NEPHROLOGY

G68 HOME COLLECTION OF URINE FOR CULTURE FROM INFANTS BY THREE DIFFERENT METHODS: PARENTS' PREFERENCES AND BACTERIAL CONTAMINATION RATES

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Aims: To determine the most reliable and convenient method for parents to collect urine from infants at home to exclude urine infections.

Methods: The parents of well children aged 0.1 to 1.5 years were asked to volunteer to collect three urine samples at home on one day. Each urine sample collected was inoculate onto a culture dipslide using a sterile swab-stick, and then incubated. The order of collection was randomised, and each parent used all of the following methods:

- urine collection pad
- sterile adhesive bag
- clean catch

Parents were asked to comment on each method, and to give a rank order.

Results: 44 mothers volunteered. 2% were unable to obtain urine from pads, 9% failed using bags, and 20% failed by clean catch. Urine infection was excluded definitively in 70% of children using pad collections, in 66% of children using bag collections, and in 75% of children using clean catch.

Some samples collected by each method grew $>10^5$/ml coliforms in 5 of the children, despite the fact that urine infection was definitely excluded by repeated sampling in each case.

Most parents considered the clean catch method highly impractical to carry out at home, and ranked it worst. Urine pads were considered more comfortable than bags, were ranked slightly higher, and are cheaper.

Conclusions: Clean catch urine collection is a poor option for parents to use at home. Urine pads and bags produce similar quality urine specimens, but parents prefer pads. Non-invasive urine collection will inevitably produce some false-positive diagnoses.

G69 INCIDENCE AND INVESTIGATION OF FIRST URINARY TRACT INFECTION IN CHILDREN

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Aims: To determine the incidence of first urinary tract infection (UTI) and pattern of subsequent imaging in a defined child population.

Methods: A retrospective analysis of first childhood UTI (pure bacterial growth $>10^5$cfu/ml) in Shropshire (children <16 years = 89477); ascertainment of follow-up investigations from the radiology database.

Results: 11093 urine samples were submitted from 8086 children over 1 year. 624 (0.7%) children had their first UTI during this period. The incidence of first UTI was 2.6%, 1% and 0.4% among infants, 1-5 year olds and 6-15 year olds, respectively with 38%, 58% and 72% being pyuric (>10 white cells/μl). Coliforms accounted for 84% of positive urines. 11.5% of positive urines in infants originated from primary care. Only 52 of 130 infants with first UTI underwent any imaging. 30% of the investigated infants had major renal abnormalities. 124 of 216 1-5 year olds with UTI underwent no radiological investigation. Failure to refer was the major reason. 75% of children >5 years did not undergo any imaging studies at all.

Conclusions: Despite the published guidelines, only a minority of children are investigated, often incompletely but renal abnormalities are frequently found in investigated infants. Easy and simple methods for urine collection in primary care, and greater awareness of the need for renal imaging are needed to improve diagnosis and management of childhood UTI.

G70 VALUE OF DMSA SCANNING AFTER URINARY TRACT INFECTION : EVALUATION OF NATIONAL GUIDELINES

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Aim: To assess the impact and outcome of imaging investigations carried out in children in accordance with national guidelines (1991) following urinary tract infection (UTI). The minimum recommendation was ultrasound alone with DMSA in addition for children under 6 years and MCUG in addition for children under 12 months.

Method: Retrospective audit of inpatients and outpatients referred to UHW Healthcare Trust with UTIs over a 12 month period February 1997 to January 1998.

Results: 164 children (51 male, 113 female) were identified following the first UTI or first referral for investigation. Overall the prevalence of dilatation on ultrasound scan was 6%, renal scarring on DMSA was 11.5% and vesicoureteric reflux was 27%.

Abnormalities	Outpatients				Inpatients			
Age group	Ultrasound		DMSA		Ultrasound		DMSA	
0-12 months	0/13	0%	0/10	0%	7/43	16%	7/42	16%
1-<6 years	2/69	3%*	1/54	2%*	5/19	26%*	6/18	33%*
6-12 years	1/13	8%	1/3	33%	1/6	17%	1/3	33%
Total	3/95	3%*	2/67	3%*	13/68	19%*	14/63	22%*

Conclusion The prevalence of abnormalities among children managed as outpatients was significantly lower than in inpatients (*p<0.01). DMSA scans involve an intravenous injection, isotope exposure, staff time, resources, psychological trauma and expense (£100 approx). The low yield of positive results and lack of evidence of impact on management indicate that this test could be omitted in children with first simple UTI not sufficiently ill to be admitted to hospital.

G71 INTRAVENOUS UROGRAM (IVU)—CONTINUING PLACE IN THE INVESTIGATION OF URINARY TRACT INFECTION

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Aim: To examine the diagnostic role of IVU in patients with abnormal differential DMSA uptake without scarring.

Methods: Forty patients (age 0-19 years) were identified over a 2 year period in whom differential DMSA uptake was >10% with smooth renal outlines and no evidence of scarring. Twenty-eight had completed further radiological investigations. In 2 marked urological abnormalities were noted. In 8 patients on ultrasound a duplex system was apparent in the kidney with greater DMSA uptake. In 18 where no explanation was apparent, IVU had been undertaken.

Findings: Eight patients had a normal IVU. In the remaining 10 patients, 8 had duplex systems and 3 had appearances of scarring in the kidney with reduced DMSA uptake.

Conclusions: IVU will identify a significant number of patients with normal kidneys, unrecognised duplex systems or scarring where DMSA scan has been inconclusive. This will help in planning longer term follow up.

G72 PRIMARY HYPEROXALURIA TYPE TWO

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Introduction: The Primary Hyperoxalurias (PH1 and PH2) are rare defects of oxalate metabolism. The more frequently reported PH1 is characterised by marked phenotypic heterogeneity. PH2, confirmed by raised urine oxalate and L-glycerate, is less frequently reported, with only 23 cases documented in world literature. We describe 12 previously unreported children with PH2, representing the largest single centre cohort in the world.

Aims: 1) To describe the presenting features and clinical course of children with PH2 in order to provide more information for those treating the disorder

2) To increase awareness of PH2 among those treating children with nephrolithiasis and ensure appropriate investigations are performed.

Methods: A retrospective review of notes of all children with hyperoxaluria was performed.

Results: The mean age at diagnosis of PH2 was 3.9yrs. 8 had a positive family history, and seven of these were diagnosed by screening when asymptomatic. The remaining 5 presented with nephrolithiasis at a mean of 3.25yrs. Haematuria was common but urinary tract infection and nephrocalcinosis were not. All had normal renal function at diagnosis, and after mean follow-up of 4.25 years only one patient had suffered a significant decline in glomerular filtration rate.

Conclusions: Most symptomatic children with PH2 have presented with nephrolithiasis in early childhood. Renal impairment is not as common as in PH1. There are a significant number of children with PH2 who remain asymptomatic over a number of years. PH2 may be more common than previously thought and all children with nephrolithiasis should have a urinary L-glycerate level measured to exclude the diagnosis.

G73 ACE GENE POLYMORPHISMS ARE NOT ASSOCIATED WITH SUSCEPTIBILITY TO RENAL SCARRING IN CHILDREN WITH VESICOURETERIC REFLUX

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The D (deletion) allele of the gene encoding angiotensin I-converting enzyme (ACE) has attracted considerable interest over the last few years as a risk factor for progressive disease in a variety of renal conditions. Recent publications have also implicated the D allele in the development of renal scar formation in children with vesicoureteric reflux (VUR).

The aim of this study is to determine whether homozygosity for the D allele is associated with renal scarring in children with VUR.

One hundred and fifty five children with VUR (all grades) have been recruited from a paediatric nephrology clinic. A DMSA scan had been performed in all cases. Eighty patients (group 1) had evidence of renal scarring, 12 of whom had decreased renal function. In group 2, there were 75 patients with no evidence of renal scarring.

ACE genotype was determined on all patients and DD polymorphisms repeated to prevent mistyping.

Allele frequencies in group 1 were I:D 0.53:0.47; and in group 2 were: I:D 0.42: 0.58. Genotype frequencies in group 1 were: II: 22, ID: 40 and DD: 18, and II: 11, ID: 44, DD: 20 in group 2. There was no association between the DD polymorphism and the presence of renal scarring (p=0.15). Neither was there evidence supporting a 'dominant' D allele; indeed, the I allele was more prominent in the scarred group.

In conclusion, we cannot confirm previous reports that the deletion polymorphism of the ACE gene is a genetic susceptibility factor in the development of renal scarring.

G74 A LOCUS FOR FAMILIAL FOCAL SEGMENTAL GLOMERULOSCLEROSIS MAPS TO CHROMOSOME 1q25-q31

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Aims: Familial forms of FSGS that exhibit autosomal dominant and recessive patterns of inheritance have been described. We have therefore studied a cohort of 4 families with clinical diagnoses of FSGS to see if they map to known loci.

Methods: Four autosomal consanguineous families (2 Arab; 2 Pakistani) were ascertained presenting with proteinuria/nephrotic syndrome. Families were compared for clinical and genetic heterogeneity. The ABI Prism Linkage mapping panel version (Applied Biosystem) was used to performed a genome wide search on families. Five microsatellite markers from the ABI linkage set and 7 polymorphic markers from the genome database were used for fine mapping on chromosome 1q. Data were evaluated using two point linkage analysis and multipoint analysis.

Results: A genome wide screen revealed the presence of a single autozygous region in both Arab families at chromosome 1q25-q31. An autozygous region at chromosome 1q25-q31 was also identified in one of the Pakistani families. A combined multipoint lod score of 8.4 over a region of approximately 7 cM in chromosome 1q, was generated using Homoz Mapmaker. The minimal critical region was calculated at approximately 10 cM.

Conclusions: We have mapped a locus for an autosomal recessive form of renal disease with clinical presentation of FSGS to a 7-10 cM interval at chromosome 1q25-q31 in 3 out of 4 families. In doing so we have excluded three candidate loci (WTI, CNS-Finnish NPHSI, MPV-17). Our work further confirms there is both clinical and genetic heterogeneity in familial FSGS.

G75 PAEDIATRIC RENAL TRANSPLANTATION IN NORTHERN IRELAND 1984-1998

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This paper aims to review paediatric renal transplantation in a geographically isolated centre with a small population. Using data compiled locally and from the UK. Transplant Support Service, a 15 year review of renal transplantation in patients under the age of 19 years has been performed for the years 1984-1998. During this time period a total of 77 transplants were undertaken. The most common causes of end stage renal failure were reflux nephropathy, congenital renal dysplasia and glomerulonephritis. The 5 year graft survival was 64% with a mortality rate of 2.6%. Our median waiting time to transplantation has risen from 87 days in the period 1984-1988 to 316 days in the 5 year period ending in 1998. The age range of kidney donors during the 15 year period has fallen progressively and they are now predominately from a paediatric population. A major advance is seen in the success of transplantation in the youngest children between the ages of 2 and 4. The graft failure rate continues to be highest in the early post operative period (13% in the first 30 days). From 1984-1998 117 offers of organs were declined most frequently because a better tissue match was required. Unfortunately a significant number were refused because of resource restrictions. The figures demonstrate that the short and long term graft survival and patient mortality in Belfast is comparable to other similar centres nation-wide.

G76 MYCOPHENOLATE MOFETIL RESCUE OF CALCINEURIN INHIBITOR RELATED NEPHROTOXICITY IN CHILDREN AFTER LIVER TRANSPLANT

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Calcineurin inhibitors (Cyclosporin (CyA) and Tacrolimus (Tac)) have significantly improved the patient and graft survival after liver transplant (LT), but nephrotoxicity associated with the use of these drugs has lead to renal replacement therapy with dialysis or renal transplant in some long term survivors of LT. Mycophenolate Mofetil (MMF) belongs to the purine analogue group of immunosuppressive agents without nephrotoxicity making it an attractive anti-rejection drug. The aim of our study was to evaluate the use of MMF as calcineurin inhibitor sparing agent in a selected group of children with impaired renal function after LT.

Patients: Twelve children (5 male), 11 on CyA and 1 on Tac, with glomerular filtration rate [GFR] by chromium EDTA <75ml/min/1.73sq.m at a median (range) interval from LT of 54 months (1-112). Indication for LT was non AE acute liver failure in 4, alpha-1-antirtypsin deficiency in 2, biliary atresia in 2, Alagille syndrome in 2 and Crigler Najjar syndrome in 2.

Methods: MMF was introduced at the dose of 20 mg/kg/day and increased to 40 mg/kg/day after 1 week. Cyclosporin dose was reduced by 25% after 1 week of MMF introduction and further reduced every two weeks to achieve 75% reduction in blood levels.

Results: There was a significant increase in GFR at 6 and 12 months after introduction of MMF, median (range) GFR mls/min/1.73sq.m at 0, 6 and 12 months being 51.5 (31.3-71), 70.5 (38-111) and 87 (44-100) respectively, $p \leq 0.02$ for all. Median (range) of CyA levels (μg/L) at 0, 6 and 12 months were 98 (21-242), 44 (15-56) and 20 (undetectable - 98 respectively). Two children on CyA developed acute rejection leading to conversion to Tac in 1, while further reduction of CyA dosage could not be achieved in the other. The child with Alagille syndrome on Tac who had an initial GFR of 33 ml/min/1.73sq.m has normal graft function and GFR value of 56mls/min/1.73 sq.m, with a level of less than 3 μg/L one year after LT. MMF was tolerated well with transient lymphopenia in two.

Conclusions: In paediatric LT MMF permits the recovery of renal toxicity due to calcineurin inhibitors by allowing reduction of their dose.

G77 THE BURDEN OF NEPHROTIC SYNDROME IN YORKSHIRE

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There is a gap in the literature documenting the occurrence of glomerular disease in a defined population; this study aimed to describe the incidence pattern of nephrotic syndrome in Yorkshire.

Listings of children (0-15 years) diagnosed with glomerular disease, including nephrotic syndrome, were collected from routine hospital episode statistics and consultant paediatricians and paediatric nephrologists within Yorkshire from 1987 to 1998. Demographic, clinical and diagnostic details were abstracted from hospital records. Annual mid-year 1991 census population estimates were used to calculate age-standardised incidence by sex and age, and over time and geographical area.

Of 396 children registered with some form of glomerular disease, 181 had nephrotic syndrome (46%). Of the nephrotics, 158 (87%) had steroid responsive disease (SRNS) and 23 (13%) were non-responsive. 74 (41%) of nephrotics had a biopsy performed. The sex ratios (M:F) for SRNS and non-responsive (NRNS) were 1.8:1 and 1.1:1 respectively. Between the ages of 0-15 years, the overall age-standardised incidence was $2.0/10^5$/year (95%CI=[1.7-2.3]), with little variation between West Yorkshire, North Yorkshire and Humberside. The incidence of nephrotic syndrome in Yorkshire has remained relatively stable over the last 12 years, only rising slightly from 1.5 to $2.0/10^5$/year (P=0.57) (on average, 1.4%/year).

The Yorkshire database of children with nephrotic syndrome is considered to be of sufficiently high quality to provide an accurate assessment of disease incidence. Recent rates appear to be similar to previous figures from the UK. In contrast to other conditions such as diabetes and certain childhood cancers, there does not appear to be a major increase in the burden of this condition over time.

G78 CLINICOPATHOLOGICAL FINDINGS IN ATYPICAL HAEMOLYTIC URAEMIC SYNDROME

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Design: Clinicopathological correlation of renal findings in children with clinically atypical HUS.

Method: Retrospective review of notes of cases identified by a UK national survey. Biopsies and necropsy kidneys analysed by two pathologists unaware of clinical features.

Results: 34 cases studied, 23 from two centres. Males exceeded females 23:11, especially in infancy, 9:1. Five children died, 4 of them infants, and 10 developed end-stage renal failure (ESRF). Eighteen had relapses, 6 of whom proceeded to end stage, 11 to chronic renal failure. Seven children had good outcome. This included 2 cases of TF cryptantigen exposure. Two children developed HUS in association with chemotherapy. Seven were familial or had persistent hypocomplementaemia. Of these one died, 2 have ESRF and 3 chronic renal failure (CRF).

One child had normal kidney on biopsy and recovered. One had isolated glomerular thrombosis typical of diarrhoea associated (D+) HUS, and one showed almost complete cortical atrophy. The remaining 31 cases had early

or late glomerulopathy with endocapillary hypercellularity or mesangial expansion and duplication of basement membranes, and often other features such as crescents. Additionally 8 had arteriolar lesions of thrombosis and intimal swelling, and 7 others had similar arterial changes. Of these 15, 2 died, 4 have ESRF and 8 have CRF.

Conclusion: The renal findings in atypical HUS usually include glomerular and vascular changes that are different from those seen in D+HUS. Extraglomerular vascular lesions are associated with an adverse outcome.

G79 DOES ORAL L-ARGININE IMPROVE ENDOTHELIAL FUNCTION IN CHILDREN WITH CHRONIC RENAL FAILURE?

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Aims: Cardiovascular disease is a major cause of mortality amongst patients with chronic renal failure (CRF). This project was designed to investigate the mechanism of premature atherosclerosis and a treatment strategy at a time when the process maybe reversible. In humans L-arginine has been used to improve endothelial function by increasing nitric oxide (NO) production and in animal models this in turn has attenuated the progression of atherosclerosis.

Methods: We conducted a randomised double-blind crossover trial of L-arginine (the precursor of NO) in 25 normotensive children aged 12 +/-3 (6-19) years with CRF (GFR 27.4 +/- 13.2 ml/min/1.73m^2) in whom endothelial dysfunction had previously been demonstrated. We examined the effect of L-arginine on the endothelial response to shear stress (NO-dependent) using a non-invasive technique of high-resolution ultrasound. Each subject was studied before and after 4 weeks of L-arginine (2.5g/m^2 x 3/day) or placebo, separated by a rest period of 4 weeks.

Brachial artery diameter was measured at rest, during increased flow (endothelial-dependent dilatation) and after 25mcg of glyceryl trinitrate (endothelial-independent dilatation) at each visit.

Results: After oral L-arginine, plasma L-arginine levels rose from 82 +/- 20 to 179 +/- 110 micromol/l ($p<0.001$). No significant change in endothelial-dependent dilatation during L-arginine (7.96 +/- 2.35 to 7.71 +/- 3.22 % $p>0.05$) or placebo (8.2 +/- 2.89 to 8.3 +/- 3.14% $P>0.05$) was noted. This was also true for endothelial-independent dilatation.

Conclusion: Endothelial function was not improved with L-arginine. This suggests that raising L-arginine levels has no effect on NO bioavailability or that the mechanism of premature atherosclerosis is independent of NO bioavailability at this stage.

G80 ACHIEVING NATIONAL STANDARDS IN PERITONEAL DIALYSIS

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28 measures of the quality of care in peritoneal dialysis for children were developed from a National Standards document produced by the Renal Association and the British Association for Paediatric Nephrology in 1995. These 28 quality measures have been audited at six monthly intervals over the last 4 years.

10 of these quality measures are entirely within the control of the professionals and include measures with direct impact on clinical risk such as the safety of equipment and the Hepatitis B status of patients and staff. In the first cycle of audit three of these measures failed the agreed standard. Over the last two years (four audit cycles) only two points have failed and in the last two cycles there were no failures.

18 of the 28 quality measures are influenced by patient and family characteristics particularly adherence to treatment. Even so analysis of failures in achieving the agreed standards has presented opportunities for the multidisciplinary team to reflect and develop new strategies for improving care. In anaemia control and growth, regular multidisciplinary meetings are now held with clear targets and informal consensus guidelines. Using this approach the percentage of patients with adequate control of anaemia has increased from 27% to 89% during the four years. Growth, one of the most important outcomes of treatment in renal failure has also shown similar improvement. In the latest audit cycle all patients were above the 3rd centile for height. Preliminary review of patient characteristics show that improvement is not due to a change in patient population.

In contrast blood pressure control and bone disease treatment for which we currently do not have guidelines and clear targets have not shown similar improvements.

These data show that it is possible to achieve national standards for care in peritoneal dialysis in children. The use of informal consensus guidelines, target setting, re-organisation of the clinical service and regular structured audit have improved the outcome for growth and anaemia control.