, M.G. 157
Saeyah, E. 230, 232
Saiidi, G. 200
Saijyo, T. 191
Salari, S. 211
Santimbreaanu, C. 195
Sapilak, B.J. 162
Saran, R. 94
Sarjou, A.A. 235
Savita, G. 180
Sayegh, M.H. 95, 96
Schmitz, S. 206
Sedor, J.R. 97
Shah, H. 209
Shaheen, F.A.M. 115
Shahinfar, S. 155
Shaibani, K. 204
Shaker, D. 123
Shamsaei, F. 225
Sharma, P.K. 146
Sheikh, S.S. 149
Sherif, A.Z. 202
Shibata, K. 130
Shimamoto, K. 210
Shimura, G. 130
Shin, M.J. 176
Shin, Y.S. 176
Shintani, K. 219
Short, C.D. 208
Shurlev, V. 131
Silva, J.G. 125
Simin, S.B. 121, 122
Singhal, V. 238
Sja'bani, M. 167
Soehardy, Z. 178
Song, H.C. 133, 134, 176, 190
Sreekrishna, V. 192–194
Steciwo, A. 135, 162, 175, 207
Stefanidis, I. 199
Stephen, T.H.C. 154
Stranik, L. 182
Stranks, S. 136, 137
Strock, E. 98
Sue, Y.-M. 203
Sufi, M.S. 154
Suhardi, D.A. 167
Sung, J.-M. 173, 128
Surani, S. 232

- Suriani, A. 232
 Svinarov, D. 132
 Svoboda, L. 182

 Takahashi, Y. 191
 Taleb, H.R. 211
 Tan, E.-K. 120
 Tan, H.-B. 120
 Tan, S.H. 159
 Tanaka, Y. 191
 Taniyama, Y. 205
 Tarazamani, M.K. 152
 Tattersall, J. 99–103
 Tay, S.C.J. 163
 Tenstad, O. 181
 Terada, I. 222

 Tervaert, J.W.C. 104, 105
 Thiruventhiran, T. 227
 Thomas, M. 155
 Toi, M. 114
 Tomino, Y. 106
 Tomita, N. 205
 Tone, Y. 113
 Torres, A. 138
 Tsai, T.-W. 173
 Tseng, C.-C. 173, 203

 Umemura, S. 130

 Vasina, N.V. 188
 Vedran, K. 172

 Venkataraman, N. 107, 238–240
 Vesna, G.D. 144
 Vikram, A. 146
 Vinko, K. 172

 Waeleghem, J.-P. Van 108
 Wang, M.-C. 173
 Webster, I. 140, 177
 Westheim, A. 156
 White, Y. 223
 Wiig, H. 181
 Winchester, J. 62
 Winn, M.P. 109
 Wissing, M. 206

 Wong, K.S. 120, 154, 155, 192–194
 Woo, K.-T. 120, 154
 Xinggang, D. 118, 119

 Yang, S.-C. 166
 Yang, W.-C. 136, 137, 171
 Yap, H.K. 120
 Yasuda, G. 130
 Yetti, K. 110, 111
 Yoon, S.A. 133, 134, 176, 190
 Yukawa, S. 113

 Zhao, Y. 120
 Zhu, A.L. 153
 Zouaghi, K. 183–185