### Paediatric Intensive Care Group/British Association for Paediatric Nephrology

G44

A PROSPECTIVE QUESTIONNAIRE ASSESSMENT
OF KNOWLEDGE AND APPLICATION OF ESTIMATED
GLOMERULAR FILTRATION RATES AMONGST PAEDIATRIC
TRAINEES

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**Aims** To determine awareness of estimated glomerular filtration rates (eGFR) and its application in prescribing and managing paediatric patients.

**Methods** This was a cross-sectional, prospective, questionnaire based study. The questionnaires were distributed at the regional deanery teaching for Paediatric trainees at levels ST1–8 in Autumn 2012.

**Results** 40 questionnaires were completed, with a 50% response rate. Trainee groups were categorised as junior trainees, ST1–3 (n = 17), senior trainees, ST4–8 (n = 16) or trainees specifically with renal experience (n = 7). Almost a third of the total number of participants had never performed an eGFR, three-quarters of whom were junior trainees. Not surprisingly therefore, one-third of junior trainees had never adjusted medication in consideration of renal impairment. Likewise, three-quarters of trainees were unable to suggest a formula for calculating an eGFR. Of significance, from the 25% who were able to give a formula, 30% wrote it incorrectly.

In the clinical scenarios 80% correctly identified an abnormal creatinine but less than half realised the need to dose adjust acyclovir. In the second case 75% appropriately indicated the use of Gentamycin in renal impairment but there was no clear consensus on the dosing regime and when levels should be checked. Only 20% were aware of the 24-hour dosing schedule with almost half opting to look it up or discuss with the renal team. Overall those with more training (ST4-8) or with renal experience (ST1-8) were more knowledgeable. Conclusions There is significant room for improvement in the knowledge and appropriate use of eGFR amongst Paediatric trainees, particularly at the junior level. An increasing awareness of these simple tests would improve prescribing practise; potentially preventing the inappropriate use of nephrotoxic drugs in those with renal impairment or conversely denying a patient gentamicin when it is the most suitable antibiotic and safe if used appropriately. We hope to establish simple regional guidelines through the local nephrology network, develop practical prescribing modules to improve prescribing in renal impairment and consequently improve clinical decisionmaking and reduce the burden on tertiary nephrology services.

G45

THE DIAGNOSIS OF URINARY TRACT INFECTION IN YOUNG CHILDREN (DUTY) STUDY: THE DEVELOPMENT OF A CLINICAL ALGORITHM TO IMPROVE THE RECOGNITION OF URINARY TRACT INFECTION (UTI) IN PRE-SCHOOL CHILDREN PRESENTING TO PRIMARY CARE

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**Aim** To develop a clinical algorithm based on symptoms, signs and urine dipstick results to assist the identification of children who require urine sampling, antibiotic treatment and/or laboratory analysis.

Methods We conducted a diagnostic cohort study of children <5 years presenting acutely (≤28 days) unwell to primary care in the UK. We collected detailed information on the presence/absence and severity of presenting symptoms and signs, as well as socio-demographic and past medical history data. Urine was sampled by clean catch (preferred) or nappy pad, 'dipsticked' and sent to (i) the local NHS laboratory (the priority sample) and (ii) a reference laboratory. Blind to children's clinical symptoms and signs, the NHS and reference laboratories processed urine samples according to their standard operating procedures.

**Results (preliminary)** 7,163 children were recruited with NHS and research urine sample results available for 6,328 (88%) and 5,257 (73%) respectively. Of the 5,017 children without missing data and with urine results from both laboratories: mean age was 2.2 years (s.d. = 1.4); 49% were male; 54% urines via clean catch, 45% via nappy pads and 1% via bag. UTI rates were 2.8% and 3% from clean catch and pad samples respectively. Among clean catch samples, the following were independently associated with UTI: history of UTI; parental report of smelly urine; pain/crying while passing urine; clinician's global impression of illness severity; and on dipstick: nitrites, leukocytes and blood (area under the ROC = 0.87 (95% CI 0.82 to 0.92). Among the nappy pad samples, the factors were: female gender; age; smelly urine; darker urine; and on dipstick: nitrites, leukocytes and blood (AUROC = 0.78 (0.72 to 0.83)).

**Conclusions** Symptoms, signs and dipstick testing have diagnostic utility for UTI. These results will be developed into an algorithm to help clinicians select which should have: a urine sample obtained; a sample sent for laboratory culture and receive immediate antibiotic treatment.

G46

#### DEVELOPING A HUMAN PROXIMAL TUBULAR CELL MODEL FOR CYSTINURIA

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**Aims** The inherited stone-forming condition cystinuria is most commonly caused by mutations in the SLC3A1 or SLC7A9 genes. These encode the two subunits, rBAT and  $b^{0,+}$ AT, of the heterodimeric cystine transporter, which is located on the apical membrane of proximal tubular cells (PTC). Defects in this transporter cause multiple, bilateral and recurrent cystine stones. Trafficking of the rBAT/ $b^{0,+}$ AT transporter has been shown to be disrupted by mutations of SLC3A1 and SLC7A9 in other cell lines, but this has not yet been demonstrated in a relevant cell type. Our aim is to interrogate cystine transport in vitro to identify new therapeutic targets at the molecular level.

**Methods** PTC from urine of healthy patients were conditionally immortalised using a temperature sensitive SV40 construct. Fluorescent tags for wild type and mutated SLC3A1 and SLC7A9 sequences were generated, and used to study the trafficking of the rBAT/b $^{0,+}$ AT heterodimer, and quantify cystine uptake using radiolabelled cystine assays.

**Results** Constructs for wild type and mutated rBAT and  $b^{0,+}AT$  were transfected into human conditionally immortalised PTC, and imaged in real time to demonstrate transporter trafficking. Functional assays of cystine transport are underway to quantify the effects of clinically relevant cystinuria mutations.

**Conclusion** We have established an in vitro study of the cystine heterodimer rBAT/ $b^{0,+}$ AT in human PTC which can be used to investigate known and discovered cystinuria mutations, and ultimately facilitate development of novel therapies for this disease.

G47

## INVESTIGATING NEW BIOMARKERS FOR EARLY DETECTION OF ACUTE KIDNEY INJURY IN PAEDIATRIC INTENSIVE CARE

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Critically ill children and neonates admitted to Intensive Care are at high risk of developing acute kidney injury (AKI) and do so early in the course of their illness. AKI is associated with increased duration of stay in intensive care, short and long term renal impairment, increased mortality, and increased hospital costs. AKI is currently diagnosed when serum creatinine (SCr) levels rise, however there may be a 48 hour delay between renal insult and detectable increase in SCr levels. This can delay diagnosis of AKI and hence potential intervention to mitigate renal damage. New AKI biomarkers can aid early diagnosis in patient groups where there is a timed potential renal insult (eg: cardiac surgery), however their utility has not been assessed in a mixed patient cohort.

We conducted a pilot study for all admissions to PICU at the Royal Manchester Children's Hospital over a 6 month period to identify risk factors for developing AKI and to measure the correlations between SCr and new AKI biomarkers. We defined AKI as eGFR <100 ml/min/1.73m² (Schwartz formula calculation). We collected urine and plasma from 50 children (age 16 days-15 years, 46% male) for the measurement of Cystatin C, KIM-1 and NGAL. We observed a 30% incidence of AKI in this cohort and age <12 months was a significant risk factor for AKI. New biomarker analysis correlated with SCr in 93% of cases and preceded the rise by 24–48 hours in 20% of patients. The utility of new biomarkers for early detection was limited by the presence of AKI at study entry.

This investigation demonstrates feasibility of new AKI biomarker testing and in combination with risk stratification, could identify children who need to be protected from secondary renal injury during their inpatient admission.

G48

#### OUTCOME OF ACUTE KIDNEY INJURY MANAGED IN A REGIONAL PAEDIATRIC TERTIARY NEPHROLOGY CENTRE

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**Introduction** Acute kidney injury (AKI), characterised by acute decline in renal function is associated with significant morbidity and mortality in children. This study reviewed the aetiology, treatment modalities and outcome of children with AKI managed in the paediatric nephrology unit at the University hospital of Wales, Cardiff.

**Method** Retrospective analysis of referral practises, aetiology, and management of 38 children with AKI over the last 5 years. Outcomes noted as complete recovery, residual renal injury, renal replacement therapy (RRT) dependency or death. Children primarily treated in intensive care were excluded.

**Result** 34% of the total 38 patients were under 5 years of age. Haemolytic uraemic syndrome (HUS) was the commonest cause

of AKI 18/38 (47.3%) with E coli 0157 accounting for most (15/18). Significant number of these cases required dialysis (10/15). 3 children had atypical HUS, one secondary to pneumococcal infection and other 2 with no known cause despite thorough workup. Obstructive renal failure (5 cases) was second most common and renal function improved following relief of obstruction. Overall, supportive management sufficed in 23/38 cases and 15 received renal replacement therapy (RRT). Most children on dialysis were oliguric (14/15). Peritoneal dialysis was the commonest mode of RRT used. 2 children needed plasma exchange. Outcome was equally favourable irrespective of mode of RRT. At 3 months there were no deaths; 29 (76%) had completely recovered, 5 children had estimated glomerular filtration rate (eGFR) between 40- 60 ml/ min/1.73m<sup>2</sup>, 2 had mild to moderate proteinuria and one was hypertensive. One child who remained dialysis dependant with moderate hypertension and proteinuria needed renal transplantation 2 years later. On most recent follow up eGFR had normalised in 2 and improved, between 70-75 ml/min/1.73m<sup>2</sup> in other 3 children. Proteinuria had resolved in one but persisted in the

**Discussion** Prognosis following AKI was excellent in children not needing intensive care probably because of lack of multiorgan dysfunction. HUS was the commonest cause of AKI. AKIs with oliguria are more likely to require dialysis and should be referred early to the nephrology team. All cases should have long-term follow up to ensure renal recovery and detect delayed complications.

G49

# RESILIENCE, POST-TRAUMATIC STRESS, BURNOUT AND COPING IN MEDICAL STAFF ON THE PAEDIATRIC AND NEONATAL INTENSIVE CARE UNIT (P/NICU) – A SURVEY

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**Aims** Working on intensive care (ICU) can be stressful, Adult-ICU studies demonstrate staff burnout and post-traumatic stress disorder, (PTSD) although *resilience* is associated with a healthier psychological state in ICU nurses. This study aims to determine whether resilience is related to the prevalence of burnout and PTSD symptoms in PICU/NICU staff, and to establish any differences in coping strategies with varying levels of resilience.

**Methods** Workplace questionnaire: demographic data, questions on coping strategies and extracts: (1) **Brief Resilience Scale** 6 items scored on a 5-point scale, higher scores indicate greater resilience) (2) **Trauma Screening Questionnaire** 10 statements answered 'yes' or 'no'. Score of > 6 predicts PTSD (3) **abbreviated Maslach Burnout Inventory** — 3 separate subscales: Emotional Exhaustion (EE) = reduced energy and job enthusiasm, Depersonalization (DP) = cynicism, treatment of patients as inanimate, Personal Accomplishment (PA) = Sense of efficacy and effectiveness.

**Results** 58 respondents (50 female) 32 nurses, 22 doctors, 4 other HCPs. Years qualified: Range 0–32; P/NICU experience: Range 0–28 years.

Mean score for resilience = 3.58 (1.83-5) 1 = lowest level of resilience and <math>5 = highest.

Mean burnout measure: PA = 12.5, DP = 2.6 and EE = 8.0 (Scale 'felt this way' 0 = never to 18 = everyday).

All staff admitted to symptoms of emotional exhaustion on some level, 22 experienced some depersonalization. Scores for personal achievement ranged from 2–18.

Higher resilience levels were significantly associated with lower PTSD symptoms (r = -0.41, p = 0.001).

 $10\ \mathrm{HCPs}$  met criteria suggestive of PTSD,  $38\ \mathrm{had}$  lower but concerning scores.