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Abstracts

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Prognosis of chronic glomerulonephritis (CGN)

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Chronic glomerulonephritis (CGN) remains an important cause of chronic renal failure, accounting for 24% of patients on renal replacement therapy. Early studies suggested approximately 50% survival off dialysis at 10 years for patients with CGN. In order to determine the current prognosis we analysed retrospectively the outcomes of 185 patients with biopsy-proven CGN presenting to the renal unit in Glasgow Royal Infirmary since 1986. We have used both survival analysis (renal and non-renal death) and linear regression analysis to measure outcomes and discuss the merits and potential problems of both methods. Our results showed that 22 patients (12%) required renal replacement therapy and 15 patients (8%) died during a median follow-up of 40 months post-biopsy (range 2–139). Five- and 10-year survival of all patients off dialysis was 81 and 72%. Univariate analysis showed creatinine clearance, proteinuria, and mean arterial pressure at biopsy to be important prognostic factors in survival but only creatmnine clearance and age to be independent prognostic factors in the multivariate analysis. In order to determine factors specifically associated with progression of renal failure, we examined the rate of decline of creatinine clearance(CrCl) for each patient followed up more than 1 year. The median decline was 2.8 ml/min/year (range −26 to +23 ml/min/year). Univariate and multivariate analysis failed to confirm any of the factors identified in the survival analysis as significantly associated with renal progression. Factors tested included proteinuria, MAP, sex, diagnosis, CrCl, and cholesterol.

When both survival and linear regression analyses are used, several assumptions are made which are crucial to the interpretation of the data. If these assumptions are not met, false conclusions can be drawn, There is a striking lack of consistency in the reporting of outcome data in CGN over the last 10 years. The majority of studies incorporate survival, analysis but even within this group there is variation in the selection of patients, definition of end-points, and use of statistical analyses. This makes comparison of of outcomes between groups difficult and it is not always clear that the implicit assumptions of survival analysis have been met, More recently, studies on progression of renal failure have concentrated on linear regression analysis with the hope that it will help predict when an individual patient may require RRT. It is clear that this analysis answers a different question and cannot be used synonymously with survival analysis. We are now in an age of sophisticated statistical programmes which allow us to quote many more 'P values'. We should ensure that we are more explicit about the limitations of these analyses and standardize our methods of reporting outcome in order to aid comparison of results.

The role of endogenous steroid hormones in the generation of Th2-mediated autoimmunity in mercuric-chloride-treated Brown Norway rats

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Injection of Brown Norway rats with mercuric chloride (HgCl2) activates a Th2-type autoimmune response with production of a number of autoantibodies, and vasculitis primarily affecting the gut. Glucocorticoids have been shown to suppress Th1 and to promote the development of Th2-type responses. Conversely dehydroepiandrosterone (DHEA) promotes Th1 responses with suppression of Th2 responses. This study set out to define the role of these hormones in setting the Th1/Th2 balance in this animal model.

Rats were adrenalectomized (Adx) with no steroid replacement ($n=11$), Adx with basal steroid replacement given by a 25 mg corticosterone pellet inserted subcutaneously ($n=13$) or sham Adx ($n=14$) prior to administration of HgCl2. In both groups of adrenalectomized animals there was a delay in the production of IgE, and serum concentrations on day 9 were marginally lower ($P=0.035$, repeated measures ANOVA). All of the animals Adx with no steroid replacement and two Adx animals with steroid replacement died between 10 and 14 days after HgCl2 challenge, presumably due to failure to suppress cytokine production. There was no difference in the severity of caecal vasculitis between the groups. A significant increase in adrenal size was noted following administration of $HgCl_2$

Administration of subcutaneous DHEA implants (100 mg and 200 mg) had no significant effect on IgE concentrations or severity of vasculitis.

These observations do not support the hypothesis that corticosterone and DHEA play a central role in setting the Th1/Th2 balance in this experimental Th2-mediated autoimmune disease; in contrast with the Th1-mediated autoimmune disease experimental allergic encephalomyelitis, where corticosterone plays a key role in immunoregulation

Impaired lipoprotein metabolism in patients with proteinuria is associated with VLDL apolipoprotein C and E deficiency

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Patients with heavy proteinuria have hyperlipidaemia and increased atherogenesis. Total cholesterol, LDL-C, triglycerides (TG) and VLDL-C are frequently raised due to increased production, impaired catabolism, and reduced receptor-mediated clearance of lipoproteins. VLDL can be divided into VLDL1 (large, light, and TG rich) and VLDL2 (small, dense, and cholesterol rich). Each is under independent meta-

bolic regulation. Proteinuric patients have delayed catabolism of VLDL1 to VLDL2 and increased production of VLDL2. Lipoprotein lipase (LpL) converts VLDL1 to VLDL2, is activated by the cofactor apolipoprotein (apo) CII, and inhibited by apoCIII. VLDL can also be removed directly by hepatic receptors which recognize apoE.

To identify the origin of the delayed VLDL1 catabolism, we compared lipase activities and plasma and VLDL1 apoB, CII, CIII, and E levels in 27 patients with glomerular disease, urinary albumin >2 g/24 h and creatinine <300 □mmol/l with 27 age- and sex-matched controls.

Patients had raised cholesterol, TG, LDL-C, and VLDL-C. Urinary albumin was 3.9 ± 0.5 g and creatiine 139 ± 11 μmol/l (Cr Cl was >50 in 20/27 patients). VLDL1 and VLDL2 masses were both raised (182 ± 39 vs $54+7$ $P<0.0001$ and 112 ± 11 vs 36 ± 4 $P<0.0001$ all mg/dl). LpL and hepatic lipase (HL) activity did not differ from controls (LpL 4.1 ± 0.3 vs 4 5 ± 0 4 HL 17.6 ± 1.6 vs 14.0 ± 1.1 μmolFA/ml/h); however, plasma levels of apoB, CII, CIII and E were all increased.

After adjusting for the excess lipoprotein particles present in the patients by assessing the ratio of apoCIl, CIII and E to apoB, it was found that levels of apoCII:B and CIII:B were similar to controls (44 ± 3 vs 39 ± 3 $P=$n.s. and $228+10$ vs 230 ± 14 P n.s., all $\times10^{-3}$); however, apoE:B was reduced in the patients (34 ± 2 vs 41 ± 2 $P=0.03$ all $\times10^{-3}$), suggesting a relative plasma deficiency of apoE. Analysing the apolipoprotein content of each VLDL1 particle revealed that each particle in the patient group was deplete in apoCII, apoCIII, and apoE. (All mean $\pm$ SE)

These results show that in patients with heavy proteinuria, $VLDL_1$ particles are deficient in essential cofactors required for both lipolysis of lipoproteins and hepatic uptake via the VLDL receptor. The low apoCII levels found easily account for the delayed catabolism of $VLDL_1$ found in metabolic studies in this population. This may explain the origin of the hypertriglyceridaemia and atherogenic lipoprotein phenotype found in proteinuric patients.

Plasma level (mg/dl)	Patients	Controls	*P*
ApoB	148.9 ± 9.0	186.8 ± 3.8	<0.0001
ApoCII	6.7 ± 0.6	3.3 ± 0.2	<0.0001
ApoCIII	$32.7+1.9$	$19.3+1.0$	<0.0001
ApoE	5.1 ± 0.5	3.4 ± 0.2	<0.002

VLDL particles (molar ratio)	Patients	Controls	*P*
ApoCII:ApoB	6.3 ± 1.1	14.3 ± 2.6	<0.001
ApoCIII:ApoB	21.7 ± 3.6	42.7 ± 7.5	<0.02
ApoE:ApoB	0.35 ± 0.10	1.5 ± 0.4	<0.001

Increased incidence of renal disease in silica-exposed workers

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Various types of glomerulonephritis may occur more commonly in people exposed to silica, and patients commencing dialysis are more likely to have been exposed to silica than matched controls. We describe an increased incidence of renal disease in an isolated community which appears to be related to silica exposure. The cases included are only those known to nephrologists at the time we first began to investigate the possibility of increased incidence.

The area in question is a mining community with a population of 1645. Eight of them are known to have renal disease. This compares with two cases out of the other 5600 population of that GP practice catchment area ($P=0.004$), and with 156 patients attending the district renal OP clinic, from a catchment population of 130 000. Six of the eight cases have some form of glomerulonephritis, an incidence of 4.25 per thousand, compared with 47 at the district renal clinic, an incidence of 0.36 per thousand. Two have normal serum creatinine and four have chronic renal failure, progressive in two. Two are on renal replacement therapy, compared with a prevalence of 410 p.m.p. for the district and 452 for the parent Renal Unit.

Of the eight cases, three have a positive pANCA, one IgA disease, one membranous nephritis and one membranoproliferative nephritis. At least six of the cases were occupationally exposed for years to silica dust. The gap between ceasing exposure to silica and developing clinically evident renal disease ranged from 0 to 30 years, in keeping with reports in the literature.

These cases are further evidence that exposure to silica can cause various types of glomerulonephritis, most commonly ANCA-related vasculitis. We have reported our findings to the local Health and Safety Executive and Department of Public Health, and hope to start systematically investigating the population of silica-exposed workers.

A new model for renal transplantation services in North Staffordshire

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Renal transplantation services in the UK are currently undergoing a process of centralization. Acute transplant surgical services were withdrawn from the North Staffordshire Hospital (NSH) in 1996 and centralized to the Queen Elizabeth Hospital (QEH) in Birmingham. This study reports the 12 month results of renal transplantation before and after centralization.

Forty-two cadaveric (CAD) and one living donor (LD) renal transplant (catchment population 1.25 million) were performed in the 12-month period before centralization compared with 20 CAD and I LD (catchment population 0.75 million) following centralization. Primary function rates (80% NSH; 76% QEH) and surgical complication rates (13% NSH; 14% QE) were unchanged. Early rejection rates (<3 months) were unaltered (NSH 29%; QEH 31%), but late rejection (>3 months) increased from 3 to 11%. Steroid withdrawal within 12 months was achieved in 86% before and 89% after centralization. There was no significant difference in 12-month allograft function (Median serum creatinine (SCr) 144 (94–429) vs SCr 136 (81–277) μmol/l).

A new clinical management model was established forging close links between NSH and the QEH, long-term clinical care being provided immediately after in-patient discharge from QER at NSH. Joint transplant assessment clinics and 3-monthly list review ensure close supervision of the transplant waiting list.

Incorporation of acute renal transplantation surgical services into a large centre (QEH >140 renal transplants/year) has not affected the short-term outcome of renal transplantation in North Staffordshire.

The role of pulsatility index as a prognostic indicator in renal transplantation

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We studied the role of pulsatility index in 60 consecutive adult renal transplantation patients, performed during the period 15 January 1997 to 14 January 1998. Then we correlated these findings with renal function at 3 weeks post-transplantation and currently. All the 60 patients had their duplex ultrasound and PI values measured at Western Infirmary, within 3 weeks of renal transplant.

Pulsatility index gives a measure of impedance to blood flow within the kidney. The mean PI on the day of highest measurement was taken. The range of PI for all 60 patients was 0.9–5.2. The mean of these values was 2.050, and the standard error for mean was 0.127. This divided the patients into two groups: group A with PI <2.18, and group B with PI >2.18. In group A only one kidney failed amongst 43 patients. In group B seven kidneys failed amongst 17 patients. In group B the mean creatinine at 3 weeks was more than twice the mean of group A.

We feel that PI values add up as another important prognostic indicator in predicting the outcome of transplanted kidney.

Impaired endothelial function in cyclosporin-treated renal transplant recipients

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Background. The vascular endothelium plays a pivotal role in the maintenance of vascular tone and in the prevention of atherosclerosis, principally through the production and secretion of vasoactive compounds such as nitric oxide (NO). Studies in diabetes and hypercholesterolaemia have demonstrated impaired endothelial NO production, and this is thought to be an important initial event in the development of atherosclerosis, Animal studies have shown that NO synthase expression is reduced in cyclosporin-treated rats, but whether cyclosporin use in humans is associated with impaired endothelial NO production is not known. This study was devised to examine NO production and thus endothelial function in cyclosporin-treated renal transplant recipients, using the *in vivo* technique of forearm venous plethysmography.

Subjects. Two separate studies were performed. In study 1, stimulated NO production was investigated in nine cyclosporin-treated transplant patients, seven azathioprine-treated transplant patients, and in 12 controls. In study 2, basal NO production was investigated in nine cyclosporin-treated patients and 11 controls.

Methods. Stimulated NO production was assessed using carbachol (a muscarinic agonist) and sodium nitroprusside; basal NO production was assessed using L-NMMA (inhibits NO synthase). Drugs were infused into the non-dominant arm via a sterile 27-gauge cannula inserted into the brachial artery under local anaesthesia. Forearm blood flow was measured using strain-gauge plethysmography and expressed as a ratio of infused/non-infused arm (FBF ratio). Responses to drugs were measured as the percentage change in FBF ratio from baseline.

Results. In study I vasodilatation to SNP was similar in all groups. However, cyclosporin-treated patients had markedly impaired vasodilatation to the highest dose of carbachol ($208.3 \pm 34.1\%$; mean $\pm$ s.e.m.) compared to azathioprine-treated patients ($353.2 \pm 54.4\%$) and controls ($376.7 \pm 58.1\%$); $P < 0.05$. In study 2, cyclosporin-treated patients vasoconstricted less well to the highest dose of L-NMMA compared to controls ($-24.8 \pm 6.3\%$ vs $-38.3 \pm 3.4\%$; $P = 0.056$)

Conclusion. This study demonstrated reduced basal and stimulated NO production from the vascular endothelium of cyclosporin-treated renal transplant recipients, suggesting endothelial dysfunction. Azathioprine-treated patients appeared to have preserved NO production. The presence of endothelial dysfunction in cyclosporin-treated patients is of major clinical relevance, as it has been linked to hypertension and premature atherosclerosis in other populations. Reversal of endothelial dysfunction could now be used in this group as a surrogate end-point for studies, for example with statins, aimed at slowing the progression of atherosclerosis.

Tacrolimus-induced, post-transplant diabetic ketoacidosis

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We present three cases of patients who presented with either diabetic ketoacidosis or severe diabetes 2–8 months after receiving cadaveric transplants. All were being treated with a combination of tacrolimus, prednisolone, and ganciclovir, and their diabetes resolved completely after either stopping or reducing these medications.

Case 1 was a 17-year-old man who had fulminant hepatic failure of uncertain cause. He underwent orthotopic liver transplant, and was discharged on routine post-operative treatment with tacrolimus, prednisolone, and ganciclovir as well as other routine prophylactic therapy. Two months post-transplant he was readmitted with a blood glucose of 46.5 and was treated with first i.v. then s.c. insulin. A month after discharge he had stopped both ganciclovir and prednisolone, and no longer required insulin, with his blood glucose remaining within the normal range.

Case 2 was a 50-year-old man with haemophilia A who required an orthotopic liver transplant for cirrhosis caused by hepatitis C. He was discharged on tacrolimus, prednisolone, and ganciclovir, as well as other routine prophylactic therapy. Two months later he was readmitted with a blood glucose of 51, a venous bicarbonate of 11, and ketones on dipstick urinalysis. He was treated with i.v. then s.c. insulin. His tacrolimus dose was cut and his prednisolone and ganciclovir were stopped. Two months later he no longer required insulin and had blood glucose measurements within the normal range.

Case 3 was a 49-year-old man requiring dialysis for chronic renal failure caused by congenital bladder neck obstruction. He developed cirrhosis due to hepatitis C and received a combined liver and kidney transplant. He was discharged on tacrolimus, prednisolone, and ganciclovir as well as other routine prophylactic therapy. Eight months later, having received a course of i.v.ganciclovir for CMV oesophagitis, he presented with a blood glucose of 52 and a venous bicarbonate of 17. Urinalysis was not recorded. He was treated with first i.v. then s.c. insulin. His ganciclovir was stopped and his dose of prednisolone and tacrolimus was reduced. Two months later he no longer required insulin and his blood glucose was in the normal range.

Tacrolimius is well known as a cause of post-transplant diabetes, which may be reversible and severe. Tacrolimus-induced diabetes appears to be associated with similar complications to diabetes mellitus unrelated to medication, but it is unusual to present with sudden-onset diabetes, or ketoacidosis.

Skin cancer risk in a caucasian renal transplant population

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Long-term immunosuppressive therapy is associated with a variable increase in the risk of skin cancer in renal transplant recipients. This study aimed to identify the clinical factors associated with skin cancer in a geographically stable Caucasian renal transplant population. All renal allograft recipients under follow-up at the North Staffordshire Hospital were systematically interviewed and examined by a single dermatologist (HMR) for malignant and pre-malignant skin lesions. Data was gathered on patient characteristics including skin type, sun exposure, hair and eye colour; case-notes were carefully reviewed for details of previous skin cancer.

One hundred and seventy-one (67% male) patients with a mean (SD) age at transplantation of 38 (17) years and mean (SD) follow-up interval 6.5 (5.7) years were studied. Thirteen per cent had non-melanoma skin cancer (NMSC), 15% solar keratoses, 57% viral warts, and 1% lentigo maligna melanoma ($n=2$). Forty-eight basal-cell carcinomas (BCC) occurred in 16 patients, 36 squamous-cell carcinomas (SCC) occurred in 15 patients, and eight patients had both SCC and BCC. More than one solar keratosis was associated with a significantly increased risk of NMSC; SCC (OR 56.4, $P<0.001$) and BCC (OR 24.8, $P<0.001$) Older age at transplantation, male gender and green eyes (OR 7.4, $P<0.02$) were independently associated with an increased risk of NMSC. Moreover, outdoor occupation (HR 1.07/year, $P<0.001$) was associated with a shorter time from transplantation to the development of the first SCC.

NMSC occurred in 13% of a Caucasian renal transplant population in this cross-sectional survey. Skin cancer poses a significant clinical problem post-transplantation even in temperate climates. The early identification of transplant recipients at highest risk of skin cancer may allow the development of more targeted and effective surveillance strategies than currently exist.

Comparing staff roles in chronic dialysis units in Europe

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The contribution of staffing to the overall cost of chronic dialysis varies considerably within Europe. Any evaluation of the cost-effectiveness of a chronic dialysis programme must therefore examine staffing costs, not only in terms of the total number of staff, but also the roles performed by those staff.

The aim of this project was therefore to develop an instrument that would systematically determine the categories of staff performing given tasks on the chronic dialysis units of nine centres in eight countries in East and West Europe.

Two focus group sessions were held, one for nursing staff and one for medical staff. Tasks relating to chronic dialysis that could potentially be performed by several categories of staff were identified. The two lists were then combined and presented again to the focus groups who approved the final content. A table was then constructed in which staff 'primarily responsible' and 'also responsible' for each task could be indicated. This table was used in structured interviews with two representatives from each of the participating centres.

The observation that in the majority of centres patients are seen by a doctor during each dialysis session has obvious implications for cost. There are also several tasks, such as needling fistulae, priming machines, ordering stock, and training PD patients, which are the responsibility of different categories of staff in different centres. The results of this project have contributed to the ongoing economic evaluation of chronic dialysis in these centres.

The effect of long-term steroids on adynamic bone

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The clinical importance of adynamic bone continues to be debated. The characteristic findings are of low bone turnover in association with low levels of parathyroid hormone. An increased fracture rate and osteoporosis have been suggested as long-term complications, both of which would be exacerbated by steroid therapy.

An 18-year-old girl with reflux nephropathy started regular haemodialysis in 1970. A skeletal survey at the time showed subperiosteal bone resorption as well as vascular calcification. Over the next 5 years the alkaline phosphate rose with increasing bone resorption on X-ray. Bone biopsy confirmed the features of severe hyperparathyroidism. Despite mild hypercalcaemia she commenced 1-α OHD3 therapy in 1975 but this had to be discontinued after 6 months because of disabling joint pain and stiffness. Total parathyroidectomy was performed and 1-α OHD3 restarted. Alkaline phosphate returned to the normal range 5 months later and bone resorption disappeared on X-ray and bone biopsy. A bone biopsy 20 months after parathyroidectomy showed an osteoid volume of 1% with inactive bone surfaces consistent with a diagnosis of adynamic bone.

A cadaver renal transplant in 1978 continues to function well with a current creatinine of 120 μmol/l on prednisolone and azathioprine. The prednisolone dosage has never been below 7.5 mg daily. Parathyroid hormone has been undetectable since parathyroidectomy and the patient has been maintained on 0.5–0.75 μg 1-αOHD3 daily. The appearances of the phalanges on X-ray are unchanged since 6 months post-parathyroidectomy but bone mineral density in the hip and lumbar spine is considerably increased compared to age- and sex-match controls. Long-term steroids have not induced bone loss in this patient with adynamic bone.

Measurement of left ventricular mass in patients on maintenance haemodialysis

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Introduction. Left ventricular hypertrophy is a common finding and a strong adverse prognostic factor for survival in patients with chronic renal failure. An accurate method of measuring left ventricular mass (LVM) is therefore a prerequisite in the management of these patients. Recent evidence has suggested echocardiography overestimates LVM in essential hypertensives, and this error increases with increasing

LVM. Cardiac magnetic resonance imaging (MRI) has been validated as an accurate measurement of LVM. We therefore performed a study comparing the two methods of measurement in 35 haemodialysis patients.

Methods. Patients were studied within 24 h of their last dialysis and the two tests were carried out within an hour of each other. Blood pressure, resting ECG, ambulatory blood pressure monitoring (ABPM), and blood sampling were performed or initiated at the same visit. A single observer measured LVM by echocardiography using 2D-guided M-mode and the images were analysed by one observer. MRI was performed on a machine operating at 1 tesla. Images were obtained by ECG gated, multislice, multiphase FLASH echo. Images were analysed by one radiologist who measured LVM in systole and diastole, using the diastolic values for direct comparison with echocardiography. Comparison was made using the method of Bland-Altman.

Results. Thirty-two patients had results from both methods. Clinic blood pressure, ABPM, and QT dispersion all correlated with LVM, with a stronger correlation observed for MRI values. Intra- and inter-observer variability were significantly greater for echocardiography, (though still within the accepted norm). Comparing the two methods, the difference in LVM values, (echo minus MR), increased in a linear fashion with increasing mean mass and chamber diameter.

Conclusion. Assuming the direct, 3-dimensional measurement of mass by MRI to be closer to the true LVM than a value calculated from a 1-dimensional echocardiography image, we would conclude that echocardiography significantly overestimates LVM. This overestimation increases linearly with mass and chamber diameter and is the result of the false assumptions made in the equation for echo LVM. This error is therefore amplified in dialysis patients, the majority of whom have a degree of LV dilatation and LV hypertrophy. The value of echocardiography in determining an individual dialysis patient's LVM is therefore questionable.

Efficacy of gastrostomy tube (g-tube) feeding in children receiving chronic peritoneal dialysis (CPD)

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Aim. To assess the effect of g-tube feeding on recommended caloric (%RNIC) and protein (%RNIP) intake, growth, total protein, albumin, cholesterol, triglyceride, and high-density lipoprotein (HDL) in infants and children receiving CPD.

Methods. A retrospective study of infants ($n=8$) and children ($n=7$) undergoing g-tube insertion on CPD was undertaken, with assessment at initiation of CPD, at g-tube insertion, and 6 and 12 months (m) thereafter. Mean age at initiation 0.29 years, infants, and 7.4 years, children with g-tube insertion undertaken after 0.6 years and 1.0 years respectively. All received CCPD. Triceps skinfold thickness (TSF), midarm muscle circumference (MAMC) and midarm mean circumference (MAC) were measured.

Results. Initial infant %RNIC of 77.2% increased during CPD and post-g-tube insertion to 107% at 6 m. Initial child %RNIC, 89.8%, fell during CPD increasing to 86.7% 6 m post-g-tube. Initial infant %RNIP, 61.3%, increased to 106.7% 6 m post-g-tube. Initial child %RNIP, 147.8%, fell on CPD increasing to 107% 6 m post-g-tube. Significant increases occurred in %TSF, %MAC, and %MAMC in infants. Increases in children were significant only for %MAMC. Height SDS was reduced in both with no change observed. Significant changes in percentage weight for height occurred in infants only, being most marked post-g-tube insertion. Initial hypoalbuminaemia, infants 28.8 g/l, children 30.8 g/l, increased during CPD and post-g-tube, 35.6 g/l and 34.9 g/l at 12 m respectively. Initial total protein (infants 57.1 g/l, children 58.4 g/l) increased to 64.4 g/l and 70.8 g/l at 12 m respectively. Infant cholesterol was unchanged, 5.6 mmol/l initially. In children a reduction occurred from 7.3 mmol/l to 3.3 mmol/l 6 m post-g-tube. Triglyceride fell in infants and children from 5.8 mmol/l and 3.6 mmol/l initially to 3.6 mmol/l and 3.3 mmol/l at 6 m. Initial HDL levels were unchanged at 1.4 mmol/l and 1.1 mmol/l in infants and children.

Conclusion. G-tube feeding is effective in producing statural growth in infants receiving CPD, but less so in the older age group. It also effective in correcting hypoproteinaemia in both groups and may be of benefit in preventing the hyperlipidaemia traditionally associated with CPD.

Complicatons of gastrostomy tube (g-tube) feeding in children receiving chronic peritoneal dialysis (CPD)

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Aims. To assess the complications of gastrostomy tube (g-tube)feeding in children receiving chronic peritoneal dialysis.

Methods. A 15-year retrospective study was undertaken of 150 patients receiving chronic peritoneal dialysis (PD) over 2599 patient months. Thirty-seven g-tubes were inserted in 23 patients (mean age 3.8, SD 3.2). Nine patients had g-tube insertion prior to the commencement of PD. Sixteen patients underwent g-tube insertion on PD, performed for 125 patient months prior to g-tube insertion and 758 patient months following insertion.

Results. Peritonitis occurred every 18.4 patient months in controls and 7.8 patient months in those with a g-tube. Peritonitis occurred every 6.0 patient months before and 8.1 patient months after g-tube insertion in those undergoing g-tube insertion on PD. PD catheter exit-site infection (PDESI) occurred every 18.7 patient months in controls and 16.8 patient months in those with a g-tube. PDESI occurred every 126 patient months before and 16.2 patient months following g-tube insertion. PD catheter replacement secondary to infection occurred every 109.4 patient months in controls and 39.9 patient months in those with a g-tube. It did not occur before g-tube insertion and occurred every 32.5 patient months following insertion. Thirty-four episodes of g-tube exit-site infection occurred; in 10 the same organism caused concurrent peritonitis. Peritonitis occurred immediately following g-tube placement in two patients. G-tube replacement was necessary on 37 occasions. Haemodynamically significant gastrointestinal bleeding occurred in three patients, being terminal in one.

Conclusion. G-tube insertion is not without risk in the paediatric CPD population; however, the nutrtional benefits outweigh the complications of exit-site infection and peritonitis and there is no absolute contraindication to g-tube insertion or usage within the paediatric CPD population.

(In)adequacy of sodium removal during nocturnal peritoneal dialysis (*n*PD)

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The Renal Association and DOQI guidelines for CAPD and APD do not include minimum standards for daily removal of sodium and water, whilst the European APD Group recommend that oligoanuric APD patients should have peritoneal ultrafiltration of at least 750 ml/day as well as achieving targets for small-solute clearances. In CAPD sodium removal correlates with net ultrafiltration, whereas the drained dialysate after short-dwell exchanges (*n*PD) using dextrose dialysis solutions has a relatively low sodium concentration due to the sodium sieving that occurs with peritoneal ultrafiltration during the first 60–120 min of the dwell time. We therefore evaluated the discordance between ultrafiltration volume and sodium removal during NPD and assessed the contribution of NPD to the total daily removal of sodium in 11 stable APD patients. All of the patients were prescribed four overnight exchanges in 9 h with mean infusion volume 2.3 ± 0.2 litres and dialysate dextrose concentration $1.97 \pm 0.52\%$. Daytime exchanges were performed by nine patients (two exchanges per day in eight patients) and three patients were anuric.

All patients provided a 3-day urine collection which overlapped with the collection of the individual daytime and total overnight drained dialysate. A serum sample was obtained at 14.00–15.00 hours to coincide with the mid-point of the daytime exchanges. Urea, creatinine (corrected for glucose where appropriate), sodium, and volume were measured in all dialysate and urine collections and serum samples. Residual renal function, Kt/V urea, total corrected creatinine clearance, net ultrafiltration, and sodium balance were calculated using standard methods.

Parameters of adequacy of dialysis + residual renal function appeared to be satisfactory in the APD patients studied :
weekly Kt/V urea 2.3 ± 0.5
total corrected creatinine clearance $= 75.0 \pm 15.8$ l/1.73 m^2/wk
daily peritoneal ultrafiltration $= 1.32 \pm 0.85$ l/day
daily sodium removal via APD $= 104 \pm 79$ mEq/day

However, the drained dialysate sodium concentration of the NPD exchanges averaged only 127 ± 2.9 mmol/l, which resulted in hyponatric ultrafiltration ovemight equivalent to 41 ± 24 mEq/l. In comparison the daytime peritoneal dialysis exchanges resulted in ultrafiltration equivalent to removing 132 ± 49 mEq/l. The relative contributions of renal, daytime exchanges and NPD to daily fluid and sodium removal are shown in Table 1.

Conclusions. NPD using dextrose dialysate containing 132 mEq/l sodium augments ultrafiltration disproportionately to sodium removal. APD patients with loss of residual renal function require net ultrafiltration with daytime (longer dwell) exchanges or ultralow sodium dialysate with NPD exchanges to achieve adequate daily sodium removal. Guidelines for adequacy of APD in oligoanuric patients should include standards for daily ultrafiltration and sodium removal as well as small solute clearances.

	Fluid loss (l/day)	Sodium removal (mEq/day)
Residual renal function	0.4 ± 0.6	31 ± 42
Daytime exchanges	0.7 ± 0.6	78 ± 62
NPD	0.6 ± 0.4	26 ± 19
Total	1.7 ± 0.8	$135 + 65$

Results of a postal questionnaire survey on current practice in vascular access in the United Kingdom

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A postal questionnaire covering pre-dialysis preparation, access for first dialysis, and stable haemodialysis patients was sent to 72 UK adult NHS haemodialysis facilities. Replies were received from 45 (62.5%) with the following findings:

A radial approach is the preferred site for primary arteriovenous fistulae in 97% of units, and the brachial site in 3%. The preferred secondary sites were femoral followed by brachial. To improve the chances of a successful fistula 36% of units routinely use anticoagulation. Aspirin is most popular followed by heparin, dipyridamole, and warfarin. Less than one-third of units (27%) routinely use intravenous fluids. GTN patches are sometimes used in up to 23% of units.

Among those patients followed in clinic (= 100%) the proportion of patients (weighted for the different sizes of units) coming to first haemodialysis with suitable access is 51%, the rest requiring urgent access. Of the total, 15% have had previous unsuccessful access attempts so one-third have either been missed or come to dialysis unexpectedly.

When temporary lines are needed, the most popular sequence of attempts at access is jugular, subclavian, then femoral (37%), with operators citing the avoidance of subclavian stenosis as the important principle. The second most popular sequence is subelavian then jugular (28%) with operator familiarity and patient convenience given as the reasons.

Concerning long-term vascular access, 74% of stable haemodialysis patients dialyse off arteriovenous fistulae, 18% off lines, and 8% off grafts. Forty-two units of 45 recognized the problem of clots forming in fistulae. To deal with this 22 use either aspirin or warfarin to reduce clots, 11 only aspirin, and 9 only warfarin. Of 44 units using tunnelled lines only 32% routinely use anticoagulants with 24% of these units using aspirin and the rest using warfarin. Once there is difficulty with patency then aspirin and more commonly warfarin are used. For blocked lines, urokinase is used in at least one-third of units in preference to mechanical options.

Outcome in patients requiring combined renal and respiratory support in Scottish ICUs over a 2-year period

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Objectives. To define the mortality and morbidity for combined renal and respiratory failure in Scottish ICUs, with widely varying levels of dialysis activity, and to identify the requirement for chronic renal replacement therapy, following discharge, in these patients.

Design. A retrospective audit of patients in 15 of 16 ICUs in Scotland that undertake dialysis. Patients having dialysis and ventilation were identified from daily entry of Therapeutic Intervention Scoring System data (TISS). Outcome was identified by survival at ultimate hospital discharge and severity of illness on first admission to the ICU determined by the Acute Physiology and Chronic Health Evaluation score (APACHE II). All patients identified as having both ventilation and dialysis had this confirmed by case-note review. Linkage with the Scottish Renal Registry and Audit System enabled follow-up of all survivors to determine the requirement for chronic renal support following discharge.

Subjects. For a 2-year period between 1995 and 1997 we validated 998 recorded incidences of renal support in intensive care to determine the extent of combined renal and respiratory failure (defined by the need for both dialysis and ventilation).
Results. Following the validation process, 615 patients in 15 ICUs were identified as having received both respiratory and renal support. The ultimate hospital mortality of this group of 64.3% compares with a predicted mortality (based on the first 24 h in ICU) of 52.5%. With the exception of one unit which dialysed only one patient, mortality varied between 50% and 74.3% with no obvious relationship between observed mortality or standardized mortality ratio (SMR) and volume of patients dialysed. Of the four most common admission diagnoses, septic shock and pneumonia resulted in the worst outcome. The duration of dialysis made no difference to the observed outcome. Seventy-eight patients who received renal and respiratory support in ICU had chronic renal impairment documented in their case-notes prior to acute hospital admission. Within this subgroup 19 of 61 patients, who were not receiving any form of chronic renal replacement therapy (CRRT) prior to their acute episode, went on to require CRRT following ultimate hospital discharge (Table 1). The ultimate hospital mortality rate in the 17 patients who were receiving CRRT prior to admission was 70.5%. Of those with no documented renal impairment, six required CRRT following discharge, accounting for 2% of survivors within this group.
Conclusion. Scottish ICUs demonstrate a wide range of dialysis activity. In spite of this, overall mortality for patients with combined renal and respiratory failure is as good as that previously quoted [1,2]. There is no obvious relationship between volume of patients dialysed and outcome. This suggests that no improvement in quality of patient care for this high-risk group could be produced by further centralization of care for such patients.

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Evaluation of a stop dialysate flow method of post-dialysis blood sampling

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Both the Renal Association and DOQI guidelines recently stressed the need for a standardized method of post-dialysis urea sampling to allow comparative audit. However, the recommended methods may be impractical in busy renal units, since they involve multiple steps and require accurate timing and volume of blood sampling. As an alternative we evaluated a stop dialysate flow method.
Methods. Serial measurements of blood urea were estimated from arterial and venous samples taken at time 0, 30, 60, 120, 180, 240, 300, and 360 s after stopping dialysate flow and maintaining dialyser blood flow at the end of haemodialysis in 10 patients. A peripheral blood sample was also obtained from the contralateral arm at 0 s to reflect body water urea concentration at the end of dialysis, without the effects of access and cardiopulmonary recirculation. The haemodialysis prescription was repeated in the same 10 patients using the Renal Association method to allow comparison between the two methods. The practical use of the stop dialysate flow method was then evaluated in 117 regular haemodialysis patients and compared to sampling immediately post-dialysis.
Results. Within 4 min of stopping dialysate flow there was no difference between the blood urea concentration of arterial and venous samples, indicating cessation of diffusion across the dialysis membrane. Also, the blood urea concentrations in all arterial and venous samples between 4 and 6 min after stopping dialysate flow were equivalent to the blood urea concentration of the peripheral venous sample taken at 0 s.

In 117 patients the post-dialysis blood urea sample 5 min after stopping dialysate flow averaged 5.49 ± 2.11 mmol/litre compared with 5.07 ± 2.05 mmol/litre immediately after the end of the haemodialysis session ($P < 0.0001$). This was equivalent to a reduction of URR from 71.68 ± 8.29 immediately post-dialysis to 69.07 ± 9.29 ($P < 0.0001$). In a subgroup of 23 patients who dialysed *via* double-lumen lines, there was no significant difference between blood urea concentrations taken from arterial and venous ports 5 min after stopping dialysate flow.
Conclusions. This study shows that there is a window period between 4 and 6 min after stopping dialysate flow when the blood urea concentration in a sample taken from any part of the extracorporeal circuit is equivalent to a peripheral sample taken at 0 s. The stop dialysate flow method is simple and practical in a busy renal unit, yet it is more accurate and allows more flexibility in the timing of sampling than the method recommended by the Renal Association.

Urea reduction ratio—might it be simpler to raise the target by 5%

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Measurement of dialysis adequacy is an important component of the care of renal patients who are being treated by

Table 1.

	Renal status pre-ICU		
	No renal impairment	Renal impairment, no CRRT	Renal impairment CRRT
n	537	61	17
ICU mortality	276 (51.4%)	16 (26.2%)	4 (23.5%)
Ult hosp. mortality	353 (65.7%)	30 (49.1%)	12 (70.5%)
SMR (95% CIs)	1.28 (1.20–1.36)	–	–
CRRT post-ICU (% of hosp. survivors)	6 (1.9)	19 (64.3)	5 (100)

Table 1.

Time post dialysis	Difference between contralateral arm blood urea concentration and post-dialysis blood urea concentration	Difference between contralateral arm URR and post-dialysis URR
Time 0	0.67 ± 0.87*	−3.47 ± 4.02*
RA (10 s)	0.31 ± 0.42*	−1.35 ± 1.84*
180 s	0.33 ± 0.55	−1.69 ± 2.64
240 s	0.10 ± 0.54	−0.45 ± 2.64
300 s	0.01 ± 0.51	0.01 ± 2.54
360 s	0.00 ± 0.42	0.10 ± 2.07

*$P < 0.05$ (paired t test).

haemodialysis. The urea reduction ratio (URR) is the simplest way to do this, but until now there has been disagreement on how and when to measure the post-dialysis urea sample. The Renal Association recommend a target URR of >65%, and that we should measure the post-dialysis urea by following a complex four-stage procedure, designed specifically to eliminate access recirculation. More recently, a Stop Dialysate Flow Method has been advocated with sampling from the arterial line at 3–5 min to eliminate both access and cardiopulmonary recirculation.

We analysed URR in the Dumfries haemodialysis population using the method recommended by the Renal Association (to allow for access recirculation) and compared this with URR measured in the contralateral arm 30 min after completion of dialysis (to allow for access, cardiopulmonary and tissue rebound). Average URR was 68.1% by the Renal Association method and 63.7% at 30 min. The average difference was 4.4% with a range of 0–13%; 22/30 (73%) patients achieved a Renal Association target URR > 65%, but only 16/30 (53%) met this target at 30 min.

It has been estimated that 50% of urea rebound is due to access recirculation, 15% due to cardiopulmonary recirculation, and 35% to tissue rebound. This means that even if we adopt a method of sampling for dialysis urea that eliminates access recirculation (Renal Association method) or access and cardiopulmonary recirculation (Stop Dialysate Flow Method) we could still be overestimating the true URR achieved by dialysis. Rather than ask patients to wait for an extra 30 min for a post-dialysis urea sample, it might be simpler to raise the target URR by 5%.

The simplest way yet to classify acute renal failure, acute on chronic renal failure, and chronic renal failure?

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The incidence of acute renal failure (ARF) has been studied less extensively than that of chronic renal failure (CRF), and comparisons between centres have been hampered by the use of different diagnostic criteria. Previous estimates of the incidence of ARF requiring dialysis have varied froni 18/million/year [1] to 50/million/year [2]. These are likely to be underestimates as both studies excluded patients requiring dialysis whose serum creatinine was less than 500 μmol/l at the initiation of treatment. Moreover, it is likely that only a minority of patients with acute renal failure in either study were referred to a Nephrologist.

Against this background, a survey of the need for short term dialysis in Dumfries and Galloway has shown that 130 adults (188/million/year) required dialysis or haemofiltration for less than 90 days between January 1994 and September 1998. This was a heterogeneous group comprising patients with ARF and acute on chronic renal failure who recovered or died; patients with CRF who died within 90 days; peritoneal dialysis patients who spent less than 90 days on haemodialysis, usually because their catheters failed to drain or became infected and required to be removed; and a small number of patients with heart failure who underwent dialysis or haemofiltration to remove fluid after conventional treatment had failed. Patients with malignancy were included. There was no Cardiac Surgery Unit in Dumfries.

Although many of our patients would have been excluded from the analyses conducted by Feest and Khan [1,2]. our data nevertheless allow an estimate to be made of the need for short-term dialysis in an unselected population in the 1990s. If it is possible to draw any conclusions from these studies, it might simply be that our failure to collect data in a systematic fashion does not allow an estimate of the incidence of ARF to be made with any precision whatsoever. Given the difficulties likely to be encountered in agreeing criteria for a definition of ARE, a national audit of patients who require haemodialvsis or haemofiltration for less than 90 days is recommended.

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Is there equality of utilization of long-term renal replacement therapy in Scotland?

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We have undertaken a 1-year (1/10/97–30/9/98) prospective study of all patients commencing long-term renal replacement therapy (RRT) in adult renal units in Scotland. We investigated whether long-term RRT was utilized equally across the country.

During the year of study 538 patients commenced long-term RRT of whom 10 unexpectedly recovered enough renal function to become independent of dialysis; these 10 are excluded from analysis. The registrar general for Scotland gives the total population to be 5 122 500 (Mid-1997 Population Estimates: Scotland); the incidence of new patients in the year studied was therefore 103 per million. The population 'at risk' i.e. those above the age of 15 years is 4166 641; the annual incidence, excluding the under 15s, is 127 per million. New patient incidence per million of each age group is shown below.

bAge band (years)	15–49	50–64	65–75	>75
Incidence/million	48	178	384	254

The incidence of new patients in each health board area was standardized such that if the national incidence is taken to be 100%, the range of incidence was from 49% of the national rate in Orkney health board area to 165% in Dumfries and Galloway, with all other areas lying within $\pm 20\%$ of the national rate except the Western Isles (69%).

Social circumstance (as measured by the Carstairs deprivation index) of the incident population mirrors that of the general population of Scotland, implying there is no bias in patient acceptance to RRT programmes. Carstairs scores are significantly lower (more affluent) with increasing age in patients starting long-term RRT, however ($P = 0.019$ Kruskal–Wallis).

Provision of RRT to the population at risk in each health board area in Scotland in the year studied was consistent within 20% of the national rate for all but three areas, and showed no overall evidence of social bias