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A Comparison of Indication and Diagnosis in Native Renal Biopsies Performed in Three Scottish Centres

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Background Evidence regarding indication for renal biopsy is sparse. Aim: The aim of this study was to compare frequency, indication and diagnosis of native renal biopsies performed in Western Infirmary, Glasgow, (WIG), Glasgow Royal Infirmary (GRI) and Ninewells Hospital Dundee (NHD). **Methods** Data on each renal biopsy are collected prospectively using an electronic data base and previously agreed codes for indication in each centre. This study included all native renal biopsies performed in a 1 year period between 2005 and 2006. Diagnoses were categorised as "glomerulonephritis", "vasculitis & SLE", "interstitial nephritis", "acute tubular necrosis", "chronic ischaemic", "diabetic nephropathy", "others". **Results** In WIG, GRI and NHD 96, 69 and 75 biopsies were performed respectively giving an incidence per million population (pmp) per year of 113.0, 96.5 and 166.7 respectively. The incidence of biopsy for the indication "acute renal failure" (ARF) was similar in WIG, GRI and NHD (34.1, 25.2, 31.1 pmp/year respectively), but was highest in NHD for "nephrotic syndrome" (22.4, 14.0, 28.9 pmp/year), "mild proteinuria, normal renal function \pm microscopic haematuria" (1.2, 2.8, 22.2 pmp/year), "moderate proteinuria, normal renal function \pm microscopic haematuria" (23.6, 19.6, 40.0 pmp/year), and "proteinuria, reduced renal function \pm microscopic haematuria" (7.1, 2.8, 31.1 pmp/year) with these last 4 indications accounting for most of the difference in overall incidence between centres. The major differences in histological diagnosis between WIG, GRI and NHD were for "glomerulonephritis" (37.7, 48.9, 68.9 pmp/year respectively), "vasculitis & SLE" (20.0, 14.0, 26.7 pmp/year) and "diabetic nephropathy" (10.6, 4.2, 22.2 pmp/year). **Conclusions** There is substantial variation in the incidence of renal biopsy between centres. This is mainly explained by an increased incidence of biopsy for mild and moderate proteinuria with or without preserved renal function in NHD. The differences in indication probably explain most of the difference in histological diagnosis between centres. Further study is required to determine if variation in biopsy practice results in differences in clinical outcomes.

Renal Biopsy for Proteinuria with Preserved Renal Function?

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Introduction Practice varies amongst nephrologists in whether to biopsy patients with proteinuria and preserved renal function. To compare practice between units and look at how often management was influenced by biopsying this group of patients we examined data from 3 Scottish centres. **Methods** Retrospective data on all patients biopsied for proteinuria (with or without microscopic haematuria) with preserved renal function were obtained from Glasgow Royal (2000-2006) and Western (2005-2006) infirmaries and Ninewells Hospital, Dundee (2003-2006). Biopsy details were retrieved from the shared biopsy database and clinical information was then retrieved from electronic and paper clinical records. **Results** Clinico-pathological data on 152 patients, (88 male), biopsied between Jan 2000 and May 2006 in Glasgow and Dundee were analysed. The median level of proteinuria was 1.5g/day (range 0.2-11g/day). The median eGFR was 81.0ml/min (range 29-145 ml/min). 127 patients (83.6%) had an eGFR \geq 60ml/min. The biopsy rate for this indication was: 22.4, 22.4, 43.8 pmp/year for GRI, WIG and Dundee respectively. 83 patients (54.6%) had glomerulonephritis; [31 (20.4%) IgA, 19 (12.5%) FSGS, 17 (11.2%) membranous, 7 (4.5%) minimal change disease, 5 (3.3%) mesangial proliferation other than IgA, 2 (1.3%) MCGN, 2 (1.3%) post infectious]; 19 (12.5%) vasculitis [9 (5.8%) lupus, 6 (3.9%) HSP, 4 (2.6%) pauci-immune vasculitis]; 13 (8.6%) diabetic nephropathy; 12 (7.9%) vascular disease [hypertensive and ischaemic nephropathy]; 14 (9.2%) other diagnoses [7 (4.6%) amyloid/fibrillary gn, 4 (2.6%) Alports, 3 (2%) thin bm]; 5 (3.3%) non-

diagnostic, 3 (2%) normal, 3 (2%) technical failure. There was a significantly greater number of patients with vascular disease diagnosed by biopsy in Dundee. 24 patients (15.8%) received disease specific therapy following their biopsy, (12 Dundee, 9 GRI, 3 WIG). Excluding those with positive immunology or HSP, 11 patients (7.2%) received disease specific therapy; [6 amyloid, 2 minimal change, 2 FSGS, 1 MCGN]. No patient in this group had urinary protein excretion $<$ 0.9g/day. **Conclusion** When patients are biopsied for proteinuria and preserved renal function the diagnostic yield resulting in initiation of disease specific therapy is low. Significantly more biopsies are performed for this indication in Dundee. This increased rate of biopsy did not result in a higher rate of disease specific therapy. This data would appear to support the practice of using 1g/day urinary protein excretion as a threshold for biopsy, however the numbers are small to base this conclusion on and prospective data from a national biopsy database would allow us to answer this question.

Prediction of Outcomes in Acute Renal Failure

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We aimed to test the hypothesis that the RIFLE classification predicts outcomes in patients with Acute Renal Failure (ARF) in a defined population (523390) served by a single laboratory system. All patients with serum creatinine concentrations $>$ 150 μ mol/l (male) or $>$ 130 μ mol/l (female) between 1/1/2003 to 30/6/2003 who fulfilled the GFR criteria for ARF were included irrespective of hospital treatment setting or requirement for renal replacement therapy (RRT). Clinical outcomes were taken from the patients' hospital case records (98% of which were obtained). 474 patients with ARF and 88 with acute on chronic renal failure were identified (incidence 1803 and 335 per million population respectively). Amongst ARF patients, significantly fewer in F category had full renal recovery and significantly more required RRT (table refer to www.smj.org.uk). RIFLE also predicted length of hospital stay (particularly when those dying during admission were excluded) and in-hospital mortality but not mortality at 90 days or at 6 months. In conclusion this population-based study showed that incidence of ARF is much higher than previously thought, with important implications for service planning and the provision of information to colleagues so that early action can be taken to prevent deterioration of renal function. The RIFLE classification was useful for predicting in hospital mortality, the need for RRT, the length of hospital stay and the likelihood of recovery of renal function but not survival at 90 days or 6 months. This classification therefore should be used to identify the patients at greatest risk of an adverse short term outcomes. Kidney Research UK supported this research.

Acute HIT should be Considered when Cardio-Respiratory Arrest Follows Line Insertion and / or Heparin Administration

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An 81 year old man with peripheral vascular disease, diet-controlled diabetes, and impaired left ventricular function underwent an elective endovascular repair of an infra-renal abdominal aortic aneurysm. Intra-operatively he received a 3000u intravenous bolus of unfractionated heparin, and he subsequently continued on 2500u of dalteparinTM (a low molecular weight heparin) for three days. Post-operatively his renal function deteriorated, and nine days later he required dialysis. An internal jugular line was inserted and the catheter dead space 'locked' with unfractionated heparin (5000u/ml) according to the manufacturer's instructions. Ten minutes after insertion of the line, he collapsed and cardiac monitoring revealed pulseless electrical activity. The initial differential diagnosis included major vascular injury, pneumothorax, haemothorax, cardiac tamponade, pulmonary embolism, and anaphylactoid drug reaction. The patient was successfully resuscitated with adrenaline, atropine, and gelfosinTM. During resuscitation, it was noted that he had developed purpura and spontaneous

bleeding from venepuncture sites. A full blood count now demonstrated severe thrombocytopenia. A chest x-ray showed that the line was correctly placed and there was no evidence of haemothorax or pneumothorax. An echocardiogram excluded tamponade. The presence of a consumptive thrombocytopenia and arrest immediately after heparin exposure suggested HIT as a possible cause. Further exposure to heparin was avoided, and the patient was transferred to the intensive care unit for ongoing care. Over the next few days, his platelet count spontaneously recovered and he had no further bleeding, therefore anticoagulation with danaparoid was started. A platelet aggregation test for HIT was positive, confirming the diagnosis. Unfortunately the patient continued to deteriorate, and following discussion with his family, a decision was made to withdraw active care. He died eleven days after admission to ICU. Hyperacute HIT was documented on the death certificate as a major contributory factor in his death. HIT is a common condition, affecting 1-3% of patients who receive intravenous unfractionated heparin. It is mediated by the formation of antibodies directed against platelet factor 4. Patients present with thrombocytopenia in association with an extreme pro-thrombotic tendency. HIT typically develops 4-14 days after heparin exposure, but can occur much more rapidly in patients who have previously been exposed to heparin. Such patients have pre-formed antibodies, and can develop cardio-respiratory collapse within minutes of heparin re-exposure. HIT's potential to present as an acute catastrophic illness is not well-recognised by many doctors. Failure to recognise the condition may lead to more prolonged heparin exposure and delay appropriate intervention. Since heparin is widely used both to lock dialysis lines and during haemodialysis, we suggest that acute HIT should be included in the differential diagnosis for any patient who experiences circulatory collapse after line insertion or during dialysis.

Do All Patients with eGFRs<60 Really Have CKD??

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Introduction Chronic kidney disease (CKD) is a growing public health concern due to our aging population and the increasing incidence of diabetes. There is strong evidence associating CKD and cardiovascular disease. In addition early identification and optimal treatment can reduce the rate of progressive disease and may obviate the need for future RRT. Despite this, detailed information regarding the epidemiology and natural history of CKD is limited, as many studies have based their incidence largely on a single creatinine measurement with no reference to case records. We propose to establish with increased accuracy the incidence of CKD in the Grampian Region (pop.500,000) and determine morbidity and disease progression. **Methods** We identified all patients with a serum creatinine of $\geq 150\mu\text{mol/l}$ in males and $\geq 130\mu\text{mol/l}$ in females during a six-month period in 2003. These patients were then grouped as ARF, ACRF or CKD. 1891 patients could not initially be categorised into these groupings, as they did not fulfil our original criteria. These patients either had too few creatinines to be accurately grouped or did not have a sustained or large enough rise in creatinine. Using the abbreviated MDRD formula we converted all creatinines to eGFRs then grouped patients according to their likelihood of having CKD (unlikely, possible, probable). Then, together with a review of case records we have staged them using the K/DOQI classification. **Results** 5700 patients were identified as having an elevated creatinine. Patients were classified as follows: CKD 2200; ACRF 88; ARF 474; Unclassified 1891. So far we have completed data collection for 1405 of these 1891 patients. 67% of these patients have evidence of CKD based on their eGFRs alone ("Probable" group). 10% had "Insufficient" creatinine data to be categorised and 6% were found to be "Unlikely" to have CKD based on their eGFRs being $>60\text{mls/min}$. 17% of patients are in the "Possible" group. A further 4% of the Unlikely, Insufficient and Possible collectively had a marker of kidney damage present. 14% have no definite evidence of CKD. Thus 71% had convincing evidence of CKD. Of these, 94% have Stage 3-5 CKD based on their index creatinine. The remaining 6% are the group with markers of CKD in the "Unlikely, possible and insufficient groups" and probably represent Stage 1 or 2 CKD. The most common co-morbid conditions were hypertension and ischaemic heart disease, 22% of those in Stage 3 were diabetics. Co-morbidities were more common in those in the "probable" category compared to those in the "possible" or "unlikely" groups. The mortality for patients in Stage 3 CKD was 45% at follow-up (30-36 months). **Conclusion** Following a thorough review of case notes and creatinines we have identified a substantial subset of patients with a creatinine $\geq 150/130\mu\text{mol/l}$ who have no conclusive evidence of CKD. This is particularly noteworthy as these patients may have been included in other prevalence studies thus overestimating the incidence of CKD. In light of the new

QOF it will be particularly important to know the characteristics of patients with an abnormal creatinine or eGFR as this will facilitate management planning and service provision.

Slowing the Progression of Cardiovascular Disease and Chronic Kidney Disease - An Audit of a District General Hospital Nephrology Clinic

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Background A position statement from the Kidney Disease: Improving Global Outcomes (KDIGO) highlighted that the two principle outcomes of chronic kidney disease (CKD) are the progressive loss of renal function over time, and the development and progression of cardiovascular disease (CVD). We undertook an audit of modifiable risk factors for both CKD and CVD progression in the setting of a district general hospital (DGH) nephrology clinic. The aims of the audit were to assess patient demographics in a DGH nephrology clinic, to assess the frequency of CKD and CVD progression risk factors, to assess the level of control of the above risk factors, and to raise awareness of the above risk factors. The audit took place over a three month period and included all patients who attended the clinic. An audit proforma was used to prospectively collect all the data. **Findings** The average age of attending patients was 59.4years with 59% being male. Approximately one third of patients attending the clinic were at each of CKD stages 3 and 4. Approximately one third of new patients seen were at each of CKD stages 2 and 3. 55% of patients were non-smokers. 28% of patients had documented ischaemic heart disease. Diabetes was the cause of renal impairment in 22% of patients, with glomerulonephritis forming 13%, ADPKD forming 10% and renovascular disease forming 9% of incident cases. A target blood pressure was set in an average of 60% of cases, with the target being attained in under 50% of cases. Proteinuria was quantified in about 40% of cases and renin-angiotensin blockers were used in a similar proportion. HbA1c targets were achieved in less than 40% of patients. Cholesterol targets were achieved in less than 15% of patients despite 40% of patients being prescribed a "statin". **Discussion** With the establishment of estimated GFR reporting by laboratories, the expansion of the GP GMS contract into CKD and the development of UK CKD and SIGN guidelines, it is important that this opportunity is taken to reduce the burden not only of CKD progression but its attended burden of CVD. We have designed a management algorithm for CVD risk factors based around the forthcoming SIGN guidelines and the current JBS2 guidelines. The plan is to close the audit loop at the beginning of 2007.

Vascular Access for Haemodialysis in Scotland

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It is widely accepted that the native arteriovenous fistula is the best form of vascular access for haemodialysis. Central venous lines are associated with a higher risk of bacteraemia and higher mortality. NHS Quality Improvement Scotland recommends that at least 70% of haemodialysis patients use a native fistula or vein graft as vascular access, but this standard was met by only 3 of 10 units inspected in 2002. Details of vascular access used by patients with established renal failure (ERF) were collected for the first time by the Scottish Renal Registry (SRR) in April 2006. There were 1566 patients with ERF on haemodialysis, and details of vascular access were available for all but 8 of these. Arteriovenous (AV) access, predominantly native fistulas, was used in 76% of patients. There was a significant difference between men and women, with 80% of men but only 70% of women using AV access ($p < 0.001$). There was a trend to greater use of lines in older patients, but this was not significant. Patients with ERF due to diabetic nephropathy were significantly less likely to have AV access than those with ERF due to other causes. There were considerable differences between units, with prevalence of AV access ranging from 55% to 96%. This could not be explained by differences in gender distribution or primary renal diagnosis between units. The QIS standard is met in Scotland as a whole, but vascular access provision varies widely between different units. The reasons for this should be investigated further, with the aim of improving the prevalence of AV access in units with lower provision. It was surprising that the use of lines was not significantly greater in older patients. The lack of a significant effect of age was not explained by a greater proportion of men in the older groups, or by age differences between those with diabetic nephropathy and other diagnoses.

Influence of Patient Fitness on the Incidence of Tunnelled Central Venous Catheter Related Bacteraemia in Haemodialysis Patients

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Introduction and aims Vascular access related complications represent an important cause of morbidity and mortality in chronic haemodialysis (HD) patients. The use of tunnelled central venous catheters (TCVC) as long-term vascular access is increasing, especially in elderly and less fit patients. The incidence of bacteraemia is known to be higher in patients dialysing through a TCVC compared to dialysing through an arterio-venous fistula (AVF). The aim of this study was to explore how much of this increased incidence is explained by patient fitness. **Methods** Two groups of patients from seven out-patient haemodialysis units were compared: all patients who dialysed through a TCVC at any time in between 01/01/2003 and 31/12/2003 and were fit enough to subsequently have a functioning AVF or a renal transplant even if that took place after 2003 (Group 1; n=93); and those patients who dialysed through a TCVC in 2003 and were not fit enough to subsequently dialyse through an AVF or have a renal transplant (Group 2; n=119). Numbers of days of exposure to AVF and TCVC in 2003 were calculated for each group using the electronic patient records (EPR). Bacteraemic episodes in 2003 were identified from the EPR and microbiology databases. Bacteraemic episodes that were definitely not related to AVF or TCVC were excluded. **Results** Patients in Group 1 were significantly younger than patients in Group 2 (mean age 57.5 v 64.8 years; $p=0.001$). Patients in Group 1 and Group 2 were exposed to dialysis through a TCVC for 10878 days and 19363 days respectively in 2003. The incidences of bacteraemia while dialysing through TCVC in Groups 1 and 2 were 2.21 and 2.27 per 1000 days respectively ($p=0.91$). The 3 year actual patient survival from 01/01/2003 in Group 1 was significantly higher than in Group 2 (80.6% v 26.1%; $p<0.0001$) confirming the greater 'fitness' of these patients. **Conclusions** The incidence of bacteraemia in patients dialysing through a TCVC is just as high in patients who are fit enough to subsequently have a functioning AVF or a renal transplant compared with those who are not. AVF should be regarded as the optimal vascular access for all haemodialysis patients.

Multiple Cardiac Biomarkers Predict Risk Of Mortality In Haemodialysis Patients

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Introduction The cardiac troponins are now well recognised as biomarkers with prognostic significance in patients with end stage renal disease. Evidence is emerging for the prognostic utility of other markers including the natriuretic peptides and high sensitivity C-reactive protein (hsCRP). We examined whether the use of multiple biomarkers would provide greater risk stratification in patients on maintenance haemodialysis. **Methods** A cohort of 175 patients undergoing maintenance haemodialysis had blood samples taken immediately prior to dialysis which were then analysed for troponin I (TnI; Bayer), troponin T (TnT; Roche), B-type natriuretic peptide (BNP; Bayer), N-terminal pro BNP (ntPro-BNP; Roche) and hsCRP (Dade-Behring). Baseline haemodynamic and demographic parameters were recorded. The cohort was followed up for a median of 450 days, with the value of each biomarker in predicting mortality compared both individually and in combination. **Results** 20 patients died during the follow up period. Table 1 shows the hazard ratio for mortality for each biomarker using Cox regression analysis (with the upper quartile compared to the lower 3 quartiles). The incremental value of using markers in combination is shown in Figure 1 (see www.smj.org.uk). **Conclusions** This study demonstrates that higher levels of natriuretic peptides, troponin I/T and hsCRP are associated with increased all-cause mortality in patients undergoing renal dialysis. In addition there is significant added predictive power when the markers are used in combination. Funded by Cardiac Endowments ARI and the Renal Dialysis Research Fund ARI.

High Haematocrit Does not Adversely Affect the Efficiency of High-Flux Dialysis Therapies

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Background In the era of widespread erythropoietin use there is a concern that high haematocrit levels will reduce the efficiency of dialysis treatments. **Methods** We performed serial clearance measurements for urea, phosphate, β_2 microglobulin and myoglobin on twelve patients with pre-dialysis

haematocrit $>35\%$ on high flux haemodialysis (HFHD) or haemodiafiltration (HDF), and correlated this to the haematocrit during dialysis. Results: Increasing haematocrit correlates with a reduction in urea and phosphate clearance for patients on HFHD but not on HDF. No reduction in clearance occurs for β_2 microglobulin or myoglobin. **Conclusions** The reduction in diffusive clearance was most probably due to reduced efficiency in peripheral fibres of the dialysis membrane brought about by the increased viscosity. The problem was not apparent in HDF due to the protective effect of the high ultrafiltration volume. The clinical impact of these reductions in clearance was small when operating at higher prevailing haematocrit levels. Source of funding: Unit funds.

Gadolinium-Enhanced Magnetic Resonance Imaging And Nephrogenic Systemic Fibrosis - A Retrospective Case-Control Study

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Introduction Gadolinium containing contrast used for magnetic resonance imaging (MRI) has been implicated in the development of nephrogenic systemic fibrosis (NSF) by two case series. We report the first case-control series of NSF, comparing the frequency and degree of exposure to gadolinium contrast amongst our established renal failure population. **Methods** We performed a retrospective analysis of all prevalent patients on dialysis in our renal units between 1st January 2000 and 1st July 2006. Diagnoses of NSF, episodes of gadolinium-enhanced MRI and cumulative gadolinium doses were recorded. Outcomes were analysed by parametric and non-parametric testing. **Results** 14/1826 patients had a diagnosis of NSF. Mortality was similar for affected and non-affected dialysis patients. 13/14 NSF patients had undergone gadolinium-enhanced MRI compared with 412/1812 non-NSF patients ($p<0.001$). Patients with NSF received a higher cumulative dose of gadodiamide ($p<0.001$) and received more gadolinium-enhanced MRI scans ($p=0.04$) than their non-NSF, gadolinium-exposed counterparts. **Conclusion** Our data support the association between gadolinium-enhanced MRI and the development of NSF. The potential risks of this type of imaging need to be balanced against those of alternative imaging forms in patients with stage 5 kidney disease.

Study of Patients Converting from Haemodialysis to Peritoneal Dialysis Because of Poor Vascular Access

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Background Haemodialysis (HD) patients with poor vascular access represent a major management problem and such patients may be transferred to peritoneal dialysis (PD) as a last resort. A literature search has shown that there is a paucity of information about the clinical outcomes of this patient cohort. **Objective** To compare the clinical outcomes of patients who transfer from HD to PD because of poor vascular access with the outcomes of patients who start PD by choice at the onset of dialysis. **Methods** A retrospective review of the medical notes of all incident PD patients at Glasgow Royal Infirmary over a 42-month period ending December 2004 was performed to permit analysis of: a) number of days hospitalisation, number of access procedures and number of access related infections per month of HD versus PD during the study period, b) haemoglobin and albumin before and 6 months after starting PD c) patient outcomes after 12 months (PD, HD, transplanted or deceased).

Results Fifty-three patients started PD at Glasgow Royal Infirmary during the study period. 47% (n=23) of patients starting PD were transfers from HD and 44% (n=11) of the transfers from HD were because of poor vascular access. All patients in the poor vascular access group (20.7% of total study population) had had at least 1 fistula operation (mean = 3 + 2) and at least 1 central venous dialysis catheter insertion (mean = 6 + 5) before starting PD. The number of days in hospital in the poor vascular access group fell by 42% on PD compared to HD (3.5 days vs. 6 days per month of dialysis; mean duration of PD was 12.3 months and HD was 15.2 months). The average number of procedures in the poor vascular access group fell by 75% on PD compared to HD (0.3 procedures vs. 1.2 procedures per month of dialysis). Average number of access related infections in the poor vascular access group was 57% less on PD compared to HD (0.15 infections vs. 0.35 infections per month of dialysis). Mean haemoglobin in the poor vascular access group was 10.9 g/dL on HD and 11.9 g/dL on PD; mean albumin was 38 g/L on HD and 32 g/L on PD. Patient survival after 12 months PD in the poor vascular access group was comparable

to that of patients on PD through choice (82% patients alive at 12 months in both groups). More patients in the poor vascular access group remained on PD at 12 months compared to those on PD through choice (73% vs. 61%).

Conclusions Transfer to PD is an option for HD patients when vascular access is no longer available. This study shows similar outcomes for patients transferring from HD to PD due to poor vascular access compared to patients on PD through choice. In HD patients with poor vascular access transfer to PD may offer benefits of fewer days in hospital, fewer access related procedures and fewer access related infections. There were no conflicts of interest when performing this study.

Existence of the Autoreactive T Cells Found in Goodpasture's Disease is Accountable by Properties of Endosomal Processing

Background Antigen processing plays a powerful role in autoimmunity by determining what self-antigen derived peptides are displayed bound to class II and subsequently presented to T cells. Those T cells recognising high affinity self-peptide/class II complexes are deleted in the thymus thus preventing the survival of potentially autoreactive T cells in the periphery. The predominant a3(IV)NC1-specific T cells in recent onset Goodpasture's disease have a strikingly consistent peptide specificity with all patients having T cells that recognise the a3(IV)NC171-91 and a3(IV)NC1131-151 (called P14). We recently reported that the stimulatory self-peptides have in common exquisite in vitro susceptibility to rapid destruction by whole lysosomal extracts, and identified the destructive activity was mediated by the endosomal aspartic proteases Cathepsin D and E. The observations suggested that the autoimmune response in Goodpasture's disease could be focused on these peptides because they are constitutively presented at too low abundance to establish self-tolerance, as was recently suggested for a major T cell epitope in multiple sclerosis. Towards testing this hypothesis we here report an investigation of the influence of Cathepsin D activity upon in vivo a3(IV)NC1 presentation by intact human antigen presenting cells (APC). **Methods** To assess a3(IV)NC1 presentation by intact human APC we made murine T cell hybridomas specific for a3(IV)NC1 peptide/ HLA DR15 complexes by immunising DR15-transgenic mice (provided by Dr D Altmann) with a3(IV)NC1 peptides. DR15-expressing mice were immunised with P14 and P14-specific T cells expanded in vitro. Lines were fused with a human myeloma T cell line (TcR negative) and shown to produce IL-2 when incubated with intact a3(IV)NC1 as well as P14-pulsed APC and to be restricted by HLA DR15. The murine T cell hybridomas were used to measure presentation of P14 on HLA DR15 by human B cells and macrophages that had been pulsed with P14 or intact a3(IV)NC1, and to evaluate the influence on presentation of manipulations that enhanced or diminished Cathepsin D processing. **Results** Human macrophages and B cells were able to process intact a3(IV)NC1 and present the P14 epitope on HLA DR15, but presentation sufficient to stimulate the T cells was considerably retarded (2-4 hours) compared with exogenous antigens (typically 30-60 minutes). P14 presentation was abrogated by prior incubation with Cathepsin D, but both accelerated and potentiated when APC were treated with Pepstatin A, a peptide inhibitor of Cathepsin D and E. **Conclusion** Our results demonstrate that the previously in vitro-demonstrated rapid endosomal destruction of the P14 epitope by lysosomal extracts is also discernable in the kinetics of a3(IV)NC1 presentation by intact human APC, consistent with a role in shaping constitutive presentation of a3(IV)NC1 and the scope of self-tolerance.

The Identification of Patients at Risk of Developing Contrast Nephropathy and Strategies Employed for its Prevention in a General Medical Receiving Unit

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An audit was performed to assess the present attitudes towards the risk of contrast nephropathy in a general medical admissions unit. Over a three week period a total of fifty one patients had CT scans involving the use of intravenous contrast (iomeprol). Complete data, including the identification of risk factors for contrast nephropathy and the identification of any prevention strategies employed was obtained for thirty five of these patients. Nine of these thirty five patients were found to have two or more risk factors for the development of contrast nephropathy. On review of the patient notes there was no appreciation of these risk factors. Furthermore patients 'at risk' generally did not have appropriate prevention measures employed and were not always followed up by the checking of renal function post contrast. Of the nine patients with two or more risk factors only one definitely received IV fluids and four did not have a check of renal function between 24 and 72 hours post contrast. One patient with three risk factors for the development of contrast nephropathy did not have diuretic withheld. Measures should be undertaken to improve identification of

patients at risk of contrast nephropathy and to improve routine monitoring of renal function post contrast in all at risk patients.

Recovery of Renal Function after 90 Days on Dialysis: Implications for Transplantation in Patients with Potentially Reversible Causes of Renal Failure

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Background Late recovery of renal function in patients requiring dialysis is a well recognised but uncommon phenomenon. Moves to increase the number of live donor transplants and the recognition that early transplantation is associated with better graft survival means it is possible that patients who are going to recover renal function may be transplanted unnecessarily. **Design** Prospective survey of patients receiving dialysis for more than 90 days in south west Scotland from 1/1/94 to 31/12/2005. **Methods** Routine measurement of residual renal function by combined urea and creatinine clearance allowed us to detect late recovery whenever this occurred. Results: Eight of two hundred and two (4%) patients recovered sufficient renal function to stop dialysing after 90 days treatment. The likely cause of the renal failure in five of these patients was atheroembolism. One with atherosclerotic renovascular disease had been stented and would have received a live related renal transplant had his sister not had second thoughts about the procedure. **Conclusion** It may be sensible to postpone transplantation in patients with certain types of renal failure, perhaps particularly patients with renovascular disease who have recently undergone a revascularisation procedure.

Outcome of Patients who Travel to Pakistan for Living Kidney Transplant

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Aim The aim of this study was to analyse single centre experience of patients travelling from United Kingdom (UK) to Pakistan for living kidney transplantation. Reports from elsewhere in the UK have led to patients being advised that this approach is associated with unacceptably high risks.

Methods Using the electronic patient record (EPR) and review of case sheets in Glasgow we have identified all patients who travelled to Pakistan for living donor kidney transplant since 2000 (PT group). A control group of living unrelated donor transplants (LUD) performed in Glasgow from a similar period of time was also identified. The outcomes analysed were patient survival, graft survival, transplant function at one, three and twelve months, incidence of acute rejection and infective complications. **Results** 12 patients were identified in the PT group and 24 patients in the LUD group. 1 patient in the PT group died in Pakistan and therefore no follow-up data are available. There was one early graft loss due to renal vein thrombosis in the LUD group. There was no significant difference in age, sex, prevalence of diabetes or incidence of pre-emptive transplant between the 2 groups. 1 year patient survival was 91% in the PT group and 96% in the LUD group (p=NS). 1 year graft survival was 91% in the PT group and 96% in the LUD group (p=NS). Mean serum creatinine in the PT and LUD groups was similar at 1 months (151.6µmol/L v 159.65µmol/L respectively; p=0.68), 3 months (130.9µmol/L v 144.7µmol/L; p=0.34) and 12 months (128.8µmol/L v 141.25µmol/L; p=0.44). The incidence of acute rejection in the first year was 36% in the PT group and 46% in the LUD group (p=NS). There was greater use of tacrolimus and mycophenolate mofetil as primary immunosuppression in the LUD group. One PT group patient developed malaria on his return from Pakistan. There were no instances of hepatitis B, hepatitis C or HIV infection in either group. **Conclusions** These data do not support the view that the outcome of patients travelling from UK to Pakistan for living kidney transplantation is worse than LUD transplantation in UK. A national study would inform discussion with patients about this approach.

Estimating Glomerular Filtration Rate: Potential Causes of Misclassification in the Community

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Introduction Recent developments in strategies to identify early chronic kidney disease (CKD) have highlighted the use of serum creatinine measurements for the estimation of glomerular filtration rate (eGFR) which is then used for screening and classification of CKD. In routine clinical practice, creatinine is most frequently assayed using a kinetic Jaffe method. This method has been shown to suffer from numerous interferences, and modern analytical techniques attempt to minimise any resulting errors. Pre-analytic factors also

affect measured creatinine concentrations, notable offenders being delayed receipt of the sample, haemolysis and icterus. For this latter reason, many laboratories, including our own, do not report creatinine in samples with high bilirubin concentrations, although most report creatinines from samples which are only mildly icteric, are haemolysed or delayed. We evaluated these three common factors to assess their impact on measured serum creatinine levels, with subsequent effects on the eGFR. **Methods** We reviewed 50,000 consecutive serum creatinine requests received from Primary Care by the NHS Grampian Clinical Biochemistry laboratory. Of these, 37 were excluded as information was incomplete. The main analytical platform in this laboratory (Bayer Advia 24000) simultaneously assesses samples for the presence of haemolysis and/or icterus, rating the presence of each variable on a categorical scale of zero to + + + +. The mean creatinine levels for each of these categories were compared, to identify potential patterns suggestive of interferences. **Results** Mean creatinine levels for all samples was 100.0 $\mu\text{mol/l}$. The results showed a negative effect of icterus with creatinine levels being on average lower in a progressive manner as the icterus increased (Figure 1, see www.smj.org.uk). A similar pattern was identified with regard to the presence of haemolysis in the samples (see Figure 2). Delayed receipt of samples appeared to result in a slight reduction in mean creatinine levels (Figure 3). **Conclusions** The three factors assessed all have graded influences on creatinine measurement. These effects may appear to be minor, but could have a significant effect on the classification of CKD by eGFR. For example, a 20 year old female with a creatinine of 100 would have a eGFR of 59 ml/min/1.73 m^2 , placing her in stage 3 CKD. This however, would not be detected if her sample was delayed more than 12 hours, or was only mildly haemolysed (1+ or more) or icteric (2+ or more), as the resulting eGFR would be greater than 60 ml/min/1.73 m^2 . Caution is therefore advised in the classification of CKD by eGFR in samples which are haemolysed, icteric, or simply delayed in transit.

ABSTRACT OF SOCIETIES

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References for all abstracts can be found online at www.smj.org.uk

Dissociation of Phenotypic and Functional Endothelial Progenitor Cells in Patients Undergoing Percutaneous Coronary Intervention

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Objectives We sought to determine the effect of local vascular injury during percutaneous coronary intervention (PCI) on circulating endothelial progenitor cells (EPCs) in patients with stable coronary disease. **Background** EPCs are circulating mononuclear cells with the capacity to mature into endothelial cells, and to contribute to vascular repair. **Methods** EPCs were quantified and characterised by whole blood flow cytometry (CD34+KDR* phenotype) complemented by real-time PCR, and the colony forming unit (CFU-EPC) functional assay, before and during the first 24 hours after diagnostic angiography (n=20) or PCI (n=20). **Results** Diagnostic angiography did not induce systemic inflammation or myocyte necrosis, nor affect the number of circulating CD34*KDR* cells or CFU-EPCs. Coronary intervention resulted in an increase in whole blood neutrophil count ($\pm 1.31 \pm 0.35 \times 10^9/\text{L}$, $P < 0.001$) and serum C-reactive protein concentrations ($\Delta 2.5 \pm 1.5 \text{ mg/L}$, $P = 0.001$), without significant myocardial necrosis. Twenty-four hours after PCI, the number of CFU-EPCs increased 3-fold (0.6 ± 0.2 vs. $2.3 \pm 0.9 \times 10^3$, $P = 0.05$),

although circulating CD34*KDR* cells (0.019 ± 0.003 vs. 0.021 ± 0.003 % of leucocytes, $P = 0.75$) and leucocyte CD34 mRNA (relative quantity 2.3 ± 0.5 vs. 2.1 ± 0.4 , $P = 0.21$) did not. There was no correlation between CFU-EPCs and CD34*KDR* cells. **Conclusions** Acute local vascular injury following PCI results in a systemic inflammatory response and increases functional CFU-EPCs. This increase was not associated with an early mobilisation of CD34*KDR* cells, suggesting these cells are not the primary source of circulating EPCs involved in the immediate response to vascular injury.

Mechanisms of Glucocorticoid-Mediated Inhibition of Angiogenic Changes in Endothelial Cells

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Background Manipulation of angiogenesis is an attractive therapeutic goal since aberrant blood vessel growth is central to many disease pathologies. The ability of glucocorticoids to inhibit angiogenesis is well established. This investigation addressed the hypothesis that glucocorticoid-mediated inhibition of angiogenesis can be modelled in endothelial cells, is the result of impaired VEGF action, and involves reduced endothelial cell migration. **Methods** Human umbilical vein endothelial cells (HUVECs) were cultured on Matrigel in conditions that stimulate spontaneous generation of tube-like structures (TLSs). The effects of glucocorticoids on TLS formation were assessed by incubation with cortisol (300-1200nM), cortisone (300-1200nM), vehicle or vascular endothelial growth factor (VEGF; 0.5-500ng/ml; positive control) for up to 24 hours. Effects on endothelial cell migration were assessed by culturing (24h) HUVECs on porous (8.0mm) inserts in the presence of VEGF (10ng/ml) +/- cortisol (600nM). HUVECs were then labelled with Calcein-AM and migration determined using fluorescence. **Results** Cortisol, but not cortisone, induced a concentration-dependent inhibition of TLS formation ($44 \pm 7\%$, $p < 0.01$) whereas VEGF stimulated an increase in TLS number ($218 \pm 6\%$). HUVEC migration was enhanced ($p < 0.01$) by exposure to VEGF (262% migration compared with untreated control cells). Cortisol had no effect on either basal (103%) or VEGF-stimulated (258%) migration. **Conclusions** These data show that TLS formation in endothelial cells provides a model for investigating the mechanisms underlying glucocorticoid-mediated inhibition of angiogenesis. The inability of glucocorticoids to reduce migration of these cells suggests their impact on angiogenesis may be due to changes in endothelial cell proliferation or on the formation of cell-cell connections.

Endothelial Dysfunction in Pre-eclampsia Prior to Clinical Symptoms

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Background Pre-eclampsia (PET) or high blood pressure in pregnancy results in approximately 150,000 maternal deaths worldwide and continues to be a leading cause of maternal and newborn illness or death in the UK. Endothelial dysfunction is a feature of PET and it is probably an early event in the development of PET. The aim of our study was to investigate if there was any evidence of endothelial dysfunction or white blood cell (WBC) activation prior to the onset of clinical signs in women destined to develop PET. **Methods & Subjects** 100 women with singleton pregnancies attending Ninewells Hospital for a scan were invited to take part in the study. At 22 weeks gestation a venous blood sample was collected from the mother along with the normal clinical data. Serum and plasma samples were stored at -70°C for measurement of vascular endothelial growth factor receptor-1 (VEGFR-1), neopterin and sE-selectin by ELISA. Sequential samples were taken from the same women at 26 and 34 weeks gestation and at 6 weeks postnatal. Following delivery pregnancy outcome was classified as PET, intrauterine growth retardation (IUGR) without PET or uncomplicated pregnancies. **Results** 83 women completed the study. 54 had a normal pregnancy; 14 had IUGR and 15 developed PET. sVEGFR-1 and neopterin levels were significantly higher at 26 weeks gestation in the PET group compared to controls, p values of 0.01 and 0.045 respectively. sE-selectin levels were significantly higher at 22, 26 and 34 weeks in the PET group compared with the controls ($p = 0.02, 0.01, 0.024$ respectively). **Conclusion** In the past conflicting findings from various studies have been reported in women with PET. We have shown for the first time in a longitudinal prospective study that levels of the potent VEGF inhibitor sVEGFR-1, plus WBC and immune activation (reflected by increased neopterin levels) and endothelial