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ABSTRACTS

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O - 01 CAN EARLY RECOGNITION OF AKI IN CHILDREN BE ACHIEVED BY USING AN ALGORITHM (PRELIMINARY RESULTS): ON BEHALF OF BRITISH ASSOCIATION FOR PAEDIATRIC NEPHROLOGY

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Introduction: The aim of the study was to validate recently proposed algorithm 'Standardising early identification of Acute Kidney Injury' introduced by NHS England in a paediatric setting and to investigate recognition and management of AKI. This multi-centre national project was supported by UK Renal Registry and British Association for Paediatric Nephrology.
Material and methods: In part one of the audit, all creatinine measurements performed at each of six centres over a six month period were evaluated electronically using the algorithm. In part two, 180 children from six centres were randomly selected and their case notes reviewed. Here, we report preliminary results on data analysed from two tertiary children's and one district general hospital in the UK. Information was obtained from paper and electronic patient's notes. AKI stage 1 is a rise of >1.5x baseline creatinine level; AKI stage 2 is a rise of>2x baseline and AKI stage 3 is a rise of>3x baseline.
Results: 33,663 creatinine measurements were analysed during the study period using the AKI algorithm. We identified 1,940 AKI 1 episodes (604 children), 479 AKI 2 (158 children) and 756 AKI 3 (112 children). Overall 666 unique children had one or more AKI episodes. We reviewed case notes of 66 children (39 boys) age range 28 days to 17 years. On clinical review of case notes, AKI was recognised in 18 patients (27.3%) only. Of all patients, 17% had prexisting renal condition. 94% children had a follow up arranged with creatinine normalising in 75% of those tested. A third of patients had urine tested and two thirds had medication dosage adjusted to estimated GFR.
Conclusions: The proposed algorithm provides an electronic means of identifying children with AKI and highlighting its severity. Our preliminary data suggest that AKI remains clinically under recognised in clinical settings. Timely recognition and optimal management of AKI is important to improve longer term renal outcomes.

O - 02 EPIGENETIC REGULATION BY HDAC PROTEINS PLAYS A CRITICAL ROLE IN THE PROGRESSION OF RENAL FIBROSIS

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Introduction: Chronic kidney disease is associated with changes in the expression of approximately 10% of the genome. The histone deacetylases (HDACs) are a family of 10 related proteins which are among the most widely expressed and crucial regulators of gene transcription. In this study, we examine the biologic and therapeutic importance of HDAC proteins during disease progression.
Material and methods: Chronic renal injury was modeled *in vivo* in mice by unilateral ureteral obstruction (UUO). The role of HDAC proteins was assessed by using a variety of molecular techniques and treatment with the broad spectrum HDAC inhibitor Trichostatin A (TSA).
Results: UUO leads to a dramatic increase in the protein levels of 9 of the 10 HDAC isoforms. Notably, there is a 6.1-fold increase in HDAC8 expression that localizes specifically to pericyte-derived myofibroblasts, the cell population which accounts for the majority of matrix production during renal fibrosis. To better understand the importance of these findings, we treated mice with the HDAC inhibitor TSA. This resulted in a 3.4-fold increase in the anti-fibrotic gene *BMP7*, a 41.6% decrease in the matrix protein *COLIA1*, and a 61.6% decrease in the myofibroblast differentiation marker α-*SMA* following UUO. These changes in gene expression culminate in a 77.9% decrease in the interstitial proliferative response, a 43.0% decrease in myofibroblast number, 31.1% decrease in renal fibrosis, 42.8% decrease in apoptosis, and a 43.4% decrease in the loss of renal architecture. [All results are $p<0.05$]
Conclusions: Chronic renal injury is associated with a dramatic increase in HDAC protein levels that stimulates pro-fibrotic gene expression and suppresses anti-fibrotic gene expression. Importantly, treatment with HDAC inhibitors reverses these changes in gene expression and inhibits the development of renal fibrosis. This suggests that HDAC inhibitors may serve as effective therapies to inhibit disease progression.

O - 03 ECULIZUMAB TREATMENT IN SEVERE PEDIATRIC STEC-HUS, A MULTICENTRIC RETROSPECTIVE STUDY

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Introduction: Hemolytic and uremic syndrome related to Shigatoxin secreting *Escherichia Coli* infection (STEC-HUS) remains a common cause of acute renal failure in children under 3 years old. No specific treatment has yet been validated in this severe disease. Recently, experimental studies have highlighted the potential role of the complement system in the pathophysiology of STEC-HUS. Eculizumab (EC), a monoclonal antibody directed against terminal complement complex, has then been used in some severe STEC-HUS patients mostly during the german outbreak in 2011 with conflicting results.
Material and methods: On behalf of the French Society of Pediatric Nephrology, we retrospectively studied 33 pediatric patients from 15 centers treated with EC for severe STEC-HUS. EC indication was neurologic involvement in 20 patients, cardiac and neurologic involvement in 8 patients, cardiac involvement in 2 patients and digestive involvement in 3 patients. Based on their clinical and biological parameters at last follow-up, patients were divided in 2 groups of favorable (n=15) and unfavorable global outcome (n=18).
Results: In patients with favorable outcome, 10/12 patients (83%) displayed complete blockade of complement activity (based on the CH50 assay) before each EC reinjection. Conversely, in patients with unfavorable outcome only 9/15 (60%) had complete blockade. Furthermore, among the 28 patients presenting with neurological symptoms, 19 had favorable neurological outcome including 17 patients with recovery just after the first injection of EC. 2 adverse effects in 2 patients potentially related to EC treatment were reported.
Conclusions: These results support the use of EC in severe STEC-HUS patients mostly in those presenting with neurological involvement. Nevertheless, absence of a control group doesn't allow definitive conclusions and prospective trials should be carried out shortly.

O - 04 THE VALUE OF SERUM ANTIBODY DETECTION TO SHIGA TOXIN PRODUCING ESCHERICHIA COLI (STEC) O157 LIPOPOLYSACCHARIDE IN COMPARISON TO FECAL DIAGNOSTICS IN CHILDREN WITH STEC-HUS.

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Introduction: In the majority of pediatric patients, hemolytic uremic syndrome (HUS) is caused by an infection with Shiga toxin-producing Escherichia coli (STEC), mostly serotype O157. It is important to discriminate between HUS caused by STEC or complement mediated HUS (atypical HUS), concerning the difference in treatment and outcome perspectives. STEC and the Shiga toxins can only be detected in the patient's stool for a short time after the onset of disease, due to this the infectious agent may go undetected while using only fecal diagnostics. Serum antibodies to lipopolysaccharide (LPS) of STEC persist for several weeks and therefore could be of added value in the diagnosis STEC.
Material and methods: In this retrospective study, all patients, presented with clinical STEC-HUS between1990-2014 in single center pediatric nephrology department are included. Clinical and diagnostic microbiological data (fecal cultures, fecal toxin assays, PCR for Shiga toxins) were gathered. Serological IgM antibodies against LPS of serotype O157 were detected with ELISA.
Results: The microbiological assays of 66 children diagnosed with STEC-HUS in this period could be collected. Feces cultures were positive for STEC in 28 patients (42%). Serology for O157 antigen was positive in 37 patients (56%). From 50 patients, both serology and feces assays were performed. In these patients, positive fecal tests for STEC were found in 26 patients (52%). Serological antibody assay yielded another 6 patients to be confirmative for STEC (total 64%). This is an added value of 12% when fecal examination is combined with serological antibody assay to confirm the diagnosis STEC-HUS. This test will be extended with other STEC serotypes in the near future.
Conclusions: Serological antibody LPS-O157 assay clearly contributes to the microbiological procedures used in patients with HUS to diagnose STEC-HUS and could be of great importance to diagnose the cause of HUS.

O - 05 MANIFESTATIONS OF ATYPICAL HAEMOLYTIC URAEMIC SYNDROME (AHUS) IN CHILDREN AND ADULTS: DATA FROM THE GLOBAL AHUS REGISTRY

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Introduction: To characterise disease manifestations in paediatric and adult patients enrolled in the global aHUS registry before any, eculizumab,treatment.
Material and methods: All patients diagnosed with aHUS are eligible for enrolment. Exclusions: Shiga toxin *Escherichia coli*-positive HUS or ADAMTS13 activity <5%. Data are collected at enrolment and every 6 months thereafter. Baseline is date of enrolment or immediately before eculizumab treatment, whichever occurred earlier.
Results: A total of 640 patients (243 children; 381 adults) have been analysed. Of these, 17% had a positive family history for aHUS. Mutations were reported in CFH in 22%, MCP in 10%, C3 in 6%, CFI in 3%, DGKE in 10%, thrombomodulin in 3% and CFB in 1% of the patients tested for the respective gene. CFH autoantibodies were detected in 23% of patients tested. Mutation detection rates were similar in adults and children except for DGKE which was found only in children. CFH antibodies were present in 29% of children and 18% of adults tested. Median time between diagnosis and baseline was 0.7 years (interquartile range: 0.0–5.8) during which the overall reported thrombotic microangiopathy rate was 37.1 per 100 person-years; 45.8 per 100 person-years for paediatric patients and 33.0 per 100 person-years for adult patients. In the 6 months prior to baseline, 52% of patients (48% children and 57% adults) had dialysis, and 17% received a kidney transplant. Extra-renal (cardiovascular, pulmonary, central nervous system and gastrointestinal) comorbidities occurred in 9–24% of children and 14–20% of adults.
Conclusions: The aHUS registry is currently the largest aHUS patient database. The baseline analysis shows a high prevalence of genetic abnormalities and extra-renal disease manifestations both in adult and paediatric patients. Further analyses from the aHUS registry will improve our knowledge of the disease.

O - 06 VON WILLEBRAND FACTOR REGULATES COMPLEMENT ON ENDOTHELIAL CELLS AND MAY CONTRIBUTE TO ORGAN SUSCEPTIBILITY TO THROMBOTIC MICROANGIOPATHY

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Introduction: Atypical hemolytic uremic syndrome (aHUS) and thrombotic thrombocytopenic purpura (TTP) are traditionally considered separate entities, with defects in the regulation of the complement alternative pathway (AP) in aHUS, and defects in the cleavage of von Willebrand factor (VWF)-multimers in TTP. Recent studies suggest that both entities are related, as defects in the disease causing pathways overlap or show functional interactions. The aim of this study was to investigate the possible functional link of VWF-multimers and the complement system in TMA pathogenesis.

Material and methods: Blood outgrowth endothelial cells (BOECs) were obtained from 3 healthy controls and 2 patients with Type 3 von Willebrand disease (VWD) lacking VWF. Cells were exposed to a standardized complement challenge via the combination of classical and alternative pathway activation (antibody-mediated sensitization and functional blockade of membrane-bound regulators) and 50% normal human serum (NHS) resulting in complement fixation to the EC surface under static and microfluidic conditions.

Results: Under these conditions we found the expected release of VWF-multimers causing platelet adhesion in control ECs. Importantly, in VWD ECs complement (C3c) fixation ($p<0.05$) and cytotoxicity ($p<0.05$) were more pronounced than in control ECs. Studying primary glomerular ECs (GECs), we found decreased VWF gene expression and protein levels. Immunofluorescence confirmed this resulted from VWF heterogeneity. VWF was positive in 61.5% of GECs, minimally present in 7.7% and absent in 31%.

Conclusions: We determined that VWF-deficient ECs were more susceptible to complement-mediated EC injury contrary to recent suggestions. VWF multimers released by ECs contribute to EC protection by acting as complement regulator. Heterogeneous VWF expression may explain the susceptibility of the glomerular endothelium for the complement-mediated injury in aHUS. Our results provide evidence for a functional link between complement and VWF (or aHUS and TTP).

O - 07 SENSITIVE, RELIABLE AND EASY-PERFORMED LABORATORY MONITORING OF ECULIZUMAB THERAPY IN ATYPICAL HEMOLYTIC UREMIC SYNDROME

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Introduction: Atypical hemolytic uremic syndrome is a severe renal illness caused by complement dysregulation. Treatment with the complement C5 inhibitor eculizumab is effective, but associated with high costs. Laboratory monitoring of these patients with respect to complement function has not been standardized. The aim of this study was to evaluate novel complement functional assays for their application in routine follow-up of eculizumab-treated patients.

Material and methods: Complement activity in serum samples was analyzed using Wieslab® complement screen assay. The presence of eculizumab-C5 complexes in serum, EDTA plasma samples and in urine was measured using ELISA. Levels of sC5b-9 in urine were measured using electroluminescent epitope assay.

Results: First, we documented that the Wieslab® complement screen assay showed a sensitivity of 1-2% of C5 activity by adding purified C5 or normal human serum to a C5 deficient serum. Second, we found that all the patient samples obtained during the standard treatment course, were completely blocked for terminal complement pathway activity. Moreover, complement remained fully blocked when intervals between the eculizumab infusions were extended to four weeks. Levels of complexes between eculizumab and C5 were inversely correlated to the complement activity ($p=0.01$). Third, titrating serum from eculizumab-treated patients into normal serum, revealed that eculizumab was present in excess up to four weeks after infusion. Finally, we showed that increased urine sC5b-9 disappeared after eculizumab treatment.

Conclusions: We demonstrate sensitive, reliable and easy-performed assays to monitor eculizumab-treated patients, which can be used to design individual dosage regimens.

O - 08 EARLY DIAGNOSIS AND TREATMENT ARE CRUCIAL IN COBALAMIN-C DEFICIENCY-ASSOCIATED THROMBOTIC MICROANGIOPATHY

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Introduction: Cobalamin-C (CblC) deficiency is a rare cause of atypical hemolytic-uremic syndrome (aHUS). Thrombotic microangiopathy (TMA) due to CblC deficiency may manifest as aHUS and/or pulmonary arterial hypertension (PAH).We aimed to describe the genotype, phenotype, treatment, and outcome of CblC deficiency associated TMA in children.

Material and methods: Survey within the ESCAPE Network

Results: 19 children (inc. 3 sibling/cousin pairs) with CblC associated TMA were reported. All patients had mutations in MMACHC; 8 patients were homozygous (7x c.271dupA, 1x C464G>A), 11 compound-heterozygous (involving c.271dupA and/or c.276G>T).

Age at onset was 7 days to 14 (median 0.9) years. Ten patients presented with isolated aHUS, 8 with aHUS combined with PAH, and one child with isolated PAH. In 3/8 children with both conditions aHUS and PAH occurred simultaneously, whereas in 5 children PAH was diagnosed 2.5-7 years following aHUS.

LDH was elevated and haptoglobin undetectable in all patients, 12 were anemic and 16 thrombocytopenic. Mean serum homocysteine was 145 (53-207) μmol/L (normal<12). In four children CblC deficiency was diagnosed only post-mortem and in another three patients 6 to 19 years after first manifestation of aHUS. Eight children required dialysis, four were treated with plasma exchange, and one child unsuccessfully with eculizumab.

Seven children died, five at disease onset and two 5 and 7 years later from PAH complications.

Five of these seven patients had not received any vitamin B12 supplementation. Of those twelve children with timely start of hydroxycobalamin therapy, six have normal renal function, four CKD 2-5 and two are post-renal transplantation. Seven of the twelve survivors suffer from neurocognitive impairment.
Conclusions: CblC deficiency associated TMA is a most likely underdiagnosed disease entity with high mortality. With respect to the clear beneficial effect of a timely diagnosis and treatment, CblC deficiency should be excluded in all TMA patients by serum homocysteine measurement.

O - 09 ARTERIAL HYPERTENSION IN CHILDREN WITH HEMOLYTIC UREMIC SYNDROME AFTER KIDNEY TRANSPLANTATION

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Introduction: The development of arterial hypertension after kidney transplantation is a well known complication. Hemolytic uremic syndrome (HUS) is a systemic disease associated with arterial hypertension during long-term follow-up. Our goal was to report on the severity of arterial hypertension after kidney transplantation (KTX) in patients with typical and atypical HUS.
Material and methods: We analysed the course of 197 HUS patients, of which 22 (n=10 with typical HUS; n=12 with atypical HUS) developed ESRF and received KTX as renal replacement therapy. We analyzed data from 1766 casual blood pressure (BP) and 85 24-hour (ambulatory blood pressure monitoring) ABPM measurements. In addition, we evaluated the used antihypertensive strategy.
Results: Comparison between the two patient groups revealed that patients with atypical HUS had significantly higher casual SBP- and DBP-SDS values after KTX despite similar intensity of antihypertensive treatment. This data was supported by analysis of ABPM profiles showing comparable results for the interval 1 to 5 years after KTX. Patients with atypical HUS had a greater severity of arterial hypertension despite similar treatment strategies and intensity of treatment.
Conclusions: Our observation, even though in a small cohort, supports recent genetic studies showing arterial hypertension closely associated with HUS-causing mutations in patients with atypical HUS.

O - 10 HOW GOOD IS DOPPLER ULTRASOUND, MAGNETIC RESONANCE ANGIOGRAPHY (MRA), COMPUTED TOMOGRAPHY ANGIOGRAPHY (CTA) AND DMSA TO DIAGNOSE RENAL ARTERY STENOSIS?

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Introduction: To evaluate the role of doppler ultrasound, magnetic resonance angiography (MRA), computed tomography angiography (CTA) and DMSA compared to digital subtraction angiography (DSA) in the diagnosis of renal artery stenosis in children.
Material and methods: A retrospective review of data and images for all children with suspected renovascular hypertension who were referred to Great Ormond Street Children's Hospital between 2006 – 2014 was performed. This analysis includes 127 patients with performed angiography.
Children have been referred either based on a positive MRA or CTA result or based on clinical suspicion of renovascular hypertension.
Results: 127 children with suspected renovascular disease underwent angiography during the study period. 98 of 127 children were diagnosed with renovascular disease. On the basis of their renal angiograms, 37 of those had unilateral renal artery stenosis, 49 bilateral renal artery stenoses, 31 midaortic involvement and 12 intrarenal disease. 79 patients were treated with a percutanous transluminal angioplasty during the same procedure.
All children were evaluted with doppler ultrasound and 97% of children with DMSA scan. MRA was performed in 38 of 127 children (30%) before referral, CTA in 33 of 127 children (26%).
MRA showed a sensitivity of 81%, CTA of 84% in relation to number of kidneys, whereas the specifity was only 60% and 73%. MRA missed the diagnosis of renal artery stenosis in 4 children (11%), CTA in 2 children (6%). Renal doppler ultrasound showed a specificity of 100% with a sensitivity of only 65%. DMSA scan had a sensitivity of 63% with a specifity of 62%.
Conclusions: MRA and CTA are increasingly used in the diagnosis of renovascular hypertension in children. Both examinations can miss relevant renovascular disease or find suspected lesions not confirmed on the formal DSA. Angiography remains the gold standard to rule out renovascular hypertension.

O - 11 ANGIOTENSIN CONVERTING ENZYME INHIBITORS IN PEDIATRICS: STATE OF THE ART

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Introduction: Angiotensin-converting enzyme inhibitors achieved widespread usage in the treatment of children with hypertension. Despite the incentives from the FDA Modernization Act of 1997, the problem of insufficient labelling information for paediatric dosing, safety or efficacy remains.
Material and methods: A systematic review of the literature has been performed to summarize the current evidence of the dosing, safety or efficacy of ACEI in hypertensive children.
Results: The evaluation of the PK properties of captopril in 10 children (>3,5years) with chronic kidney failure and in 10 infants (2-15months) with chronic heart failure showed similar PK parameters as in adult. No RCT for captopril have been performed, only 4 small prospective studies (n=9-73) in mainly children with secondary hypertension, showing significantly and persistent blood pressure reduction. Two studies in 20 neonates (25-43weeks) demonstrated increased sensitivity for side effects. The PK properties of lisinopril in 46 children and infants (>6months) had been evaluated in a prospective trial. The efficacy and safety of lisinopril have been evaluated in one prospective (n=46) and one RCT (n=115, only >6years), and showed an effective, dose dependent blood pressure reduction with good tolerance. PK properties of enalapril have been evaluated in one study of 40 children (>2months). The safe antihypertensive effect of enalapril have been demonstrated by two large RCT, in respectively 110 children (>6year) and 281 children (>6years). However, no data children >6years receiving enalapril is available. One RCT (n=253, >6years, secondary hypertension) and two prospective studies (n=14, >5years, renal hypertension, and n=385, >3years, renal hypertension) have proved the effectively and safety profile of respectively fosinopril and ramipril. However, no PK parameters for fosinopril and ramipril in hypertensive children are available.
Conclusions: Paediatric dosing, safety or efficacy of ACE inhibitors is still poorly studied with valuable RCT and PK studies. Especially in younger children (< 6 years) and infants evidence is poor.

O - 12 PREVALENCE, DIAGNOSES AND POSTNATAL OUTCOME OF ANTENATAL DIAGNOSED ANOMALIES OF THE KIDNEY AND URINARY TRACT

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Introduction: Children with congenital anomalies of the kidney and urinary tract(CAKUT) have increased risk of upper urinary tract infection(UTI), renal insufficiency and hypertension. Since 2004 all pregnant Danish women have been offered routine prenatal screening ultrasound and since 2006 we have had a Danish CAKUT-consensus report. Aim of this study is to determine incidence and type of prenatally diagnosed CAKUT after introduction of routine prenatal screening ultrasound, to quantify infant morbidity, and to evaluate the efficacy of the Danish consensus report.
Material and methods: This cohort study include consecutive cases with prenatally diagnosed CAKUT by ultrasound in second and third trimester at Hvidovre Hospital, who were either terminated before the end of 22 gestational weeks or born in the 8-year period 2006-2013. In this period 95% of pregnant women had prenatal screening ultrasound. Postnatally the patients were followed until June 2014. If surgery was indicated, patients were referred to Rigshospitalet. The patients were examined after the Danish CAKUT-consensus report.
Results: In the cohort of 50,193 cases the CAKUT-incidence was 0.39% prenatally, 0.29% in first postnatal ultrasound (median: 7 days) and 0.22% at the end of follow-up (median: 4.1 years). Within the follow-up period and among patients with CAKUT verified postnatally; 25% had at least one UTI, 26% had surgical intervention related to CAKUT, 4% had impaired kidney function and 2% renal hypertension. The frequencies of spontaneous normalization, UTI and surgery differed with prenatal anterior-posterior diameter of the renal pelvis at 10-12mm, 12-15mm and >15mm, respectively ($p<0.0001$, $p=0.0367$, $p<0.0001$).
Conclusions: The observed incidences of prenatally diagnosed CAKUT are lower than previously reported. Frequency of termination and ultrasound selection criteria are major confounding factors. The Danish consensus report is a valuable tool.

O - 13 PREDICTING CHRONIC KIDNEY DISEASE IN INFANTS AND YOUNG CHILDREN WITH POSTERIOR URETHRAL VALVES: OBJECTIVE ANALYSIS OF INITIAL ULTRASOUND KIDNEY CHARACTERISTICS AND VALIDATION OF PARENCHYMA AREA AS FORECASTERS OF RENAL RESERVE

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Introduction: Obstructive uropathy secondary to posterior urethral valves (PUV) is a common cause of chronic kidney disease (CKD) in childhood. There are few early markers to help prognosticate an individual child's risk of renal deterioration. Based on recent data estimating renal mass by measuring the renal parenchymal area (RPA), we hypothesized that early measurement of both quantity (RPA) and quality (renal echogenicity [RE] and cortico-medullary differentiation [CMD]) of the total renal mass could help predict future function. We sought to validate existing RPA data and evaluate RE and CMD as forecasters of renal reserve.
Material and methods: Initial postnatal US images from serial children diagnosed with PUV were analyzed using NIH sponsored image-processing software. Echogenicity was objectively measured as a ratio relative to the adjacent liver or spleen. CMD was calculated by indexing the pixel density of identically sized areas of the renal cortex and medulla from a single representative US image. The primary outcome, renal function at last follow up, was determined based on serum creatinine and need for renal replacement therapy (CKD).
Results: 75 patients were evaluated; 16 of these had progressively developed CKD at a median follow up of 58.8 (IQR=30.8-94.7) months. Mean RPA was 21.41 cm^2 in Non-CKD vs 16cm^2 in CKD groups ($p<0.001$). Mean CMD was 1.77 in Non-CKD vs 1.21 in CKD ($p<0.001$). Bilateral echogenic kidneys were associated with development of CKD ($p=0.004$). These findings remained statistically significant on multivariable and time to event analyses. CMD index showed a trend that reflects deterioration as measured by serum creatinine at last follow-up.
Conclusions: RPA, CMD, and RE, measured on initial postnatal US have prognostic value for determining risk of CKD in PUV patients. These data are promising for developing prognostic tools to help risk stratify patients, counsel parents, and help plan monitoring protocols for children with PUV.

O - 14 OUTCOME OF CHILDREN WITH PRUNE BELLY SYNDROME

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Introduction: Prune Belly Syndrome (PBS) is one of the important causes of end stage renal disease in infants and very young children who were believed to have poor outcome on renal replacement therapy (RRT) and transplantation. However, valid outcome data for PBS are missing.
Material and methods: Patients aged < 20 years who started RRT between 1990 and 2012 in 34 countries providing data to the ESPN/ERA–EDTA Registry were included in the study.
Results: Eighty-six patients with PBS were identified. One thousand thirty five patients with congenital obstructive uropathy (COU) and 1905 patients with congenital renal hypoplasia (CRH) or dysplasia (CRD) served as controls. Median age at onset of RRT was 7.4 (IQR: 1.6-11.7) years in the PBS group, significantly lower compared to patients with COU (9.6; IQR:3.2-14.0 years). Unadjusted ten-year patient survival was 88% for PBS, 94% for COU and 92% for CRH and CRD. The age- and sex-adjusted survival of PBS was similar to CRH and CRD (HR:1.62, 95% CI:0.88-2.95), but significantly higher as compared to COU (HR:1.72, 95% CI:1.01-2.93). Seventy four (86%) patients with PBS received first kidney transplantation after a median time on dialysis of 7.6 (IQR: 0.0-20.8) months. The time spent on dialysis before transplantation was similar in PBS patients and controls, as was the chance of receiving a first renal transplant within 5 years. After adjustment for sex and age at transplantation, death-censored risk of graft loss was not

significantly different for patients with PBS as compared to patients with COU (HR: 0.95, 95% CI: 0.64-1.42) or patients with CRH or CRD (HR: 1.10, 95% CI: 0.72-1.69).

Conclusions: This study in the largest cohort of patients with PBS receiving RRT to date demonstrates that the outcome of patients with PBS on dialysis and transplantation are not different from that of patients with RRT for other forms of CAKUT. Although, the survival of PBS was significantly higher than COU, this difference is unlikely to be clinically relevant.

O - 15 ESRD IN INFANTS: ATTITUDES OF PAEDIATRIC NEPHROLOGISTS AND INTENSIVISTS. A FRENCH NATIONAL SURVEY

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Introduction: Dialysing infants with ESRD is feasible, time-consuming and burdensome. European registers allowed spreading data on medium-term follow-up. Medical practices depend on advancing technology and cultural and legislative background. We aimed at drawing an objective map of current medical decision making process and practices in France in neonates with pre- and ESRD.

Material and methods: French national internet survey. Paediatric nephrologists and neonatal and paediatric intensivists answered questions *a priori* or related to case reports.

Results: 135 doctors from all over France answered the national enquiry, 104 senior doctors and 31 junior neonatologists.

A priori questions revealed 48% doctors were willing to start RRT in new-borns with ESRD, 68% agreed for palliative care. When neurological development was compromised, 18% favoured RRT and 84% palliative care. In pre-ESRD, 76% doctors chose RRT, 33% palliative care and this increased to 60% in case of neurological impairment.

In antenatal care, 90% decided TOP in case of severe kidney hypoplasia with oligohydramnios, 15% performing terminal sedation in the delivery room and 60% treating discomfort rather than protecting residual kidney function. TOP choice was less precise in case of syndromic hypoplastic hyperechogenic kidneys with uncertainty regarding time at ESRD and degree of neurological development.

In a neonate with APKD, 15% thought palliative decision only concerned intensivists.

Difference in attitudes chosen by paediatric nephrologists were: more surgery and RRT in new-borns with CAKUT (respectively 81% *versus* 58%, and 77% *vs.* 52%, P<0.05), and less importance left to the intensivists in all decisions taken.

Parents' point-of-view was always of importance.

Width of the sanitary region < 2.5 million inhabitants favoured RRT in ESRD infants. Doctors with experience > 21 years sought more for consensus among all doctors and parents, whereas some junior doctors thought parents should not decide.

Conclusions: Such decisions are multi-factorial, and remain case-specific.

O - 16 TARGETED PANEL SEQUENCING OF 399 RENAL GENES RECLASSIFIES PRIMARY DISEASE DIAGNOSES IN YOUNG ESRD PATIENTS

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Introduction: About 20% of patients with end stage renal disease (ESRD) before age 30 do not have a primary renal disease diagnosis. Undetected genetic renal disease may hamper their transplantation career and leaves relatives at risk undetected. So far, genetic studies have focused on specific clinical diagnoses. We took an innovative approach by sequencing a panel of 399 renal disease genes in 200 cases with ESRD onset before age 30, regardless of their clinical diagnosis.

Material and methods: We designed the "RENome" using SureSelect/Agilent with 399 genes involved in hereditary renal disease and/or urinary tract development. We used SOLiD™ 5500XL for sequencing and an in-house developed bioinformatics pipeline for mapping, variant calling and QC. Variants were annotated using CARTAGENIA software.

Samples were selected (based on age at onset of ESRD) from the REGaTTA cohort.

Quality parameters: Median sequence coverage per sample: 108X (48X-198X). On average >95% of in target bases were genotyped, with >99% sensitivity and specificity. Out of a first selection of 180 variants, 92% were validated as true positives. On average >95% of in target bases were genotyped, with >99% sensitivity and specificity. Stringent filtering criteria allowed only for coding variants with percentage variant reads of >15%, either novel or with allele frequency of <0.005, that were listed as disease-causing in HGMD Pro, had a SIFT score <0.05 and were not predicted to be benign in PolyPhen2. 54 variants in 46 (of 132) cases were manually curated. We also selected samples with likely homo- or hemizygous whole gene deletions.

Results: Our strict filtering strategy yielded a molecular diagnosis in 19 out of the first 132 patients (14.4%), confirming the registered primary disease in 11, and unexpectedly reclassifying it in 8 (6%). Examples of revised diagnoses are a patient who is registered as having IgA-nephropathy with an *ACTN4* mutation (FSGS), and two patients with CAKUT diagnoses, with a nephronophthisis genotype. It should be noted that for the confirmed clinical diagnoses, the fact that the disease is hereditary and might occur in relatives was not alway known (illustrated by a case with oligomeganephronia and a *PAX2* mutation). An extended filtering strategy, for the whole cohort (200 samples), will be presented at the meeting.

Conclusions: Considering the stringency of filtering, these numbers underestimate the diagnostic potential of our innovative approach. Adding early RENome sequencing to the diagnostic work-up in young ESRD patients, is likely to improve etiologic classification and genetic counseling. We do not only detect new diagnoses in patients with previously unknown diagnoses, but also likely revise the diagnosis in at least 6% of patients. Therefore our data unequivocally demonstrate the added value of routine panel based genetic testing in all young adult ESRD patients, and hint at the potential in adolescent kidney disease patients.

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O - 17 CHARACTERIZATION OF THE MUTATIONAL LOAD IN 152 PATIENTS WITH BARDET-BIEDL SYNDROME AND IDENTIFICATION OF C8ORF37 AS A NEW GENE FOR BBS

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Introduction: Bardet-Biedl syndrome (BBS) is a clinically and genetically heterogeneous ciliopathy. Primary features are obesity, polydactyly,

retinal dystrophy, renal abnormalities, hypogonadism and learning difficulties, but most patients do not present with the full clinical picture. Phenotypic and genetic overlap exists with other cilia-related disorders.
Material and methods: We performed genetic testing in 152 unrelated BBS patients which represents the largest study to date. Initially, we tested for the *BBS1* and *BBS10* hotspot mutations. NGS multi-gene panel testing for ciliopathies (currently targeting 381 genes) was performed in 91 patients.
Results: More than 95% of typical BBS patients harboured mutations in one of the known disease genes. We identified homozygous or compound heterozygous mutations in a single *BBS* gene or *ALMS1* in all but four families who fulfilled the diagnostic criteria. Most mutations were not described so far. High-coverage NGS enabled the detection of causative copy-number variations which were key to the diagnosis in hitherto unsolved constellations. All deletions would have been most probably missed by conventional techniques, as no MLPA kit is available for any of the *BBS* genes. Most patients carried additional mutations at other loci. However, in contrast to published data in favour of oligogenic inheritance patterns, we postulate a recessive disease model for BBS in which modifiers may play a role for variable expressivity. In a BBS patient without a mutation in recognized genes, we were able to identify a convincing homozygous mutation in *C8orf37* as a new gene for BBS.
Conclusions: Overall, our study widely resolves the long-standing enigma of triallelic or oligogenic inheritance in BBS. The data is of major importance for genetic counselling, prenatal diagnostic testing and the clinical management of patients with Bardet-Biedl syndrome.

O - 18 EVIDENCE FOR A DOSAGE-SENSITIVE MUTATIONAL NETWORK IN A COHORT OF 308 PATIENTS WITH EARLY AND SEVERE FORMS OF POLYCYSTIC KIDNEY DISEASE

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Introduction: Polycystic kidney disease (PKD) is the most common potentially life-threatening human genetic disorder. In addition to recessive ARPKD, 2-5% of patients with dominant ADPKD show early and severe disease. Genetic testing is cumbersome because of the size and structure of major disease genes and increasing genetic heterogeneity.
Material and methods: We established a novel customized sequence capture based Next-Generation Sequencing (NGS) panel for PKD that allows the parallel analysis of 95 genes that are currently targeted. By using high-coverage NGS data and a comprehensive bioinformatics approach, we extended our analysis to additionally uncover copy number variations (CNVs). All mutations and CNVs detected by NGS were subsequently validated by Sanger sequencing and MLPA.
Results: We analysed a cohort of 308 patients with early and severe PKD. The majority of patients carried mutations in *PKD1*, *PKD2*, and *PKHD1*, however a subgroup harboured mutations in genes typically related to other ciliopathies such as nephronophthisis, Joubert, Meckel, and Bardet-Biedl syndrome. We demonstrate that *PKD1* is a driver for early and severe manifestations in families with dominant ADPKD. Notably, mutations in both ADPKD genes can also be identified in patients with recessive PKD. A proportion of patients carry aggravating mutations in more than just one single gene/allele in the context of a functionally proven dosage-sensitive network. Zebrafish and Xenopus are used as models for validation of some of our findings.
Conclusions: This is the most comprehensive study performed so far by which we propose a dosage-sensitive model for early and severe forms of PKD. Our NGS panel allows the parallel analysis of all disease genes including the pseudogene-variable *PKD1* gene which plays a decisive role in cyst initiation. An accurate genetic diagnosis is crucial for genetic counselling, prenatal diagnostics and the clinical management of patients.

O - 19 LONG-TERM RENAL OUTCOME OF A LARGE COHORT OF PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX

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Introduction: Tuberous Sclerosis Complex (TSC) is an autosomal dominant neurocutaneous disorder characterized by the growth of hamartomas in multiple organs. Renal involvement represents the second most important cause of morbidity and mortality at all ages, and the most common cause of mortality after the age of 30 years. However, very little is known about the natural history of these renal features in adults and even less in children and adolescents affected by TSC. The purpose of this study is to explore the renal phenotype and long-term renal outcome in a large TSC cohort.
Material and methods: We assessed the clinical records and the renal imaging of TSC patients from two tertiary hospitals in a cross-sectional study. Demographics, renal phenotype, renal outcome and co-morbidity data were assessed retrospectively.
Results: We included 82 TSC patients, 50 females (61%) with a male/female sex ratio of 1.6. Fifty (62%) patients were younger than 18 years. Median (minimum-maximum) age at last follow-up was 15.4 (1.4-72.5) years with a median follow-up duration of 11.1 (0.9-56.6) years. Presenting features (N=69) were neurological complications in 45 (55%) patients and only 4 (5%) patients had renal symptoms as the first clinical sign. *TSC1* and *TSC2* mutations (N=63) were found in 17 (27%) and 37 (59%) patients respectively. Two patients (3%) had a contiguous gene deletion syndrome. Renal ultrasound at last follow-up (N=65) showed renal angiomyolipomas in 39 (59%) patients and renal cysts in 36 (55%) patients. Renal function (N=73) showed end-stage-renal-disease (ESRD) in 6 (8%) patients with a median age at start of renal replacement therapy of 47.0 (21.0-64.0) years. Estimated glomerular filtration rate (eGFR) was <90 ml/min/m² in 24 (33%) TSC patients. Three of the 6 patients with ESRD underwent a nephrectomy due to renal cell carcinoma (RCC). Hypertension (N=60), proteinuria (N=41) and renal complications (bleeding, RCC or surgery) were found in 14 (23%), 6 (15%) and 9 (11%) patients respectively.
Conclusions: This study describes the long-term renal outcome in a large cohort of TSC patients. Our findings confirm the high rate of renal involvement in TSC. Therefore, we advocate regular renal surveillance of these patients for the timely and optimal managing of the renal co-morbidities.

O - 20 EFFECT OF EVEROLIMUS ON RENAL ANGIOMYOLIPOMA IN PEDIATRIC PATIENTS FROM THE FINAL ANALYSIS OF EXIST-1

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Introduction: Data from the final analysis of the EXIST-1 study (NCT00789828) are presented to assess the long-term effect of everolimus on renal angiomyolipoma in pediatric patients being treated for tuberous sclerosis (TSC)–associated subependymal giant cell astrocytoma (SEGA).
Material and methods: Patients (any age) with TSC and new or worsening SEGA were randomly assigned (2:1) to receive everolimus 4.5 mg/m2 (target blood trough 5-15 ng/mL) or placebo. After achieving positive results for SEGA response rate (primary endpoint) during the study's core phase (cutoff March 2, 2011), all remaining patients could receive open-label everolimus in an extension phase. This post hoc analysis focuses on the subset of patients <18 years of age with ≥1 target renal angiomyolipoma (lesion longest diameter ≥1.0 cm). Renal angiomyolipoma response rate was defined as the proportion of patients with ≥50% reduction in renal angiomyolipoma volume relative to baseline, with no new lesions ≥1 cm in longest diameter, no increase in kidney volume ≥20% from nadir, and no angiomyolipoma-related bleeding grade ≥2 (CTCAE, version 3.0). Adverse events (AEs) were assessed every visit and graded using CTCAE, version 3.0.
Results: In total, 33 patients aged <18 years with target renal angiomyolipoma received ≥1 dose of everolimus and are included in this analysis (cutoff October 2, 2014). Median (range) age was 11.5 (5.4-17.5) years. Median duration of everolimus exposure was 44.8 months. Renal angiomyolipoma response rate was 75.8% (95% confidence interval [57.7%-88.9%]). The most common AEs experienced in ≥20% of these patients included convulsion and mouth ulceration (45.5% each), stomatitis (42.4%), cough (27.3%), nasopharyngitis (24.2%), and headache, sinusitis, and upper respiratory tract infection (21.2% each). Four patients (12.1%) experienced a drug-related serious AE. Three patients (9.1%) discontinued due to an adverse event.
Conclusions: Everolimus appears safe and effective in the long-term reduction of renal angiomyolipoma volume in patients aged <18 years treated for TSC-associated SEGA.

O - 21 EARLY FLUID OVERLOAD IS ASSOCIATED WITH ACUTE KIDNEY INJURY AND PREDICTS PICU MORTALITY IN CRITICALLY ILL CHILDREN

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Introduction: Fluid overload (FO) has been associated with an increased risk for adverse outcomes in critically ill patients. Information on the impact of FO on mortality in a general population of pediatric intensive care unit (PICU) is limited. We aimed to determine the association of early FO with the development of acute kidney injury (AKI) and mortality during PICU stay and evaluate early FO as predictor of mortality, even after adjustment for illness severity assessed by pediatric risk of mortality (PRISM) III score.
Material and methods: This prospective study enrolled 370 critically ill children admitted to the PICU. The early FO was calculated based on the first 24-hour totals of fluid intake and output after admission and defined as cumulative fluid accumulation ≥5% of admission body weight.
Results: Of the patients, 64 (17.3%) developed early FO during the first 24 hours after admission. The PICU mortality rate of the whole cohort was 18 of 370 (4.9%). The independent factors significantly associated with early FO were PRISM III score (unstandardized coefficients [B] =0.163, standard error [SE] =0.041, p <0.001), age (B =-1.093, SE =0.304, p <0.001), AKI (B =2.584, SE =0.878, p =0.003), and blood bicarbonate level at admission (B =-3.668, SE =1.519, p =0.016). The early FO was associated with AKI (odds ratio [OR] =1.31, 95% CI =1.17-1.46, p <0.001) and mortality (OR =1.36, 95% CI =1.20-1.55, p <0.001). The association of early FO with mortality remained significant after adjusting for potential confounders including illness severity assessed by the PRISM III, age, the use of mechanical ventilation, and the presence of AKI (OR =1.17, 95% CI =1.01-1.37, p =0.035). The area under-the-receiver-operating-characteristic curve (AUC) of early FO for predicting mortality was 0.78 (95% CI =0.65-0.91, p <0.001), which was not better than PRISM III score (AUC =0.85, 95% CI =0.74-0.96, p <0.001). However, there was no significant difference between the two AUCs (p =0.422).
Conclusions: Early FO was associated with increased risk for AKI and mortality even after adjustment. A higher early FO was independently predictive of PICU mortality in critically ill children.

O - 22 NON LINEAR TRAJECTORIES OF GFR IN CHILDREN WITH CKD: A BAYESIAN APPROACH

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Introduction: Change in glomerular filtration rate (GFR) is a key element of surveillance in children with chronic kidney disease (CKD). Decline of GFR over time has been mainly estimated by linear or log-linear regressions which are practical but too simplistic approaches for such complex situations. Moreover, epidemiological studies amongst CKD adults go against the assumption of linear decline of GFR.
Material and methods: Longitudinal data from 90 children with CKD (GFR 20-75 ml/min/1.73 m² at inclusion) followed at a single centre between January 2008 and January 2015 (median follow-up 45 months [IQR 28-61]) were collected and censored at the date of last follow-up or first renal replacement therapy. GFR was calculated every 3-6 months according to the updated Schwartz formula. A Bayesian model was performed to estimate each individual's GFR trajectory allowing for estimating probabilities of nonlinear progression and of non progression. For each patient, the Bayesian approach product 1,0000 curves (Monte-Carlo samples) to approximate the a posteriori distribution of all parameters. The yearly slope was calculated by the average of these curves. A trajectory was defined as nonlinear if the mean slope for the half of follow-up with faster decline and the mean slope for the other half with slower decline differed by > 5 ml/min/1.73 m²/year. The posterior probability that a patient's GFR trajectory was nonlinear was then calculated as the proportion of the 1,000 Monte-Carlo trajectories that satisfied this criterion.
Results: A third of children (n=31) reached ESRD and required RRT during the follow-up. The majority of children (n=55, 61%) had a significant probability (> 0.5) of having either a nonlinear trajectory or a prolonged non progression period (probability > 0.5). Ten patients (11%) had both a substantial period of stable or increasing GFR and a substantial period of rapid GFR decline. Baseline GFR > 45 ml/min/1.73 m², hypodysplasia as primary renal disease, and urine protein-creatinine < 100 mg/mmol were factors associated with a higher likelihood of a non progression period.
Conclusions: Contrary to the paradigm of a steady linear decline of GFR over time, most children with CKD experience a nonlinear progression of GFR or periods of non progression. These findings may be helpful for physicians to counsel patients and families on the planning for ESRD care.

O - 23 THE PD MEMBRANE IN HEALTH, UREMIA AND PD – RESULTS FROM THE INTERNATIONAL PEDIATRIC PERITONEAL DIALYSIS BIOPSY BANK

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Introduction: The global pediatric PD biobank systematically defines age dependent PD membrane ultrastructure in health, the impact of uremia and of PD treatment over time.
Material and methods: 297 standardized peritoneal and 183 omental specimens were obtained in 28 centers (15 countries) from 96 healthy children and 31 adults (0.1-65.0 years), 101 children at time of first PD catheter insertion and from 76 children on PD (0.1-20.1 years), 64 children treated with low GDP fluid. Stained sections underwent automated analysis (Aperio®).
Results: In controls the calretinin/podoplanin/CA125 stained mesothelial cell layer was largely intact, a submesothelial compact zone, as described in adult PD patients, not delineated. Median total submesothelial zone thickness increased from 258 in infants to 378μm in adolescents. Submesothelial capillaries, lymphatic vessels and nerve fibers were predominately located in 3 distinct layers, 36, 96 and 192μm below the mesothelium. Total vascular exchange area decreased with age (7.6/2.4/1.8/2.1/2.5% of peritoneal surface area below 1/2/6/12/18 years), lymphatic vessel density was age-independent. Uremia induced minor peritoneal inflammation.
At PD onset the mesothelial cell layer was intact in 72% of the patients and in 59 and 21% after ≤ and >2 years of PD. In patients on low GDP dialysis submesothelial thickness, vessel density, endothelial exchange area, ASMA positive, activated fibroblast, CD45/CD68+ macrophage number, VEGF and TGF-ß induced pSMAD abundance increased with time. Capillary morphology and lymphatic vessel density, however, remained unaltered. Epithelial to mesenchymal transition and CD90 positive fibroblasts were mainly detected with high GDP dialysis, capillary and lymphatic vessel angiogenesis was more pronounced. Transcriptomics (Illumina®) and proteomics (tandem mass tag-based LC-MS) of microdissected vessels point to a central role of the complement system.
Conclusions: The healthy peritoneum exhibits substantial age dependent particularities, which disappear during PD. Major time-dependent peritoneal membrane transformation develops with low GDP dialysis, albeit distinct and less pronounced than with high GDP fluid usage.

O - 24 THE CONCEPT OF ADAPTED APD (A-APD): PROVE THE PRINCIPLE

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Introduction: It is of importance to individualize the prescription of patients on peritoneal dialysis (PD), taking into account his peritoneal permeability (dwell time) and his body surface area (fill volume). The concept of adapted automated PD (A-APD) is based on the impact of varying dwell time and fill volume on peritoneal exchange permeability: a short small cycle favors ultrafiltration (UF), conversely, a long large cycle favors purification[1,2]. This concept of a sequence of short small cycles before a sequence of long large cycle (A-APD) has been suggested to be more efficient regarding solute and water removal as compared to a standard regime (conventional APD, a repetition of the same fill/dwell time).
Material and methods: We performed a modified peritoneal equilibration test (PET) in 4 children (12 to 35 kg body weight): either two consecutive cycles each consisting of 1000mL/m^2 volume and of 75 min dwell time, or a short small cycle (600mL/m^2 for 30min) followed by a long large cycle (1400mL/m^2 for 120 min). This PET was analyzed regarding clinical symptoms, UF and dialysis adequacy parameters, intraperitoneal pressure and bioimpedance (hydration before the PET).
Results: The superiority of delivering the same amount of dialysate (2L/m^2) over the same duration (150min) applying a short small cycle before a long large cycle compared to the repetition of two identical cycles in terms of dwell/fill could be shown:

	Conventional APD 1L/m^2-75 min +1L/m^2-75 min	A-APD 0.6L/m^2-30 min +1.4L/m^2-120 min	Balance individual mean changes (%)
UF (ml)	-30	+125	+131(-44 to+257)
Na removal (mmol)	+2.8	+12.2	+39.9 (-74 to+178)
Glucose absorbed (mmol)	+48.4	+43.1	-12.8 (-38 to 7.8)

Conclusions:
Conclusion: Based on this pilot study, the European Dialysis Working Group should conduct a multicenter study.
[1] *Advances Perit Dialysis 1994*; *10*: *307-309*;
[2] *Perit Dial Int 2011*; *31*: *450-458*

O - 25 VASCULAR ACCESS CHOICE AND COMPLICATIONS IN PEDIATRIC HEMODIALYSIS: FINDINGS FROM THE INTERNATIONAL PEDIATRIC HEMODIALYSIS NETWORK (IPHN)

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Introduction: To compare the performance of different hemodialysis access modalities documented in the International Pediatric Hemodialysis Network (IPHN) Registry.
Material and methods: Analysis of 394 prospective records of 234 chronic HD/HDF patients from 31 pediatric dialysis units in 19 countries.
Results: 172 patients (73%) had central venous lines (CVL), 58 (25%) arteriovenous fistulas (AVF), and 4 (2%) grafts (AVG) as initial access. The choice of vascular access was driven by patient age, which averaged 11.5±5.1 (range 0.3-19) yrs in patients started on CVL vs. 16±3.6 (range 4.2-20) yrs with AVF/AVG ($p<0.001$). 21 patients (9%) had transient CVL before AVF placement. Access placement-related complications (thrombosis, hemorrhage, infection) were reported in 10 patients with AVF (16%) and 8 patients with CVL (5%). The predominant site for CVL was right internal jugular vein (n=125, 73%), while AVF/AVG was most often placed on left forearm (n=21, 34%). Infectious complications (n=34) were exclusively reported with CVL at a rate of 1/40 months, requiring CVL removal in 44% of cases. Catheter malfunction (n=69, rate 1/18 mo), defined most commonly as insufficient blood flow (39%), leakage/breakage (19%) or obstruction (14%), required access change in 57 cases (82%). AVF/AVG dysfunction rate was 1/49 mo and included thrombosis (n=5), insufficient blood flow (n=2), puncture failure (n=2) and aneurysm (n=1). In 5 cases successful AVF/AVG revision was performed, while the remaining 5 pts required a new access. The risk of access dysfunction was increased by the use of CVL (OR 4.52, $p=0.001$) independently of patient age, diagnosis and access site.
Conclusions: This is the largest prospective report on vascular access in children undergoing chronic hemodialysis. CVL still represent the first access choice despite much higher complication rates. Infectious complications exclusively occurred in pts with CVL and access dysfunction risk was substantially higher with CVL use, even after correction for patient age.

O - 26 A PROPENSITY-MATCHED COMPARISON OF HARD OUTCOMES IN CHILDREN ON CHRONIC DIALYSIS: THE ITALIAN REGISTRY EXPERIENCE

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Introduction: Data concerning outcomes of children on HD and PD are scarce and frequently refer to single center experiences. To better investigate the association between dialysis treatment modality and patient outcomes, we compared survival and transplantation rate in a large cohort of incident PD children propensity-matched to those on HD .
Material and methods: We retrospectively reviewed all patients starting dialysis under 18 years of age, collected over 10 years (2004-2013) by the Italian Registry of Pediatric Chronic Dialysis. Patients starting PD were propensity-matched to those starting HD. The propensity scores were estimated using the logistic regression model, which included gender, age, primary cause of ESRD, number and type of comorbidities, and duration of dialysis cycle. Cox models were used to compare outcomes using an intent-to-treat analysis.
Results: A total of 310 matched pairs (155 in each group) were obtained from 452 incident patients (261 PD and 191 HD). In the unmatched cohort, PD patients were significantly younger (median age of 5.1yrs [interquartile range 1.1-11.4] vs 13.9yrs [IQR 9.4-15.6]; $p<0.001$), more likely to be diagnosed with CAKUT (47.1% vs 36.1%; $p=0.007$), with lower body weight (15.5kg [IQR 8.8-31] vs 38.2kg [IQR 25-46]; $p<0.001$), and larger urinary volume (1.4ml/kg/day [IQR 0.7-2.5] vs 0.9ml/kg/day [IQR 0.3-1.6]; $p=0.0005$) than HD patients. After propensity score-matching, covariates were well balanced between the two groups and the cumulative hazard ratio (cHR) for transplantation was 0.99 (95%CI 0.73-1.34; $p=0.95$) for HD relative to PD children. Transplantation rate at 3 years after the first dialysis cycle initiation was 67% for PD and 62% for HD patients ($p=0.49$). The cHR for shifting dialysis modality was 1.39 (95% CI 0.78-2.50; $p=0.26$) and the cHR for death was 1.57 (95% CI 0.46-5.36; $p=0.47$) for HD as compared to PD patients. The survival probabilities for PD and HD patients were 98% and 97% at 12 months, 96.3% and 95% at 24 months, and 90% and 91.2% at 24 months ($p=0.47$).
Conclusions: Incident children undergoing PD and HD have distinct characteristics, that may influence the interpretation of outcomes. After adjusting for potential confounders and controlling for treatment-selection biases, no single type of dialysis seems to be superior to the other in terms of hard clinical endpoints.

O - 27 ISOLATED NOCTURNAL HYPERTENSION IS ASSOCIATED WITH INCREASED PULSE WAVE VELOCITY AND CAROTID INTIMA-MEDIA THICKNESS IN CHILDREN WITH CHRONIC KIDNEY DISEASE (CKD): RESULTS FROM THE 4C STUDY

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Introduction: Children with CKD are at high risk for cardiovascular (CV) morbidity and mortality. In the Cardiovascular Comorbidity in Children with Chronic Kidney Disease (4C) Study ambulatory blood pressure monitoring (ABPM), measurements of left ventricular mass index (LVMI), pulse wave velocity (PWV) and carotid intima-media thickness (cIMT) are performed annually as children progress towards end-stage renal disease.
Material and methods: ABPM profiles were analyzed in 456 children with CKD stage II-IV at baseline (64.3% males, 71.3% CAKUT, age 12.5 ±3.2 years, eGFR 28.9±12.2 ml/min/1.73m^2). Patients with normotension (including controlled hypertension), isolated nocturnal hypertension, and uncontrolled daytime or 24-hour hypertension were compared regarding their PWV, cIMT, and LVMI values.
Results: ABPM revealed normal BP profiles in 294 children (64.5%), uncontrolled hypertension in 101 children (22.1%), and isolated nocturnal hypertension in 61 children (13.4%). PWV-SDS and cIMT-SDS were significantly higher in children with uncontrolled and isolated nocturnal hypertension, compared to patients with normal ABPM profiles. LVMI

was significantly increased in patients with uncontrolled hypertension, but not in isolated nocturnal hypertension.

Measurements	ABPM findings		
	Uncontrolled HT	Isolated nocturnal HT	Normal ABPM
eGFR (ml/min/ 1.73m²)	28.2 ± 13.4	29.4 ± 10.7	29.1 ± 12.1
Albuminuria (mg/g creatinine)	864 [2123] *	487 [1960] *	264 [857]
PWV-SDS	1.27 ± 1.86*, #	0.55 ± 1.42*	-0.13 ± 1.53
cIMT-SDS	2.08 ± 1.59*	2.06 ± 1.20*	1.49 ± 1.29
LVMI (g/m$^{2.7}$)	43.8 ± 14.3*	39.7 ± 13.8	36.5 ± 14.0

*p <0.01; compared to patients with normal ABPM; #: p <0.05; compared to patients with isolated nocturnal HT
Whereas eGFR did not differ between groups, albuminuria was significantly higher in children with uncontrolled and isolated nocturnal hypertension

Conclusions: In children with CKD isolated nocturnal HT is associated with increased PWV and cIMT. Whether these changes in PWV and cIMT precede an increase in LVMI remains to be shown by longitudinal data analysis.

O - 28 INDEXING LEFT VENTRICULAR MASS

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Introduction: A number of disciplines rely on the assessment of left ventricular hypertrophy (LVH) to help determine disease severity and guide management decisions. Our study aims to comprehensively analyze reproducibility of four left ventricular mass (LVM) indexing methods in children and classification errors of LVH.
Material and methods: A total of 230 transthoracic echocardiograms of children without complex congenital heart disease or cardiomyopathy were randomly selected from a single institution's pre-existing database: 100 with structurally normal hearts, 100 with hypertension, and 30 with LVH. LVM in all children was indexed to body surface area (BSA), height and height$^{2.7}$, and additionally to lean body mass (LBM) in children over the age of 5 years. The results were transformed into LVM Z scores; LVH was defined as a Z score ≥1.65. Statistical analysis was performed using intraclass correlation coefficient (ICC), Kappa and Bland-Altman analysis.
Results: There were 126 males (54.7%); median age was 11.6 years. Mean LV mass Z score varied significantly by method, from -0.55 (BSA) to the majority of the group falling between the 75th-90th percentile when indexed to height$^{2.7}$. Bland-Altman analyses of Z scores revealed bias and wide limits of agreement between methods. The indexing method determined the proportion of individuals classified as having LVH. In children under the age of 5 years, indexing to BSA or height classified about 7% of the group with LVH, whereas 19% were categorized as LVH when indexed to height$^{2.7}$. In children over the age of 5 years, the differences were even greater, with a range of 5% to 43% being classified with LVH depending on the indexing method. The differences in classification persisted when using a cutoff of greater than 97.5th percentile (Z score ≥ 2) to define LVH. Kappa statistics confirmed best reliability in children under the age of 5 years between indexing measures of BSA and height. In children over the age of 5 years, kappa values were lower overall.
Conclusions: Classification of LVH is heavily biased and depends directly on indexing technique. There is poor reliability and agreement between the four key indexing methods which are not interchangeable. Moving between Z score indexing methods could lead to inaccurate clinical decisions.

O - 29 EFFECTIVE TREATMENT OF NOCTURNAL ENURESIS RESULTS IN AMELIORATION OF NEUROCOGNITIVE DYSFUNCTION AND DISRUPTED SLEEP

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Introduction: The high comorbidity between nocturnal enuresis, sleep disorders and psychological problems is suggestive of a common pathway in the central nervous system. This study aims to evaluate the effect of a simple therapeutic intervention for nocturnal enuresis on the major comorbidities: disrupted sleep and neuropsychological dysfunction.
Material and methods: In this open-label, prospective phase IV study, children with monosymptomatic nocturnal enuresis associated with nocturnal polyuria, underwent standardized video-polysomnographic testing and multi-informant neuropsychological testing at baseline and 6 months after the start of desmopressin treatment. The primary endpoints were the change in sleep and neuropsychological functioning. Neuropsychological functioning was measured on five domains: quality of life, attention, executive function, internalizing problems and externalizing problems. The secondary endpoint was the change in the first undisturbed sleep period or the time to the first void.
Results: Thirty-nine patients were screened and 35 patients were included in the study and completed the first examination. Thirty children (23 boys and 7 girls) between 6 and 16 years (mean 10.43, SD 3.08)completed the study. Response rate to desmopressin was 82%. The study demonstrated a significant decrease in periodic limb movements during sleep and a prolonged first undisturbed sleep period.Additionally neuropsychological functioning was improved on several domains: quality of life, executive functioning, internalizing problems and externalizing problems.
Conclusions: This study demonstrates that effective treatment of nocturnal polyuria in children with monosymptomatic nocturnal enuresis has a beneficial effect on sleep disruption and neuropsychological dysfunction.

O - 30 POSTURE AND MOBILITY CHANGES IN PATIENTS WITH NOCTURNAL ENURESIS

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Introduction: Posture refers to body alignment maintaining proper conditions to perform movements. Neuro-muscular system integration is required for maintenance of posture as well for adequate voiding function. Patients with enuresis were assessed for changes of posture and hip and spine mobility.

Material and methods: Ninety seven patients with nocturnal enuresis (EG) ranging from 7-16 years were paired with 60 asymptomatic kids (CG) for gender, age, and body mass index. Posture was assessed placing anatomical land markers in the process mastoid (PM); 7th cervical vertebrae (C7); anterior superior iliac spines (ASIS); posterior superior iliac spines (PSIS); greater trocanter (GT) and lateral maleolus (LM). A photograph was acquired while quiet standing. Angles and distances were obtained from landmarks connections using a software to assess the posture variables: ante/retroversion of pelvis, ante/retropulsion of pelvis, and protusion/retraction of head. The mobility of hip flexion, extension and spine flexibility were measured using goniometry, index of Schober/Stibor and Bank of Wells.
Results: EG showed higher angles of anterversion of pelvis than CG ($p<0.001$). Head protraction was presented in 76% of EG while head retraction was presented in 61% of CG. EG showed less spine mobility than CG ($p=0.001$); goniometry showed lower hip extension in EG than CG ($p<0.001$).
Conclusions: Kids with enuresis presented alterations in posture with anterversion of pelvis and head protraction. Diminished mobility and motion extension range of hip was also observed.

O - 31 AUTOMATED FLOW CYTOMETER AND DIPSTICKS FOR PREDICTING URINARY TRACT INFECTION IN FEBRILE CHILDREN

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Introduction: Rapid and sensitive diagnostic tests for urinary tract infection (UTI) are currently lacking and suspected episodes require urine culture . The present study compared the predictive values of urinary dipstick and automated flow cytometerurinalyses as diagnostic tests for UTI in febrile children
Material and methods: We prospectively collected data on 1247 febrile episodes in 1224 children. Urine was assessed for white blood cell (WBC), red blood cell (RBC) and bacterial counts using an automated flow cytometer. Urinary leucocyte esterase and nitrites were tested by dipstick and the diagnosis of UTI established by urine culture. The diagnostic performance of these tests and their optimal cut-off points to diagnose UTI were established using receiver-operating characteristic (ROC) analysis. Reduction of diagnostic uncertainty by cytometer analysis was modeled for populations with different prevalences of UTI.
Results: Urinary and biological data were analyzed for 1247 infectious episodes, among which 221 UTI (17.7%). The area under the ROC curve for cytometer WBC counts (0.99) was significantly superior ($P < 0.0001$) to urinary dipstick analysis (0.92), RBC (0.74) and bacterial counts (0.89). For cytometer WBC counts, the presence of ≥35 WBC/μl was the most useful cut-off point, yielding both high sensitivity (99.5%) and acceptable specificity (80.6%). Only one episode of UTI was associated with a WBC cytometer count of <35/μL (NPV of 99.9%). Modelling diagnostic performance for populations with a prevalence of UTI between 10 and 90% showed that the NPV of cytometer WBC counts remained always ≥95%.
Conclusions: Cytometer WBC counts provide precise prediction of UTI in febrile children. The presence of ≥35 WBC/μl in urinary specimens is the optimum cut-off value for identifying febrile infants for whom urine culture is warranted. The diagnostic performance of the test remains excellent for populations with a wide range of prevalence of UTI.

O - 32 PROTEASOME TO IMMUNOPROTEASOME SWITCH IN IGA NEPHROPATHY AND ITS GENETIC CONTROL: A POST-VALIGA EUROPEAN RESEARCH STUDY

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Introduction: α - and γ-interferons induce proteasome (PS) β type catalytic subunits PSMB5, PSMB6 and PSMB7 substitution with PSMB8, PSMB9 and PSMB10 leading to formation of immunoproteasomes (IPS). Mutations and single nucleotide polymorphisms (SNPs) in IPS subunit PSMB8 are associated with inflammatory and autoimmune diseases and up-regulation of PSMB8 mRNA with IgA nephropathy (IgAN) .
The locus encoding PSMB8 and PSMB9 genes was associated with increased IgAN risk in genome-wide association studies (GWAS). Aim of this study is to validate our observations of increased PS to IPS switch in a large cohort of European IgAN patients and to test if the top SNP at the PSMB8/PSMB9 locus (rs9357155) contributes to genetic control of this process.
Material and methods: We analyzed mRNA of constitutive (PSMB 5, -6, -7) and corresponding IPS subunits (PSMB 8, -9, -10) by RT-PCR in PBMCs from 150 VALIGA IgAN patients, 77 of which with DNA available for rs9357155 genotyping.
Results: We detected a highly significant increased expression of IPS subunit PSMB8 and corresponding PS/IPS switch in comparison to healthy controls (HC) (PSMB8:IgAN median value 2.09, IQR 1.6- 3.2;HC 1.2, 0.7- 1.9, $p< 0.0001$;PSMB8/PSMB5 IgAN 1.70, 1.3-2.3; HC 1.02, 0.9-1.2, $p=0.0002$) and of IPS subunit PSMB9 and corresponding PS/IPS switch (PSMB9 IgAN 1.80, 1.2 -2.4; HC 0.44, 0.3-0.7, $p<0.0001$; PSMB9/PSMB6 IgAN 1.25, 0.9-1.9, HC 0.49. 0.3-0.7 , $P< 0.0001$).
PSMB10 and PSMB10/PSMB7 expression was similar to HC. The frequency of IgAN risk allele rs9357155-C was 0.87, similar to 0.83 in the CEU HapMap population (European controls). Patients with CC genotype tended to have higher IPS switch compared to CT/TT genotypes, but these preliminary results did not reach statistical significance.
Conclusions: This large multicenter European study confirms enhanced immunoproteasome activation in PBMCs from IgAN patients. We also observed a trend for increased PS/IPS switch in homozygotes for the GWAS risk allele at PSMB8/PSMB9 locus, although low power of our genetic association study precludes definitive conclusions; we expect to confirm this trend increasing sample size for the genetic arm of this study.

O - 33 APPLICATION OF KATAFUCHI SEMI-QUANTITATIVE CRITERIA AND THE OXFORD CLASSIFICATION IN CHIDREN WITH IGA NEPHROLOGY

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Introduction: To compare the differences and similarities of Katafuchi semi-quantitative criteria and the Oxford classification of IgA nephrology(IgAN) in scoring the degrees of glomerular and tubulointerstitial lesions in chidren with IgA neprology
Material and methods: Clinical and pathological data was retrospectively analyzed in children with IgAN initially diagnosed by renal biopsy in the Department of pediatric nephrology, the First Affiliated Hospital of Sun Yat-sen University from June 2008 to June 2014. The degrees of glomerular and tubulointerstitial lesions were scored according to the Katafuchi semi-quantitative criteria and the Oxford classification of IgAN respectively
Results: 117 children (male: 81 cases, female:36 cases) with IgAN were included, The median age was 8.8 years. All cases were divided into isolated haematuria group (18), hematuria and proteinuria group (52), acute glomerulonephritis (12) and nephrotic syndrome group (32) as well as into three groups according to pathologic grades according the 1982 Lee's level criteria: grade I+II (19), grade III (67) and grade IV+V (31) groups. According to the Katafuchi semiquantitative critiria of IgAN, the severity scores of glomerullar and tubulo-interstitial lesions in pediatric patients were positively correlated with either different IgAN clincal or pathological groups($P<0.01$). In the Oxford classification of IgAN, the severity scores of mesangial hypercellularity, endocapillary hypercellularity, tubular atrophy/interstitial fibrosis and segmental glomerulosclerosis/adhension were positively correlated with different IgAN clincal ($P<0.05$). While in different IgAN pathological groups , the severity of mesangial hypercellularity, endocapilarity hypercellularity, segmental glomerulosclerosis/adhension,tubular atrophy/intersitial fibrosis and cellular/fibrocellular crecents were all positively correlated with different IgAN pathological groups ($P<0.05$)
Conclusions: The severity scores of renal lesions according either Katafuchi semiquantitative critiria or the Oxford classification of IgAN were both positively correlated with different IgAN pathological groups, but it showed that Katafuchi semiquantitative critiria indicated a better positively correlationship with different IgAN clinical groups

O - 34 PRETERM NEONATAL URINE AS A NOVEL SOURCE OF HIGHLY POTENT KIDNEY PROGENITOR CELLS

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Introduction: Human urinary sediment is currently a noninvasive source of cells from different locations of the urinary tract. Recently, subpopulations of cells from amniotic fluid (AF) and adult urine were shown to express kidney progenitor cell features with multipotential of differentiation. We aimed to study urine of preterm neonates before the completion of nephrogenesis for the presence of kidney neonatal stem/progenitor cells (nKSPC) and the ability of these cells to differentiate into functional podocytes.
Material and methods: Clonal cell lines were characterized as KSPC and KSPC-derived podocytes by gene expression analyses using quantitative rt-PCR and protein expression by flow cytometry and immunofluorescence. Podocytes differentiation was induced by incubation of cells in medium containing retinoic acid and vitamin D. Function of podocytes was assessed by albumin endocytosis and calcium influx assays. Results were compared to conditionally immortalized podocytes (ciPodocytes) and podocytes differentiated from amniotic fluid stem cells (AFSC) and adult urine progenitor cells (aUPC).
Results: nKSPCs expressed mesenchymal stem cell markers and kidney progenitor cell markers as SIX2, CD24, CD133, Vimentin and *CITED1* maintaining these characteristics up to passage 17. nKSPC-derived podocytes presented mesenchymal-to-epithelial transition acquiring arborized cytoplasm comparable to ciPodocytes. Cells presented upregulation of podocyte-specific genes and proteins and were able to endocytose albumin and uptake calcium via transient receptor potential cation channel, subfamily C, member 6 (TRPC6).
Conclusions: Preterm neonatal urine represents a novel noninvasive source of self-reviewing kidney progenitor cells with potential to differentiate into functional podocytes and may be a promising tool for regenerative medicine aiming kidney repair and a model for studying renal disease.

O - 35 COMPLEMENT ACTIVATION AFFECTS ENDOTHELIAL REPAIR VIA IMPAIRED CELL MIGRATION

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Introduction: Complement-mediated thrombotic microangiopathy (TMA) is characterized by platelet rich thrombi in the microvasculature resulting from endothelial cell (EC) injury. The possible consequences of EC complement deposition not resulting in cell death (sublytic), however, are not understood. We hypothesized that sublytic EC complement exposure impairs EC wound healing and investigated the underlying mechanism.
Material and methods: Blood outgrowth ECs were exposed to complement by blocking EC surface regulators (CD46, CD55, CD59) and incubating ECs with 50% normal human serum (NHS; complement active). Heat inactivated serum (HIS; complement inactive), C5-depleted serum (terminal pathway inactive) and media served as controls. A wound was created in a microfluidic system using 0.05% trypsin/EDTA, and wound closure was measured using ImageJ software. Reduction of EC wound area, indicative of healing, was determined in presence of media followed by HIS, C5-depleted serum or NHS for 1.5 h each.
Results: During media perfusion, wound area decreased to 62.5±4%. Subsequent HIS perfusion allowed for further wound area reduction to 38±6%, an effect similar to the one observed with C5-depleted serum (remaining wound area 46±5%). By contrast, NHS perfusion prevented further wound closure (remaining wound area 63±7%). While these results indicated a complement-mediated (NHS vs. HIS) and terminal pathway-dependent (HIS vs. C5-depleted serum) impairment of EC wound healing, the exact mechanism – proliferation vs. viability vs. migration – was unclear. The proliferation rate (% BrdU positive cells after 2 h) was not different between controls and complement-exposed ECs (20 ±2 vs. 21±3%), and no apoptosis was detected within a 4 h observation period (Annexin V). However, live cell imaging identified cyto-skeletal, cell-cell contact and cell motility abnormalities in complement-exposed ECs, which were in keeping with defective cell migration.
Conclusions: Our data suggest that sublytic EC complement exposure results in impaired cell migration leading to defects in EC wound healing – findings extending our current concept of TMA pathogenesis.

O - 36 DEVELOPMENTAL CONTEXT HAS A SIGNIFICANT IMPACT ON DISEASE PROGRESSION IN THE OBSTRUCTED KIDNEY AND POTENTIAL TREATMENT STRATEGIES

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Introduction: Inflammation and fibrosis are widely accepted as the key processes driving the progression of renal injuries to kidney disease in the mature kidney. However, congenital defects are the leading cause of

pediatric kidney disease and the pathogenesis of renal injury in the developing kidney remains poorly understood. In this study, we provide the first direct comparison of injury responses during each of the critical stages of kidney development.
Material and methods: Disease progression was examined in chronic and reversible murine models of unilateral ureteral obstruction (UUO) at several developmental time points: (1) P1, during nephrogenesis/nephron maturation, (2) P14, during proliferative growth, and (3) P60, in the mature kidney. Renal pathology was assessed by immunostaining for molecular markers of key processes in kidney development and the pathogenesis of renal injury.
Results: UUO at either P1 or P14 in the developing kidney leads to decreased kidney growth, reduced proliferative expansion of nephrons, increased apoptosis in progenitor cells, and impaired nephron differentiation. There is also a notable absence of fibroblast and macrophage recruitment, inflammation, and fibrosis in the developing kidney. This contrasts the mature kidney where there is a marked increase in reparative proliferation, inflammation, and fibrosis. [All results are n=10, $p<0.05$]
Conclusions: This study reveals that developmental context has a significant impact on the pathogenesis of renal injuries. In contrast to the mature kidney, injury in the developing kidney is characterized by profound developmental deficits and a distinct absence of inflammation and fibrosis. This suggests that treatment strategies for pediatric kidney disease can be optimized by stimulating proliferation and minimizing apoptosis at early stages of development while inhibiting inflammation and fibrosis at later stages.

O - 37 ASSESSING THE EFFECTS OF HUMAN KIDNEY-DERIVED CELLS IN A CISPLATIN-INDUCED ACUTE KIDNEY INJURY MODEL

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Introduction: Previous studies have suggested that CD133+ cells isolated from human kidney can ameliorate injury in rodent models of kidney disease by differentiating to replace damaged renal cells. However, the effect of the cells on the glomerular filtration rate (GFR) has not previously been assessed. Our objectives are to: (1) assess the differentiation capacity of CD133+ and CD133- human kidney cells using established*in vitro* differentiation assays; (2) evaluate the effect of the cells on GFR following intravenous administration into immunodeficient rats with cisplastin (CP)-induced injury; (3) assess whether the cells can replace damaged renal cells in the CP rat model.
Material and methods: Cells isolated from the cortex of human juvenile kidney were sorted into CD133+ and CD133- populations using FACS and characterized using flow cytometry. The potential of the cells to generate podocytes and proximal tubule cells (PTCs) was assayed *in vitro*. On days 2 and 7 following a single dose of CP (7mg/kg b.w.), rats received either saline or $1x10^6$ $CD133^+$ or $CD133^-$ cells. Cells were labeled with a GFP lentivirus and the membrane dye PKH26 so that their fate could be monitored histologically. Kidney function was sequentially assessed over 14 days via transcutaneous GFR measurements. In addition, urinary and plasma parameters, as well as histological changes were evaluated.
Results: Both $CD133^+$ and $CD133^-$ cells can generate cells *in vitro* that display some of the characteristics of PTCs and podocytes. Both cell types similarly improve renal function in the CP rat model as determined by transcutaneous GFR measurements. Additional renal biomarkers, as well as the biodistribution of GFP+/PKH26+ cells are currently being analysed.
Conclusions: CD133 expression has no significant relevance for the *in vitro* differentiation potential, nor the *in vivo* therapeutic potential of human kidney cells. Biodistribution results will indicate if the therapeutic efficacy of the cells is associated with engraftment in the kidney.

O - 38 ANALYZES OF A LARGE COHORT OF FAMILIAL STEROID-SENSITIVE NEPHROTIC SYNDROME CONFIRMS THE HETEROGENEITY OF THE DISEASE

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Introduction: Steroid-sensitive nephrotic syndrome (SSNS) accounts for >80% of cases of idiopathic nephrotic syndrome (NS) in childhood. An immune-related origin has been postulated since the 70's, and clinical and experimental evidence suggests that circulating factors (CF) are involved in its pathogenesis. Familial cases are rare, and only a few have been published. Mutations in the*EMP2* gene were recently identified in some of them. We present here clinics and genetics about a large familial SSNS cohort.
Material and methods: We enrolled 61 families (132 affected cases) presenting two or more individuals with NS, but at least one with SSNS at diagnosis.
Results: Transmission was compatible with an autosomal recessive (AR - n=34) or dominant (AD – n=27) mode of inheritance. Clinical data were not different between the AR and AD groups. All but seven patients were primary steroid-sensitive. Among primary steroid-resistant patients, none evolved to end-stage renal disease (ESRD), and all were sensitive to intensive immunosuppressive therapy (IS), whereas 12 steroid-sensitive patients evolved to resistance and 7/12 to ESRD. Six were transplanted and 2 relapsed after engraftment and were finally sensitive to intensive IS. Most of families (>50%) shared both frequent relapsers (FR) and non-FR in their related cases. Exome sequencing was performed in 13 AR families and did not reveal pathogenic mutation shared by more than two families. Among the 22 potentially mutated genes in individual families, two responded to CF criterias but did not co-segregate with the disease in the families. Among all the potential AR families, no mutation was found in *EMP2* gene.
Conclusions: Altogether, these results suggest both a high clinical and genetic heterogeneity in familial SSNS. Transmission seems to be more complex than a Mendelian monogenic one. Furthermore IS sensitivity in all individuals, comprising primary steroid resistant cases, confirms the immune origin in all the patients of these families.

O - 39 RESPONSE TO INTENSIFIED IMMUNOSUPPRESSIVE THERAPY AND IDENTIFICATION OF GENETIC DISEASE ARE HIGHLY PREDICTIVE OF LONG-TERM RENAL OUTCOME IN CHILDREN WITH STEROID RESISTANT NEPHROTIC SYNDROME (SRNS)

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Introduction: To evaluate the long-term course of renal function in patients with SRNS - dependent on the underlying cause.
Material and methods: Out of 1718 pediatric patients reported to the PodoNet Registry by 67 centers in 21 countries, 645 patients were included in the evaluation of long-term prognosis. Detailed longitudinal information on proteinuria and medications allowing to classify responsiveness to intensified immunosuppression (IIS) was available in 416 patients. Among these, 56 cases had a genetic disorder, 19 familial disease without an identified genetic cause, and 341 were sporadic cases. Treatment response was based on defined criteria regarding proteinuria and serum albumin. Cox regression was performed with adjustment for center effects.
Results: 123 out of 416 children achieved complete (30%) and 61 (15%) partial remission with IIS, whereas 232 (56%) were multidrug resistant. 47 of 232 multidrug-resistant cases had a genetic disorder and 6 children familial disease. 47% and 21% of the familial cases and 4% and 13% of the genetic cases showed complete or partial IIS responsiveness respectively. In children achieving complete remission on IIS, the risk of developing ESRD within 12 years, conditioned on surviving at least one year, was 2.4% as compared to 50.7% in multidrug-resistant patients (HR=11.9 [3.7; 38.3]). Children with a genetic cause had a 12-year ESRD risk of 77.8% (HR 26.2 [8.2;83.6]) compared to IIS-sensitive patients. Children with genetic disease also had a poorer outcome (12-y ESRD risk 41.9%) than those with familial disease without identifiable genetic cause (HR=2.2 [1.6;3.1]).
Conclusions: Proteinuria remission during IIS is highly predictive of a favourable long-term renal prognosis in SRNS patients. Multidrug resistance is associated with guarded long-term outcome but prognosis is still significantly better than in children with hereditary podocytopathies. In conclusion, IIS responsiveness is a positive, and the identification of genetic disease a negative predictor of long-term outcome in SRNS.
This analysis emphasizes the importance of genetic testing in evaluation of long-term prognosis of SRNS.

O - 40 RISK FACTORS FOR POST-TRANSPLANT RECURRENCE OF STEROID RESISTANT NEPHROTIC SYNDROME (SRNS): RESULTS FROM THE PODONET REGISTRY

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Introduction: Children with end-stage renal disease due to SRNS are at risk to develop proteinuria after transplantation. We evaluated possible risk factors for disease recurrence in the PodoNet SRNS cohort.
Material and methods: Among 1766 children with SRNS enrolled in the registry at 67 centers in 21 countries, 260 patients underwent kidney transplantation. In 233 of these, information on the post-transplant course is available. Multivariate logistic regression analysis was performed to explore the prognostic value of clinical, pharmacological, genetic and histopathological factors in predicting post-transplant proteinuria recurrence.
Results: Proteinuria recurred in 37/233 patients (15.8%). Disease recurrence was observed in 29 of 105 children with idiopathic nephrotic syndrome (27.8%), but only in 4 of 107 genetic cases (all pathogenic *NPHS2*mutations).
Patients with and without recurrence did not differ with regard to histopathological diagnosis in the native kidneys (FSGS in 69.7% vs. 64%), response to intensified immunosuppression (79.2 vs. 85.5%), time from

diagnosis to ESRD (Median (IQR): 3.3 (2.1-6.5) vs. 2.7 (1.3-5.7) years), age at transplantation (11.6 vs. 10.3 yrs) and duration of dialysis (1.6 vs. 1.6 years). Disease recurred in 3 of 67 children with disease manifestation during first year of life compared to 34/166 children first manifesting later in childhood (p=0.001). Children with post-transplant recurrence were characterised by more severe clinical symptoms at initial disease manifestation (severe oedema in 32% vs. 9.4%; p=0.002). Detection of genetic diagnosis was the strongest negative predictive value for post-transplant disease recurrence (Odds Ratio 0.1, 95%CI 0.03-0.3; p<0.0001). When adjusting for genetic status, initial clinical presentation was predictive of recurrence (severe oedema: OR 4.03 (1.45;11.2), p=0.008), whereas clinical, histopathological or treatment response data did not influence the risk of disease recurrence significantly.
Conclusions: Detection of a genetic diagnosis remains the only relevant predictive criterion in risk evaluation of post-transplant disease recurrence in children with SRNS.

O - 41 POOR PROGNOSIS OF PLASMA CELL RICH ACUTE REJECTION EPISODES IN PAEDIATRIC RENAL TRANSPLANT RECIPIENTS

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Introduction: The aetiopathogenesis and immunological reason for plasma cell rich acute rejection episodes in paediatric renal transplant recipients (pRTR) remains unknown. We investigated the incidence and prognosis in pRTR in a case-control study.
Material and methods: We conducted a retrospective study on plasma cell rich acute rejections in pRTR from April 1996 to March 2014. Cases were defined as all pRTR with ≥10% plasma cells in renal transplant biopsies and were matched to a control cohort for grade of rejection according to Banff classification, type of Tx (LRD vs DD), age at Tx and Tx age at biopsy.
Results: Plasma cell infiltrates were present in 14 (9%) out of 162 pRTR, aged 3.2 - 17.5 (median 13.4) years at time of transplantation of whom 13 (93%) received deceased donor renal transplants. Compared to 14 pRTR whose renal transplant biopsies had < 10% plasma cells there were no significant differences in mismatch, CMV/EBV status of recipient and patient at Tx and baseline eGFR. There was no significant difference in the number and grade of rejection according to Banff classification between cases and controls. Plasma cells were present in case biopsies with a density of 14 - 116 (median 33) cells/hpf/x40. Plasma cells were associated with decreased eGFR at biopsy (22 vs 49mls/min/1.73m^2; p < 0.001), despite comparable eGFR four weeks prior to biopsy. Mean eGFR post biopsy was significantly lower in patients with plasma cells (26 vs 56mls/min/1.73m^2; p < 0.001). Plasma cells were associated with renal allograft loss (71% vs 7%; p < 0.001) at 0 - 27 (median 2) months after biopsy.
Conclusions: Plasma cell rich acute rejection episodes in pRTR are associated with reduced renal allograft survival. In the future, bortezomib, a proteasome inhibitor which induces apoptosis in mature plasma cells, may play a role in patient management.

O - 42 OUTCOMES OF ABO INCOMPATIBLE KIDNEY TRANSPLANTATION IN CHILDREN

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Introduction: A shortage of suitable donors has driven transplantation across the blood group barrier. Whilst encouraging data is emerging on short and medium term graft outcomes in adults, ABO incompatible(ABOi) kidney transplantation in children is rare as pre-transplant conditioning remains challenging and concerns persist about an increased risk of rejection. Encouraged by good results in a large number of adult ABOi transplants, we extended our programme to paediatric recipients , and here report the largest European cohort using a tailored desensitisation strategy.
Material and methods: A retrospective analysis of all ABOi paediatric renal transplant recipients in the two largest centres in the UK, sharing the same tailored desensitisation protocol. Desensitisation protocol tailored to antibody titres is shown in the flowchart. Tacrolimus and mycophenolate mofetil were started one week pre-op. No routine post-op antibody removal was performed. Graft survival, biopsy proven rejections and eGFR were compared to fifty randomly selected ABO compatible transplants(ABOc).
Results: Eleven children (aged 2 -14 years) underwent an ABOi kidney transplant. One patient died from gastrointestinal failure with a functioning graft. Baseline titres, tailored desensitisation and eGFR are shown in the table. One patient developed grade 2a rejection successfully treated with anti-thymocyte globulin. Another patient had a rise in titre of 2 dilutions at week one treated with two immunoadsorption sessions. There was no histological evidence of rejection in other patients. All had good graft function with eGFR ranging from 27 to 77ml/min/1.73m^2 at last follow up (range 1-66 months). One patient developed CMV/BK and another EBV/BK. Death censored graft survival was 100% in ABOi vs. 98% in ABOc; biopsy confirmed rejection rates were ABOi 8% vs. ABOc 37%.
Conclusions: ABOi transplantation in children has a good outcome with graft survival and rejection rates comparable to ABOc transplants.

O - 43 PACAP DEFICIENCY AS A CAUSE OF INCREASED PLATELET AGGREGABILITY IN IDIOPATHIC NEPHROTIC SYNDROME

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Introduction: Patients with nephrotic syndrome (NS) have an increased risk for thrombosis, including both deep venous and arterial thrombosis, which significantly increases morbidity and mortality rates. The pituitary adenylate cyclase-activating polypeptide (PACAP) was recently identified as an inhibitor of megakaryopoiesis and platelet aggregability. We recently demonstrated urinary losses of PACAP and its binding protein ceruloplasmin in children with congenital NS (CNS), resulting in plasma PACAP deficiency, associated with increased megakaryopoiesis, thrombocytosis and platelet hyperaggregability. We now studied PACAP levels in children with idiopathic NS (INS), and its role in thrombocytosis and platelet hyperaggregability.
Material and methods: Plasma and urine levels of PACAP and ceruloplasmin were measured in 24 children with INS (29 nephrotic episodes),

as well as platelet counts and platelet aggregation responses to collagen. All tests were performed during nephrotic and non-nephrotic state.
Results: Urinary losses of PACAP and ceruloplasmin were documented during the nephrotic state, leading to plasma PACAP deficiency, and normalizing in the non-nephrotic state. Thrombocytosis was observed in 11/29 cases during nephrotic state, but no correlation between platelet counts and PACAP plasma levels was found. Platelet hyperaggregability was observed during nephrotic state and the addition of recombinant PACAP to patients' platelets resulted in decreased aggregation. Platelet aggregation correlated inversely with plasma PACAP levels, while not with serum albumin levels.
Conclusions: We demonstrate plasma PACAP deficiency in children with INS, probably playing a role in the platelet hyperaggregability and the increased risk for thrombosis in NS.

O - 44 GLUCOCORTICOID THERAPY REVERSES THE HYPERDYNAMIC NATURE OF THE PROTEINURIC GLOMERULAR FILTRATION BARRIER

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Introduction: Children presenting with nephrotic syndrome (NS) typically receive an empiric course of glucocorticoid (Gc) therapy. Glucocorticoids mediate their effects through the glucocorticoid receptor (GR), which is a ligand-activated transcription factor. However, neither the mechanism of action, nor target cell, of Gc therapy in NS are known. We postulate that glomerular podocytes are the direct target cell of Gc therapy, and that eliciting the relevant mechanism of action may identify novel therapeutic targets.
Material and methods: We combined chromatin immunoprecipitation sequencing (ChIP-Seq) and DNA microarray technologies to define the GR cistrome. We coupled this readout with mass spectrometry to investigate Gc-regulated protein expression in human podocytes and validated findings with live cell imaging, GTPase activation assays, and Electric Cell-substrate Impedance Sensing (ECIS). To complement our *in vitro* studies we generated a mouse line with podocyte-specific deletion of GR using the Cre-Lox system.
Results: Gene onotology analysis of the transcriptomics data highlighted prominent Gc effects on podocyte motility. Live-cell imaging confirmed that Gc treatment reversed the disease-associated podocyte hypermotility (podocyte speed 0.006328 μm/sec following puromycin aminonucleoside (PAN) treatment Vs. 0.003483 μm/sec with PAN/Gc treatment, $p<0.0001$). Gc reduced the activity of the pro-migratory controller of cell motility Rac1, and had a direct, functionally relevant effect on the podocyte filtration barrier by protecting against PAN-induced damage.
Conclusions: Our data suggests that Gc efficacy in NS may be explained by a direct effect on the filtration barrier, rather than though an indirect immunosuppressive mechanism. Gc exposure reverses the hypermotile proteinuria-associated podocyte phenotype and reduces activity of the pro-migratory motility-regulator Rac1. Generation of the Podocin-Cre+ $GR^{fl/fl}$ mice will allow us to investigate the podocyte as the potential target cell of action of Gc therapy *in vivo*.

O - 45 URINARY AQP2 EXCRETION IS INCREASED DURING NEPHROTIC SYNDROME AND IS ASSOCIATED WITH REDUCED URINE PRODUCTION

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Introduction: Edema is a hallmark of nephrotic syndrome (NS) and has largely been attributed to sodium retention. Yet low plasma sodium is frequently observed in children with acute NS suggesting that a disturbance in renal water handling may coexist together with sodium retention. The aims of the study were to investigate the urinary excretion of the renal water channel AQP2 and it´s correlation to urine production in children with NS.
Material and methods: A total of 20 (7 girls) children with NS were included with a mean age of 9.1(SD 3.2)yrs. Urine samples were collected from the second morning void at debut/relapse of NS and at remission. Urinary AQP2(uAQP2) concentration was determined using an ELISA assay. Urinary osmolality was determined by freezing-point depression. At debut/relapse, a 6 hour pretreatment urine collection was performed and at remission a 24 hour urine collection was performed.
Results: The concentration of uAQP2 was significantly higher during active NS compared to remission, 9.9 ng/ml (CI95% 4.3-22.5 ng/ml) vs. 3.9 ng/ml (CI95% 1.5-10.5 ng/ml), $p=0.003$. Mean urine production was 1.3 ml/h/kg during active NS compared to 1.0 ml/h/kg at remission, $p=0.25$. A linear regression analysis revealed a significant negative relationship between uAQP2 and urine production (r^2=-0.20, $p=0.05$). Urine osmolality and urine production was negatively correlated (r^2=-0.44, $p=0.009$) though urine osmolality did not differ comparing NS to remission 671±58 mOsm/kg vs. 703±44 mOsm/kg, $p=0.62$.
Conclusions: During active NS, patients exhibit an increased excretion of AQP2 in urine compared with remission and increased uAQP2 concentration correlated with reduced urine production. Further studies are needed to investigate if uAQP2 is associated with a positive free water balance in NS independently of sodium retention.

O - 46 MAC-2BP IS INCREASED IN PLASMA DURING NEPHROTIC SYNDROME AND IS PRODUCED BY PBMC

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Introduction: The pathogenesis of idiopathic nephrotic syndrome (NS) is believed to be a result of a circulating permeability factor (CPF) released by peripheral blood mononuclear cells (PBMC). MAC-2BP is a glycoprotein binding GAL1 and GAL3. GAL1 is located in close relation to nephrin. GAL3 mediates contact between integrin $\alpha2\beta1$ and collagen I-IV establishing contact between podocyte footprocesses and the basement membrane. The aims of the study were to identify a possible CPF, its presence in plasma and production by PBMC.
Material and methods: Mass spectrometry was performed using plasma from 4 patients comparing active NS with remission. The identified protein was validated in plasma of 20 children with NS using ELISA comparing active NS with remission. The protein was also measured in 18 healthy age and gender match controls. PBMC was obtained from 5 patients at active NS and from 5 patients at remission. PBMC were isolated, cultured and concentration of MAC-2BP was measured with ELISA in the supernatant.
Results: Plasma proteomics identified 388 proteins to be altered comparing NS with remission. Among these, MAC-2BP was identified. Plasma MAC-2BP was 8,848±3,326 ng/ml at active NS higher than remission of 6,050±2,866 ng/ml, $p=0.007$. MAC-2BP concentration in the healthy control group was 3,064±1,859 ng/ml, significantly lower than the concentration of MAC-2BP at remission, $p=0.0005$. MAC-2BP was identified in the supernatant from PBMC from active NS patients with a median of 41(20-170)ng/mL while MAC-2BP was undetectable in the supernatant from PBMC isolated from patients in remission.

Conclusions: Plasma MAC-2BP is increased in plasma during active NS compared to remission. Plasma MAC-2BP from patients with active disease and in remission was significantly higher than plasma MAC-BP levels of healthy controls. Furthermore, MAC-2BP was produced by PBMC isolated from nephrotic patients. Further studies are needed to investigate if MAC-2BP affects the podocyte and slit diaphragm function and integrity.

O - 47 REFRACTORY STEROID-DEPENDENT NEPHROTIC SYNDROME UNDER B CELL DEPLETION AFTER RITUXIMAB TREATMENT

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Introduction: Rituximab, an anti-CD20 antibody that targets B cells, is a promising agent against steroid-dependent and steroid-resistant nephrotic syndrome in children. We have previously reported that RTX significantly reduces the number of relapses and doses of steroid in patients with refractory SDNS. In previous studies, CD19 depletion was shown to be correlated with remission and they have showed that nephrotic syndrome relapse occurred frequently a few months after CD19 recovery and proposed a prolonged B-cell depletion could sustain longer remission. We found rare cases who had relapsed under B cell depletion after RTX infusion. These cases has not, to the best of our knowledge, been previously described in the literature.
Material and methods: We retrospectively analyzed 82 patients with SDNS who were treated with RTX from January 2007 until December 2012 in the National Center for Child Health and Development, Tokyo, Japan.
Results: All patients achieved B cell depletion. Six of 82 patients (5 males, one female) had relapsed under B cell depletion after RTX infusion (relapsed-patients). Another 76 patients have never relapsed under B cell depletion (non-relapsed patients). We analyzed relapsed- patients and compared with other non-relapsed patients under B cell depletion.Times of relapses and history of steroid resistance in the relapsed-patients were more than those in the non-relapsed patients, but there was no statistical difference. Duration to steroid-off and duration of B-cell depletion were not significantly different. Duration to first relapse after RTX infusion in patients with relapse under B-cell depletion was significantly longer than those in patients without relapse (median 77 vs 277 days, p=0.005). Times of relapse during one year after RTX infusion in patients with relapse were significantly more than those in patients without relapse (median 2.5 vs 0.9 times/year, p=0.002). In relapsed-patients, half of patients had relapsed under B cell depletion repeatedly, all patients also experienced sustaining remisson under B cell depletion after another RTX infusions. Duration to relapses from B cell recovery was shorter than non-relapsed patients (median 30 vs 91 days, p=0.005).
Conclusions: We found that 7.3 percent of patients with SDNS who were treated with RTX had experienced relapses under B cell depletion. It is interestingly in clarifying cause of nephrotic syndrome, because in such patients, B cell independent mechanism should worked. Although we have focused on effectiveness of RTX therapy, there are a few RTX resistance patients. It is issue we should make strategy for these patients with a larger number of patients together with a longer follow-up are necessary for future studies.

O - 48 PLCE CONTROLS PODOCYTE RESPONSE TO TGF-B1 BY MODULATION OF THE SMAD2/3 RATIO

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Introduction: Mutations in PLCE1 are a known cause of nephrotic syndrome. However, within a group of so-called "nephrotic genes", PLCE1 is somewhat the odd-one-out. The gene products of the "nephrotic genes" are generally components of the slit diaphragm, involved in anchoring the slit diaphragm to the actin cytoskeleton or regulate the actin cytoskeleton. PLCe is involved in lipid signalling at the membrane: converting PIP_2 into the secondary messengers IP_3 and DAG. Therefore the link between protien function and podocyte function overall is less clear.
A conditionally immortal human podocyte cell line was generated from explant tissue from a Denys-Drash patient. The 321C>T mutation induces an early stop codon which severely truncates the protein. Essentially PLCe in this cell line is functionally null.
Material and methods: Both mutant and wild-type conditionally immortalised podocyte cell lines were treated with recombinant human TGF-B1 to ascertian the signalling and functional response in both cell lines. Western blots were performed to study the signalling responses and scratch assays and ECIS were performed to study the functional effects of TGF-B1 exposure. siRNA was used to knock down PLCE1 in the wild-type podocyte cell line in order to replicate the mutant genotype.
Results: PLCE1 Mutant pododcytes displayed only limited SMAD2 phosphorylation compared to their wild-type counterparts. The PLCE1 mutants readily phosphorylated SMAD3 in response to TGF-B1 stimulation. Wild-type podocytes also demonstrated increased motility in response to TGF-B1 whereas the mutant podocytes exhibited no-such response. Upon further inspection it was discovered that the wild-type podocytes have twice the amount of SMAD2 as SMAD3 while the mutant podocytes expressed equal amounts of SMAD2 and SMAD3.
Conclusions: SMAD3 is known to control the pro fibrotic response to TGF-B1. As the wild-type podocytes express twice the amount of SMAD2 compared to SMAD3 their TGF-B1 signalling responses are biased towards SMAD2. The mutant podocytes express equivalent amounts of SMAD2 and SMAD3, their limited SMAD2 phosphorylation suggests that SMAD3 is capable of dominating SMAD2. This work suggests a clear mechanism by which PLCE mutations in the podocyte could be contributing to podocyte damage leading to nephrotic syndrome.

O - 49 PLA2R AUTOANTIBODIES IN PAEDIATRIC MEMBRANOUS NEPHROPATHY

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Introduction: Membranous nephropathy (MN) is the commonest cause of nephrotic syndrome in adults, with most cases being “primary”, or autoimmune in nature. Understanding of primary MN (PMN) advanced with the discovery of phospholipase A2 receptor (PLA2R) as the target autoantigen and with the detection of circulating autoantibodies in the sera of adult patients. Furthermore, identification of the major epitope within the N-terminal cysteine-rich domain of PLA2R has enhanced our understanding of autoantibody binding in the adult PMN population. Despite these recent advances, there is limited characterisation of PMN in children. In the paediatric population, PMN is rare and often presents with persistent, steroid-resistant, proteinuria and is diagnosed by typical histological features on renal biopsy. In this study, we describe the clinical phenotype, renal histological analysis, anti-PLA2R status, and autoantibody binding in 6 children with biopsy-proven PMN treated at the Royal Manchester Children’s Hospital over the past 7 years.
Material and methods: We carried out phenotypic characterisation of patients, determination of anti-PLA2R status by ELISA and histological analysis of renal biopsies. Anti-PLA2R binding was determined by

comparing autoantibody reactivity to recombinant fragments of the PLA2R under denatured and native conditions.
Results: Determination of anti-PLA2R status revealed 50% of children were seropositive. Seropositivity was associated with a severe clinical phenotype; that is, presentation with nephrotic syndrome, with or without renal impairment. Seronegative patients presented with asymptomatic proteinuria. Autoantibody reactivity patterns to recombinant fragments of the PLA2R, differed with clinical phenotype at presentation.
Conclusions: Here we report, for the first time, a series of 6 children with biopsy-proven PMN. We demonstrate a correlation between clinical phenotype and anti-PLA2R status and evaluate autoantibody-PLA2R binding in the paediatric PMN population. Our results suggest that minor, or alternative, epitopes exist within the PLA2R which may be responsible for autoantibody binding in paediatric PMN.

O - 50 IMPACT OF PAEDIATRIC RENAL REPLACEMENT THERAPY ON LONG TERM SOCIO-PROFESSIONAL OUTCOMES: A 30 YEAR FOLLOW UP STUDY

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Introduction: This nationwide Dutch cohort study evaluated socio-professional outcomes after 30 years of renal replacement therapy (RRT) and explored predictors of these outcomes.
Material and methods: The cohort comprised all Dutch patients, born before 1979, who started RRT at age <15 years in 1972-1992. Outcomes on family life (i.e. living arrangement, having offspring), level of educational attainment and employment status were established in 2000 and in 2010 in 80 out of 152 survivors. Secondly, participants completed the Course of Life Questionnaire, which retrospectively assesses the achievement of developmental milestones (autonomy, psychosexual and social development). Socio-professional outcomes in 2010 were compared with age-matched Dutch citizens and with outcomes obtained in 2000. Logistic regression analysis were performed to identify potential determinants, including both clinical- and psychosocial factors, of the socio-professional outcomes.
Results: Mean age and mean time on RRT in 2010 was 40.6 and 28.1 years respectively. Compared to age matched Dutch citizens, patients less often had offspring (28.8% vs 64.8% P<0.05) and less often were employed (62.5% vs 81.0% P<0.05). Co-morbidity, being on dialysis, short stature and lower scores on the autonomy developmental scale were associated with worse outcomes. In 2010 patients improved significantly regarding family life and educational attainment compared with 2000: 67.5% vs 33.8% (P<0.05) had a partner, 28.8% vs 16.3% (P<0.05) had children and 22.5% vs 13.9% (P<0.05) completed a high level educational degree.
Conclusions: Adult survivors of paediatric end stage renal disease gain social autonomy and optimal educational attainment at an older age as compared with healthy individuals. Awareness among health care professionals of the potential of these patients and adjusted psychosocial interventions might improve their socio-professional development on the long term.

O - 51 CARDIOVASCULAR RISK PROFILING IN CHILDREN WITH NON-RENAL TRANSPLANTS

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Introduction: Studies in adult recipients of solid organ and stem cell transplant have revealed an increased cardiovascular morbidity and mortality in this patient group. We therefore wondered how prevalent cardiovascular risk factors and subclinical organ damage are in children after lung (LuTx), liver (LiTx) and stem cell transplantation (SCTx).
Material and methods: We investigated 106 pediatric recipients of a non-renal transplant (21 LuTx, 41 LiTx and 44 SCTx). Patients were between 6 and 25 years old and had been transplanted between 1 and 15 years ago. We assessed hypertension (HTN; casual BP, ABPM), dyslipidemia and renal function. In addition, we measured aortal pulse wave velocity (PWV) and carotid intima-media thickness (IMT). Values are expressed as SDS-values where appropriate.
Results:

	LuTx	LiTx	SCTx
Hypertension (%)	75	15	24
controlled	30	3	3
uncontrolled	15	0	0
masked	30	12	21
GFR (ml/min*1.73m²)	88±19	126±48	118±27
Cholesterol	171±77	141±25	170±16
Triglycerides	155±37	102±40	133±71
PWV-SDS	0.9±1.6	0.6±1.1	0.3±1.0
IMT-SDS	1.8±1.0	1.9±1.0	1.9±1.1

The percentage of patients suffering from HTN, mean values (±SD) for other cardiovascular risk factor (cholesterol, triglycerides, GFR) and subclinical organ damage (PWV-SDS, IMT-SDS) are presented in the table.

Conclusions: Children and young adults after non-renal transplantation show a high prevalence of HTN and other cardiovascular risk factors. ABPM is crucial in detecting a high percentage of masked HTN, especially in lung transplant recipients. Our data also reveals a high burden of arterio- and atherosclerotic changes in these patients indicated by increased PWV- and IMT-SDS values. The patterns of this subclinical organ damage are different: lung transplant recipients show the greatest arteriosclerotic damage most likely reflecting the lower GFR. With more patients expected to be enrolled into this study, comparative analysis will give further insight in the underlying mechanisms driving those different patterns after transplantation.

O - 52 KIDNEY DECLINE FOR PAEDIATRIC TRANSPLANT RECIPIENTS - A NATIONAL PROSPECTIVE STUDY

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Introduction: Kidneys offered for paediatric transplantation may be declined because of donor or recipient factors. The aim of this study was to determine the reasons for kidney decline across the United Kingdom (UK) and to examine short-term outcome in declined organs.
Material and methods: Prospective data was collected for all kidneys declined for paediatric recipients (age <18 years) in the UK from January 2014 to December 2014 from the NHS Blood and Transplant registry. All 10 paediatric transplant centres in the UK were prospectively asked to provide additional data on reasons for decline of a kidney in a paediatric recipient. Data was collected on the outcome of declined organs, as well

as baseline characteristics in the donor and recipient (age, height and weight). All data was fully anonymised and ethical principles adhered to.
Results: 41 kidney offers were declined for paediatric recipients across 8 paediatric transplant centres in the UK, these were from 31 donors (62 kidneys) offered to 32 different children. Reasons for decline were provided for 98%. Mean recipient age was 10 (range 2-17) years and mean donor age was 37 (range 4-50) years. The commonest reasons for decline were donor health factors (75%) or inappropriate size (13%). Of the 62 kidneys which were declined, 76% were eventually transplanted. Of these 47 transplanted organs, 98% went to adult recipients and 2% to a paediatric recipient. All 47 transplanted organs were functioning with no failure reported at 3-month follow up.
Conclusions: This study reports the commonest reasons for kidney decline amongst paediatric transplant recipients in the UK. Adverse donor health and inappropriate size match were the commonest reasons for organ decline, but declined organs which were eventually transplanted had good short-term outcomes. Although long-term outcome data is required, clinicians could consider expanding criteria for accepting renal allografts for paediatric transplant recipients.

O - 53 STRUCTURED TRANSITION PROGRAMME LEADS TO IMPROVED RENAL ALLOGRAFT SURVIVAL FOR ADOLESCENT RENAL TRANSPLANT RECIPIENTS TRANSFERRING TO ADULT NEPHROLOGY

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Introduction: Transfer of care from paediatric to adult services is a particularly vulnerable time for renal transplant recipients (RTR) and is associated with significant morbidity. We describe our single centre adolescent renal transplant programme since 2004, offering a multi-disciplinary approach to transfer and providing support to this cohort as they become increasingly autonomous. We report the changes in patient and renal allograft survival seen prior to and following the introduction of a formalised transition process.
Material and methods: Adolescent RTR were identified retrospectively from our nephrology database and case notes. Patient and renal allograft survival data were obtained from the NHS Blood and Transplant database of patients from this transition cohort and a historical control. Patients who received a renal transplant between 1973 - 2009 with at least 12-months of follow-up data were included.
Results: Since 1973, a total of 505 patients have been transferred from GOSH paediatric services to adult care who have undergone 583 renal transplants (66 patients with their second transplant and 12 patients on their third). RTR were predominantly male (64%), undergoing transplantation from deceased donors (68%). CAKUT was the underlying primary diagnosis in 25%. Since 2006, 132 RTR have completed our transition programme (56% male) with a mean age of 17.9 years on transfer; 73% went on to adult care with a functioning first transplant and 12% with a functioning second. 19 (17%) grafts have since failed, which is lower than previously reported. One patient died with a functioning graft at time of death. When cohorted into transplant vintage, progressive improvements in renal allograft survival are seen compared with pre-transition patients.
Conclusions: We have seen ongoing improved renal allograft survival every year since the inception of our formal transition programme for adolescent RTR.

O - 54 ESCORT TRIAL - EFFECTS OF STRICT CONTROL OF BLOOD PRESSURE IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS – 2 YEAR RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

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Introduction: Arterial hypertension is a known risk factor for impaired graft survival in patients after renal transplantation (RTx). Strict control of blood pressure (BP <50th percentile) delays progression of chronic kidney diseases in children (ESCAPE trial). It is not known whether strict BP control has renoprotective effect also in children after RTx. The aim of this 3-year randomized controlled trial was to investigate whether strict BP control can protect kidney graft in children after RTx. We present 2-year data on blood pressure and proteinuria.
Material and methods: All 23 children from our paediatric renal transplantation centre who fulfilled the inclusion criteria (3-16 years, ≥1 year after RTx, no acute rejection in the last 3 months, eGFR >15 ml/min/1.73m2, 24hr mean BP ≥50thpercentile using ambulatory blood pressure monitoring ABPM) were included to the study. They were randomized to standard BP group (STAND, target 24hr MAP 50-95th percentile, n=11) or intensified BP group (INTENS, target 24hr MAP <50th percentile, n=12). All antihypertensive drugs were allowed to reach the target BP. The primary endpoint is the yearly change in eGFR (Schwartz formula, ml/min/1.73m2/year), the secondary endpoints are graft failure, change in proteinuria, blood pressure, left ventricular mass and safety of strict control of BP.
Results: A total of 21 children completed 2 year of treatment (2 children withdrawn due to steroid-resistant or antibody mediated acute rejection). The results are given in the Table.

Characteristic	All patients	STAND group	INTENS group	p (STAND vs.INTENS)
Age at baseline (years, range)	11.2 (6.2-16.8)	10.9 (6.2-16.8)	11.5 (6.6-16.7)	NS
Time after transplantation at baseline (years, range)	4.7 (1.0-13.1)	4.6 (1.0-11.1)	4.9 (1.1-13.1)	NS
24hr mean arterial pressure index at baseline	0.93 (0.85-1.11)	0.93 (0.85-1.07)	0.94 (0.86-1.11)	NS
24hr mean arterial pressure index after 1 year **(*p<0.05 **p<0.01 vs. baseline**	0.89 (0.80-1.07) **(**)**	0.90 (0.88-1.07) (NS)	0.89 (0.80-0.91) **(**)**	**p<0.05**
24hr mean arterial pressure index after 2 years **(*p<0.05 **p<0.01 vs. baseline**	0.88 (0.80-0.99) **(**)**	0.91 (0.84-0.99) (NS)	0.85 (0.80-0.94) **(**)**	**p<0.01**
Proteinuria at baseline (mg/mmol creatinine)	24.3	25.7	22.1	NS
Proteinuria after 1 year (mg/mmol creatinine)	13.9 (NS)	15.8 (NS)	13.5 (NS)	NS
Proteinuria after 2 years (mg/mmol creatinine)	14.1 (NS)	15.5 (NS)	14.1 (NS)	NS

Blood pressure (BP) index = mean BP of the patient divided by the 95th percentile, NS = not significant

Conclusions: This is the first randomized controlled trial on BP control and its effects on graft function in children after renal transplantation. 2 year data demonstrate that reduction of BP is possible in the majority of children even <50th percentile and it is sustained over time.
Supported by the project ED2.1.00/03.0076 from European Regional Development Fund.

O - 55 PUBERTAL DEVELOPMENT IN PEDIATRIC KIDNEY TRANSPLANT PATIENTS RECEIVING MAMMALIAN TARGETS OF RAPAMYCIN INHIBITORS OR CONVENTIONAL IMMUNOSUPPRESSION

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Introduction: Data regarding the onset of puberty in children receiving mammalian target of rapamycin (mTOR) inhibitors are limited.
Material and methods: Patients undergoing kidney transplantation at age <14 years were analyzed retrospectively to age 18. Immunosuppression comprised (i) standard CNI-based regimen or (ii) low-exposure mTOR inhibitor with reduced-exposure CNI, initiated either de novo or in the maintenance phase.
Results: Of 108 children analyzed, 67 received an mTOR inhibitor (56 everolimus, 11 sirolimus) and 41 did not. Mean age at transplant was 7.0 years (range 0.7–13.8 years); 66 patients were boys. The age at which girls reached Tanner stage P2 was similar with mTOR inhibitor therapy (median 11.6 [95% CI 11.2–12.1] years) or without (median 11.1 [95% CI 9.6–12.6] years) (p=0.177), as was age at stage B2 (median 11.6 [95% CI 10.8–12.4] years versus 11.2 [95% CI 10.6–11.9] years) (p=0.485). In boys, both the age of attaining Tanner stage P2 (median 12.6 [95% CI 11.3–13.9] years versus 13.0 [95% CI 12.8–13.2] years; p=0.751) and Tanner stage G2 (median 12.9 (95% 12.4–13.3 years versus 12.9 (95% CI 11.7–14.0) years; p=0.604) were also similar with or without an mTOR inhibitor. Age at menarche in girls, and age at spermarche in boys, did not differ between the two groups.
Conclusions: In this retrospective analysis, sexual maturation ages and reproductive hormone levels were comparable in adolescent kidney transplant patients receiving low-exposure mTOR inhibitors and reduced CNI therapy or conventional CNI-based immunosuppression. Long-term data on fertility are still lacking.

O - 56 CIRCULATING KLOTHO AND CARDIAC FIBROBLAST GROWTH FACTOR 23 MODULATE MYOCARDIAL FIBROSIS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Introduction: Pathologic cardiac remodeling, i.e. left ventricular hypertrophy (LVH) and myocardial fibrosis, is a major cause of cardiovascular death in patients with chronic kidney disease (CKD). As we demonstrated previously, fibroblast growth factor 23 (FGF23) is expressed in human cardiomyocytes, enhanced in patients with CKD, and associated with LVH. The impact of cardiac FGF23 on myocardial fibrosis in CKD is not known. Here we investigate the association of cardiac FGF23 and its coreceptor Klotho with myocardial fibrosis in autopsy samples of CKD patients.
Material and methods: Formalin-fixed paraffin-embedded myocardial autopsy samples of the left ventricle of 18 deceased pediatric CKD patients, and age and sex-matched controls were evaluated with human fibrosis *RT^2 Profiler^{TM} PCR Arrays* including genes responsible for fibrotic remodeling. For histological investigation of cardiac fibrosis, samples were stained with picosirius red and quantified by brightfield and polarized light microscopy. Cardiac FGF23 and soluble Klotho in cardiac tissue were assessed by qPCR and/or immunohistochemistry.
Results: The degree of cardiac fibrosis was increased in CKD patients compared with controls, and correlated positively with duration of ESRD, and dialysis treatment. Enhanced cardiac FGF23 expression was associated with the degree of fibrosis in CKD patients. The amount of circulating Klotho was reduced in myocardial tissue of CKD patients, and correlated negatively with cardiac fibrosis. Human fibrosis gene array analyses identified 31 genes regulated significantly in our patient cohort. The TGFb pathway, with *TGFb1*, *TGFbRs* and *SMAD3*, was up-regulated in CKD patients. Moreover, *TGFb1* correlated negatively with circulating Klotho. *BMP7* and *SMAD7*, which attenuate fibrotic activity, were down-regulated in CKD patients. In contrast, the pro-fibrotic target genes *CTGF* and collagen I and III were up-regulated in our patients cohort. Furthermore, CTGF correlated with collagen III.
Conclusions: Enhanced cardiac FGF23 expression in concert with Klotho deficiency is strongly associated with fibrotic cardiac remodeling processes in CKD.

O - 57 RECESSIVE MUTATIONS IN SLC34A1 (NAPI-IIA) CAUSE IDIOPATHIC INFANTILE HYPERCALCEMIA

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Introduction: Idiopathic infantile hypercalcemia (IIH) is characterized by severe hypercalcemia with failure to thrive, vomiting, dehydration, and nephrocalcinosis. Initially, mutations in *CYP24A1*, encoding the vitamin D inactivating enzyme 25-hydroxyvitamin D_3-24-hydroxylase were discovered resulting in an accumulation of the active metabolite 1, 25-$(OH)_2D_3$.
Material and methods: In a subgroup of IIH patients without mutations in *CYP24A1*, we now performed a positional candidate gene approach in order to identify a second IIH gene locus. For this purpose, four patients from three consanguineous families were subjected to homozygosity mapping. Newly identified *SLC34A1* mutations were functionally

characterized in mammalian cells and Xenopus oocytes. Changes in calcium and phosphate metabolism were evaluated in *Slc34a1* knockout mice.

Results: We identified a shared homozygous interval on chromosome 5q35 with a maximum LOD score of 6.91 encompassing *SLC34A1* as the most promising candidate gene. *SLC34A1* codes for proximal-tubularsodium-phosphate co-transporter NaPi-IIa. The *SLC34A1* sequence analysis yielded recessive mutations in the four index cases as well as in fifteen additional sporadic IIH patients. Functional studies of the mutated sodium-phosphate cotransporter NaPi-IIa in Xenopus oocytes and OK cells demonstrated a disturbed trafficking to the plasma membrane as well as a loss of phosphate transport activity. Studies in phosphate-depleted *Slc34a1* knockout mice highlight the impact of FGF-23 suppression for the development of the IIH phenotype.

Conclusions: Genetic heterogeneity in IIH is revealed by identification of recessive *SLC34A1* mutations. The mice and human data together demonstrate a critical role of phosphate depletion and FGF-23 suppression that induce an inappropriate production of 1,25-$(OH)_2D_3$ with subsequent symptomatic hypercalcemia. In affected infants, clinical and laboratory findings persist after omitting vitamin D prophylaxis but rapidly respond to phosphate supplementation. Therefore, an early differentiation between *CYP24A1* (24-hydroxylase) and *SLC34A1* (NaPi-IIa) defects appears crucial for a effective therapy in children with IIH.

O - 58 DEVELOPMENT OF AN RNAI THERAPEUTIC TARGETING GLYCOLATE OXIDASE FOR THE TREATMENT OF PRIMARY HYPEROXALURIA TYPE 1

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Introduction: Primary Hyperoxaluria Type 1 (PH1) is an autosomal recessive disorder of glyoxylate metabolism from loss of function of alanine-glyoxylate aminotransferase in hepatocyte peroxisomes of affected individuals, resulting in profound oxalate overproduction. End stage renal disease is common at an early age with necessary treatment via dual liver-kidney transplantation. RNAi therapeutics are a class of potential medicines that target a specific mRNA to reduce production of a protein known to impact disease. In PH1, inhibiting the upstream peroxisomal enzyme glycolate oxidase (GO) should starve the defective pathway of substrate and decrease oxalate synthesis. This study evaluated the impact of RNAi therapeutics targeting GO on oxalate metabolism in rodents and primates, leveraging a clinically validated conjugate platform that employs the sugar N-Acetylgalactosamine to direct therapeutic delivery through asialoglycoprotein receptors on hepatocytes - the major site of oxalate production.

Material and methods: GalNAc-siRNA were administered weekly or monthly via subcutaneous injection to mice, rats, and monkeys at doses from 0.1 to 10 mg/Kg. mRNA levels were monitored via qPCR and enzyme activity was measured from liver lysates. Glycolate levels were measured from serum and urine by ion chromatography coupled to mass spectroscopy and urinary oxalate was measured using the oxalate oxidase method.

Results: GalNAc-siRNA treatment consistently silenced the GO transcript across species to decrease enzyme activity, with >95% inhibition seen at the top doses. This translated to dose-dependent increases in circulating glycolate from 1.5x to 45x untreated levels, depending on the species, sex and degree of GO inhibition. In rodent models of PH1, GO knockdown decreased urinary oxalate by 80%, confirming the therapeutic hypothesis.

Conclusions: GalNAc-siRNA conjugates resulted in substantial knockdown of GO activity in the livers of treated animals to effectively reduce oxalate synthesis. If successful, RNAi therapeutics have significant potential to prevent oxalate synthesis in PH1 patients and the need for liver transplantation.

O - 59 A PROSPECTIVE STUDY OF PAEDIATRIC PATIENTS WITH ATYPICAL HAEMOLYTIC URAEMIC SYNDROME (AHUS) TREATED WITH ECULIZUMAB: 1-YEAR UPDATE

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Introduction: To report an update at 1-year of a prospective study of eculizumab (a terminal complement pathway inhibitor approved for the treatment of aHUS) in paediatric patients.

Material and methods: This was an open-label, single-arm, Phase 2 trial of eculizumab in paediatric patients with aHUS. Primary endpoint: proportion of patients achieving complete TMA response (platelet count ≥150 x 10^9/L, LDH <ULN, and serum creatinine decrease ≥25% from baseline, on 2 consecutive measurements ≥4 weeks apart). Dosing was weight cohort-based and designed so ≥95% of patients had complete and sustained terminal complement inhibition at all times.

Results: 22 patients (aged 1 month – 17 years) enrolled. At the 1-year update, median (range) treatment duration was 12.6 (0.0–24.5) months. At week 26 and 1 year, 14 (64%) and 15 (68%) patients achieved complete TMA response, respectively. Platelet levels and estimated glomerular filtration rate increased significantly from baseline over the 26-week study period, and improvements were maintained or increased at 1 year. Of 11 patients on dialysis at baseline, 9 (82%) discontinued dialysis and remained dialysis-free at 1-year. No patients started dialysis between baseline and the 1-year update. Eculizumab efficacy was equivalent in patients with (n=11) and without (n=11) identified complement abnormalities; by 26 weeks, complete TMA response was achieved by 8 (73%) with and 6 (55%) without abnormalities. Eculizumab was well tolerated and there were no meningococcal infections or deaths. The elimination half-life of eculizumab was 14.5 days. Generally, individual C_{min} values were >50 μg/mL and C_{max} values <700 μg/mL. After 24 hours, all 18 evaluable patients had evidence of complete terminal complement inhibition.

Conclusions: Data at the 1-year update further demonstrate the safety and continued efficacy of ongoing eculizumab in paediatric aHUS patients, whether or not a complement abnormality has been identified. Pharmacokinetic data indicate dosing by body weight cohort was appropriate.

O - 60 SILDENAFIL FOR TREATMENT OF NEPHROGENIC DIABETES INSIPIDUS

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Introduction: Congenital nephrogenic diabetes insipidus (NDI) characterized by inability to concentrate urine in response to arginine vasopressin (AVP), is caused by mutations in vasopressin receptor 2 (V2R) gene (90%) or mutations in the aquaporin 2 (AQP2) water channel (10%). Current conventional treatment regimen including adequate hydration, low sodium diet, hydrochlorothiazide (HCTZ) and nonsteroidal anti-inflammatory drugs (NSAIDs) can only partially control the NDI symptoms. Recent experimental studies have suggested that treatment with sildenafil citrate, a PDE5 inhibitor, may enhance cyclic adenosine monophosphate (cAMP)-mediated apical trafficking of AQP2 and may be effective in increasing water reabsorption in patients with congenital NDI.
Material and methods: A 4-year old bot with x-linked NDI (12bp-deletion, delta R247-G250 at Xq28 position) resistant to conventional therapy (HCTZ-amiloride and indomethacin) treated with sildenafil citrate 2mg/kg/day for 10 days after a 2-day washout period between the two treatment regimen. Aliquots of 24-hr urine collections before and after sildenafil treatment were analyzed for urine volume, osmolality and cAMP determination. Blood samples were also obtained for sodium and osmolality measurements. The primary endpoint was 24-hour urine volume after 10 days of sildenafil and conventional teatments.
Results: Compared to conventional therapy, treatment with sildenafil resulted in significant reduction in 24-hr urine volume (1698 mL vs. 851 mL) and serum sodium (164 vs.148 mEq/L) and an increase in osmolality (101 vs.687 mOsm/L) and cAMP concentration (759 vs.1501 nmol/day). Patient tolerated sildenafil well and experienced no adverse effect
Conclusions: Sildenafil citrate should be considered as an alternative agent in treatment of x-linked NDI resistant to conventional therapy.

O - 61 THE SWEDISH INFANT HIGH GRADE REFLUX TRIAL – UTI AND RENAL DAMAGE

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Introduction: Endoscopic injection is an established treatment option for vesicoureteral reflux (VUR) in children. Does endoscopic treatment of VUR grade 4-5 in infants reduce the risk of UTI recurrence and renal scarring?
Material and methods: This randomized, controlled, multicenter, 1-year follow-up trial, enrolled 77 infants (22 girls, 55 boys) <8 months of age with VUR grade 4-5(n=30/n=47), bilateral VUR in 52(68%). 39 received continuous antibiotic prophylaxis (CAP) and 38 endoscopic treatment (and prophylaxis until resolution). Voiding cystourethrogram and DMSA-scintigraphy/ MAG-3-renography were performed at study entry and after 1 year. Parenchymal defects were seen in 67(87%) children at entry, 28(36%) categorized as severe, severity more pronounced in boys. At follow-up, new scars, worsening of damaged kidneys and symptomatic UTIs (≥38.5°C=febrile) were reported.
Results: There were 27 recurrent febrile UTIs in 6(16%) children in the endoscopy group and in 10(26%) in the CAP group (p=0.43), in 8(36%) girls and 8(15%) boys (p=0.074). New renal scars were detected in 1(3%) child in the endoscopic group and in 3(8%) in the CAP group (p=0.64), deterioration in 3(8%) and 5(14%) respectively (p=0.74). New scars were seen in 3(14%) girls and 1(2%) boy (p=0.13), deterioration in 4(19%) girls and 4(8%) boys (p=0.32). There was a weak correlation between number of febrile UTIs and VUR-grade at follow-up (Spearman correlation coefficient 0.26). There was a tendency to more deterioration in children with several febrile recurrences (p=0.067). In 5 of the 8 children with deterioration, as in 2 of the 4 with new scars, there was no febrile UTI documented.
Conclusions: In this high-risk group of children, 87% of them with established renal defects in infancy, the lower risk of febrile recurrences and renal scarring seen after endoscopic treatment compared to CAP was not significant, probably due to the small study population and short observation. Renal scarring can occur in the absence of UTI.

O - 62 THE SWEDISH INFANT HIGH GRADE REFLUX TRIAL - VUR GRADE AND BLADDER FUNCTION

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Introduction: Endoscopic treatment for vesicoureteral reflux (VUR) has become an established alternative to continuous antibiotic prophylaxis (CAP) and surgical intervention in children. We aimed to study if high-grade VUR in infants can be treated with endoscopic injection and if early down-grading of VUR can prevent development of bladder dysfunction characterized by high bladder capacity and incomplete emptying.
Material and methods: In this randomized, controlled, multicenter, 1-year follow-up trial, 77 infants (55 boys, 22 girls) <8 months of age with VUR grade 4-5(n=30/n=47) were included. 52(68%) had bilateral VUR. 39 were randomized to CAP and 38 to endoscopic treatment (and prophylaxis till resolution). Voiding cystourethrogram (VCUG) and free voiding observation (FVO) were performed at study entry and after one year for evaluation of VUR grade and bladder function. Functional BC (from FVO) was compared to expected for age, and its relation to VUR grade was analyzed.
Results: Median age at inclusion was 6,7 months (SD 1,15). 21(58%) in the endoscopy group and 8(21%) in the CAP group had VUR-grade ≤2 at follow-up (p=0,0015). 19(63%) and 10(23%) of VUR grade 4 and 5 downgraded to VUR-grade ≤2 (p=0,0007). Reflux resolution was more common in unilateral (58%) than bilateral (30%) VUR (p=0,022). Functional BC was >150% of expected for age in 32(42%) at inclusion (mean 149%) and in 23(34%) at follow-up (mean 132%), similar for both treatment groups. Children with VUR-grade ≤2 at follow-up had a lower free-voiding BC than those with VUR-grade >2 (p=0,050), the difference was even more significant when comparing with bilateral VUR grade 5 (p=0,016).
Conclusions: High grade VUR in infants can be treated with injection therapy. VUR grade 4 and unilaterality is favorable for resolution or down-grading of VUR. Bladder capacity decreased in children with non-dilating VUR at follow-up, indicating that refluxing volume plays an important role in the development of bladder dysfunction.

O - 63 EFFICACY OF HIGHER DOSE LEVAMISOLE IN MAINTAINING REMISSION IN STEROID DEPENDANT NEPHROTIC SYNDROME

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Introduction: Levamisole (LEV) has been used successfully on an alternate day regime of 2.5mg/Kg in steroid dependant nephrotic syndrome (SDNS) to maintain remission. This controlled study was carried out between 2010 and 2015 at a single centre in Sri Lanka to evaluate the efficacy of LEV prescribed at 2.5mg/Kg daily.
Material and methods: Sequential children with SDNS, relapsing more than 2 times in the preceding 12 months, who had been previously treated with LEV and low dose alternate day prednisolone (0.1-0.6 mg/kg) were recruited to the study. This group received LEV (2.5 mg/kg) daily with

the same dose of alternate day prednisolone for a period of one year. Urine protein excretion was performed and recorded by parents on a daily basis and the presence of 3+ proteinuria on three consecutive days was considered as a relapse. Full blood counts and liver function tests were performed every 3 months to monitor for adverse effects.
Results: Sixty four children were enrolled to the study. Six children were excluded due to prescription of other immune suppressive drugs. Median age 7.9 years and 33 were male and 25 female. The number of relapse episodes was 163 (Mean relapse rate/patient 2.8 ± SD 0.8) with alternate day LEV and 77 (Mean 1.3 ± SD 0.9) with daily LEV during the 12 month period of observation. No major adverse events were noted. The P value 0.000 (according to the Wilcoxon Signed Ranks Test) is less than 0.001.
Conclusions: The prescription of daily LEV is effective and safe in maintaining remission in SDNS .

O - 64 INFLUENCE OF FLUID INTAKE ON FUNCTIONAL BLADDER VOLUME AND NIGHTTIME DIURESIS IN NOCTURNAL ENURESIS

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Introduction: In the management of monosymptomatic and non-monosymptomatic nocturnal enuresis, it is generally advised by the International Children's Continence Society (ICCS) guidelines to increase the fluid intake during the day and restrict drinking in the evening. The intended objective is increasing functional bladder volume and decreasing the nighttime diuresis by eliminating more water and osmotic agents during day. However, this is a very challenging task for both parents and child. More so, the presumed beneficial effect is never fully investigated. The goal of this study is to investigate the influence of increasing fluid intake during day on functional bladder volume and nighttime diuresis.
Material and methods: Children assessed for bedwetting at the children's nephrology and urology clinic at the university hospital in Ghent were admitted to a prospective uncontrolled pilot study. The families were instructed to complete a day- and nighttime voiding and drinking diary during two weeks and again after 5 weeks. At the end of the first week the children were instructed to drink at least 1500 ml/m^2 before 6 p.m. in the evening.
Results: Of the 51 included patients, only 21 completed the study. Just 13 patients filled out the diary after 5 weeks. The drinking volume is significant higher after the first week (p<0,001), but not anymore after 5 weeks (p=0,064). The maximum voided volume is significant higher after increasing drinking volume (p=0,038). There is no significant influence on nighttime diuresis after increasing drinking volume (95% confidence interval (-35, +16)).
Conclusions: In children with nocturnal enuresis, there is a significant positive effect of increasing drinking volume to 1500 ml/m^2 on functional bladder volume. However, there is no significant decrease in nighttime diuresis. On the contrary, the results suggest a possible increase of nighttime diuresis and therefore bedwetting.We suggest adjusting our drinking advice to the underlying archetype of enuresis; increasing fluid intake in patients with small functional bladder volume, but not in children with nocturnal polyuria.

O - 65 SHOULD ECULIZUMAB BE OFFERED TO ALL PATIENTS WITH ADAMTS13 DEFICIENCY AND SIGNS OF COMPLEMENT ACTIVATION?

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Introduction: A 12-year-old boy presented with haemolytic anaemia, thrombocytopenia, acute renal failure requiring haemodialysis and generalized seizures, preceded by an upper respiratory tract infection. The childhood onset, severe renal impairment, absence of prodromal diarrhoea and negative results (by stool culture and sierology) for Shiga-like toxin-producing *E.coli*, and elevated plasma levels of the terminal complement complex sC5b-9 (520 ng/ml, n.v.<300 ng/ml) were consistent with a diagnosis of complement-mediated atypical haemolytic uraemic syndrome (aHUS).
Material and methods: Given the severity of the clinical condition, on day four, Eculizumab (900 mg, i.v. 4 doses weekly, then 1200 mg every two weeks, preceeded by anti-meningococcal vaccination and antibiotic prophylaxis), was started.
Results: The response was excellent; within 3 days platelet counts, LDH and diuresis normalized, dialysis was discontinued, serum creatinine dropped to 1.78 mg/dl and anaemia ameliorated (Hb:8.9 g/dl). After the sixth Eculizumab dose, an attempt to space out subsequent infusions resulted in severe thrombocytopenia (pl:11, 000/μl with diffuse petechiae) and microangiopathic haemolysis without renal impairment (creatinine: 0.59 mg/dl). Eculizumab (1200 mg) was reintroduced, promptly resolving thrombocytopenia. The patient remained on Eculizumab biweekly till day 140, therafter the inter-dose intervals were progressively lengthened until discontinuation, with no sign of relapse during 3 months of drug-free follow-up. A recently published test for endothelium-restricted complement activation showed that serum taken from the patient during the relapse deposited high C5b-9 amounts on cultured endothelial cells and deposits normalized after Eculizumab, exactly as observed in aHUS. While the boy was already on treatment, screening of aHUS-associated genes (*CFH*, *CD46*, *CFI*, *CFB*, *C3*, and *THBD*) failed to show any mutation. Plasma anti-FH antibodies were negative both before and after Eculizumab initiation. In the meantime, measurement of plasma ADAMTS13 activity showed undetectable levels (<6% by collagen-binding assay) both during the acute phase and at remission, without inhibitory antibodies. By sequencing *ADAMTS13*, we found 2 heterozygous mutations (c.3251G>A causing a p.C1084Y amino-acid change, previously reported in thrombotic thrombocytopenic purpura, TTP, and a new c.4049delC frameshift causing protein interruption, p.E1351Rfs9X. Screening results were consistent with a diagnosis of congenital TTP.
Conclusions: The prompt disease remission after Eculizumab, paralleled by normalization of C5b-9 endothelial deposits, supports the recent notion that complement is activated in the presence of ADAMTS13 deficiency, and discloses a main role of complement in the pathophysiology of microvascular thrombosis.
Recent findings of complement components binding endothelial cell-anchored ultra-large VWF (ULVWF) strings, which preceded the formation of the complement alternative pathway C3 convertase, together with the recognized role of ADAMTS13 in cleaving ULVWF into smaller size multimers, offer a plausible molecular explanation for this patients dramatic response to anti-C5 treatment.Furthermore, while smaller VWF multimers favor degradation of the C3 activation product C3b, ULVWF multimers do not.
Conceivably, ADAMTS13 deficiency caused excessive assembly of complement components on the ULVWF-multimers anchored to microvascular endothelium, as well as complement-mediated injury, mimicking the events associated with genetic complement dysregulation of aHUS. Should Eculizumab be offered to alla patients with ADAMTS13 deficiency and signs of Complement activation? In the absence of appropriate studies this question remains unanswered. However, the spectacular clinical evolution of this patient who received anti-C5 treatment just by chance, opens an unanticipated perspective for treatment of a disease that is still burdened with a 10-20% mortality rate.

O - 66 WHOLE EXOME SEQUENCING APPROACH FOR RENAL HYPODYSPLASIA IDENTIFY INVS LIKE NOVEL CAUSATIVE GENE

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Introduction: Renal hypo-/dys-plasia (RHD), belonging to congenital anomalies of the kidney and urinary tract (CAKUT), is an important cause of chronic renal failure in children. It is due to a perturbation in the regulatory gene network during nephogenesis. In RHD patients, mutations in about 20 renal developmental genes were identified, but they account for only a small proportion of the cases, probably due to locus heterogeneity and to a greater complexity of the pathogenetic mechanisms of RHD. As part of the Strategic Project Funds BIOINFOGEN, we applied Whole Exome Sequencing in order to identify disease-causing mutations in new candidate genes in RHD patients.
Material and methods: We enrolled 20 children with sporadic non syndromic bilateral RHD, with or without associated upper urinary tract malformations. In 12 cases, it was possible to enroll also healthy relatives. Following genomic DNA quality control, a barcoded fragment library was prepared, enriched in exome sequences by TargetSeq™ Exome Enrichment System and sequenced with at least 50X average coverage.
Results: To date, analysis of variants was performed in the first 5 trios (proband and parents), using both dominant and recessive models. We observed some variants in known and unknown CAKUT genes, that have to be validated. In one trio, the proband with end-stage-renal-disease diagnosed at 18 months after birth, who came to our center for kidney transplantation at the age of 2 years with isolated RHD, carried a compound heterozygous mutation in the INVS gene. Both mutations were inherited by parents, and one was a nonsense unreported mutation.
Conclusions: INVS encodes the ciliary protein inversin, that is required for normal renal development. Mutations in INVS gene are associated with infantile nephronophthisis. Our finding suggests that INVS could be a new candidate gene for RHD or that borderline phenotypes of two kidney diseases may exist.

O - 67 SODIUM VALPROATE INDUCED FANCONI TYPE PROXIMAL RENAL TUBULAR ACIDOSIS: A CASE SERIES

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Introduction: Sodium valproate is one of the most commonly used drugs to treat epilepsy with NICE guidelines recommending it as first line treatment in many seizure types. However, there are ever increasing reports that valproate can cause proximal renal tubular injury in children which can have devastating impact on child development. To date there have been 25 reported cases of Sodium Valproate induced Fanconi's syndrome.
Material and methods: Here we report three patients with valproate induced Fanconi's syndrome with ages ranging from 5 years to 12 years at presentation.
Results: The biochemistry results from the cases reinforce the key diagnostic features of this syndrome being hypophosphatemia, glycosuria and proteinuria. The authors also add that osteopenia presenting as clinical fractures, may indicate Fanconi's, which may provide an opportunity for intervention. These cases continue to add to the evidence that there is a subpopulation of individuals who are particularly at risk of developing Fanconis, who share one or a number of features including being non-ambulatory, tube fed and/or developmentally delayed. None of our patients have confirmed mitochondrial disorders and, unlike the features described in the various publications, this case series does not demonstrate features consistent with mitochondrial toxicity. The treatment for valproate induced Fanconi's syndrome is to withdraw valproate treatment which resulted in resolution of clinical features in this case series as well. Previous case series have reported recovery time of between 2-14 months with an average 5.5 months.
Conclusions: Since the first case we discovered we have raised awareness and as a result have identified an increasing number of Valproate induced Fanconi's syndrome cases The authors advise regular urine and serum analysis for those taking valproate, especially high risk individuals.

P - 1 ACUTE KIDNEY INJURY IN CRITICALLY ILL CHILDREN: A PROSPECTIVE ANALYSIS OF RISK FACTORS.

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Introduction: Children admitted to pediatric intensive care unit (PICU) are at risk of acute kidney injury (AKI). Few studies have focused on the identification of factors potentially associated with the development of this condition. The aim of our study was to identify risk factors of AKI in a large sample of critically ill children.
Material and methods: All patients admitted to our PICU (age between 0-16 years) over a 6-months period (January-June 2014) were prospectively enrolled. AKI was defined according to KDIGO criteria. A comparison between patients with and without AKI was carried out, and the risk factors playing a significant role in the manifestation of AKI were analyzed. These factors were first evaluated by univariate analysis; a multivariate analysis by stepwise regression was then performed using odds ratio (OR) with 95% confidence interval (CI).
Results: There were 79 cases included in this study, with the incidence rate of AKI being 31.6%. In 19 out of 25 AKI cases, a stage 1 AKI was diagnosed, whereas in 6 patients CRRT was required (stage 3 AKI). Patients with and without AKI were comparable as far as gender, age, body weight and non-renal comorbidities. In the AKI group, PIM3 score was significantly higher than for non-AKI group (0.038vs.0.019;p=0.05) The most common PICU admission diagnoses in AKI cases were cardiac disease (28%), respiratory failure (24%) and infections (12%). In univariate analysis, risk factors for AKI resulted to be inotrope exposure (OR 2.57;95%CI 1.01-6.84;p=0.05), hypotension (OR 3.58;95%CI1.29-9.98;p=0.012), MODS (OR 4.08;95%CI1.23-13.55;p=0.016) and thrombocytopenia (OR 7.14;95%CI1.66-30.8;p=0.04). Overall, hypotension was the only independent risk factor for AKI in a multiple logistic regression model (p=0.0047). The mortality rate was estimated to be higher in AKI patients compared with non-AKI cases (12% vs. 1.8%; p=0.05)
Conclusions: The incidence of AKI in critically ill children is high, and this is associated with high mortality. In the PICU setting, AKI represents a marker of illness severity and it is mainly associated with hypotension.

P - 2 URINARY KIDNEY INJURY MOLECULE-1 RAPID TEST PREDICTS ACUTE KIDNEY INJURY IN EXTREMELY LOW BIRTH WEIGHT NEONATES

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Introduction: The new urinary and serum biomarkers are discovered and are being investigated. With them we can diagnose acute kidney injury (AKI) faster and more precisely and they also have a significant role in the outcome prediction.
Material and methods: The study included 22 extremely low birth weight neonates who were hospitalized in the NICU. They were divided into two groups based on serum creatinine (SCr) level - with and without AKI. Detection and quantification of urinary kidney injury molecule-1 (uKIM-1) was done on the third day of life, using commercially available KIM-1 rapid test. Subsequently, measurements were repeated only in subjects who were diagnosed with AKI, at different values of SCr.
Results: Logistic regression analysis showed that AKI is an independent risk factor for mortality. In a group of neonates with AKI, 50% of neonates administered the KIM-1 rapid test showed positive findings. KIM-1 rapid test was positive in patients with a wide range of SCr levels (range of 78.73-385 μmol/l), but all subjects had oliguria and died in the next 24h.
Conclusions: KIM-1 is a significant predictor of death. On the other hand, our study failed to prove that KIM-1 rapid test has any significance for early prediction of AKI.

P - 3 RECOGNISING ACUTE KIDNEY INJURY IN CHILDREN - HOW WELL ARE WE DOING?

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Introduction: The aim of the study was to investigate recognition and management of acute kidney injury (AKI) in paediatric patients not under renal follow up.
Material and methods: We reviewed the clinical assessment and management of children aged 1 month to 17 years who: 1) had a single creatinine measurement and, 2) the value was above the upper normal limit (UNL) for their age in a tertiary children's hospital. The 6-month study period was July-December 2012. Data was retrieved from paper and electronic patient records.
Results: There were 12,046 creatinine results in 4,103 patients during the study period. Of these, 206 patients (5.1%) had creatinines above the UNL for their age. In this subgroup, fifty-two children (25%) were not under renal follow up. Of these children 29 were male and 23 female. Their average age was 7 years old with a standard deviation of 3 years and 11 months. Review of the medical notes was done to confirm the recognition of elevated creatinines, revealing that just 2 of the abnormal results were recognised. Only 12% had their blood pressure recorded and 15% had a urinalysis performed at the time their creatinine level was tested. Follow up was arranged for 87% of patients with only a third (31%) having plans for repeat blood tests; 13% of these were requested specifically to check creatinine levels. The average time to repeating the blood tests was 6 months (range 1 week to 17 months). Of all patients, 3% had urine albumin:creatinine ratio checked on follow up visits.
Conclusions: This study suggests that recognition of AKI in children not known to have underlying renal problems/conditions is poor. Further data is needed to identify with greater precision clinically relevant levels of AKI in children. Electronic cues may be helpful along with better education.

P - 4 EARLY MARKER OF ACUTE KIDNEY INJURY IN CRITICALLY ILL TERM INFANTS

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Introduction: Using modern minimally invasive biomarkers of acute kidney injury (AKI), such as lipocalin-2, neutrophil gelatinase-associated (NGAL), kidney injury molecule-1 (KIM-1) and interleukin-18 (IL-18) in the urine of infants is especially important because allows for earlier periods diagnose AKI and timely conduct preventive measures aimed at preventing the development of AKI in children who underwent resuscitation in the neonatal period. The purpose of the work. Optimize the diagnosis of acute kidney injury in critically ill term infants.
Material and methods: A prospective observational study of the "case-control" 86 in critically ill term infants, they are the main group. In the main unit, in accordance with the classification AKIN (2011), two groups were formed: I - «AKI +», n = 12, with the level of serum creatinine ≥ 1,5 mg / dl over the age of 48 hours after birth. II - «AKI -», n = 74 - with the level of serum creatinine <1.5 mg / dL over the age of 48 hours after birth. AKI diagnosis in newborns conducted in the dynamics of 3-5th, 10-14th and 18-21th days of life. A control group comprised 26 somatically healthy term infants.
Results: The incidence of AKI in critically ill term infants 14%. Clinical manifestations AKI in critically ill term infants were: hourly urine output less than 1.5 mL / kg / h (100%, p 0,001), Edematous syndrome (100%, p 0,05), urinary syndrome as proteinuria (67%, p <0.05) and / or microhematuria (42%, p 0,05), increase of echogenicity of the renal parenchyma (67%, p <0.05), increased vascular resistance index and pulsatility index, followed by a decrease in the maximum and minimum flow velocities in the main renal arteries (p <0.05). The content of NGAL in the urine of term infants with AKI on 3-5th day of life was 2-fold higher (872,11 ± 52,64 ng / mg urine creatinine) than in infants without AKI (419, 88 ± 24,18 ng / mg urine creatinine) to 10-14 days of age, it decreased by 1.5 times, but remained significantly higher than in the control group (p <0.01). The content of KIM-1 in urine term infants with AKI on 3-5th day of life was 3 times higher (2,12 ± 0,25 ng / mg urine creatinine) than in infants without AKI (0,7 ± 0 08 ng / mg urine creatinine), and 18-21 days of age to this difference increases to 7 times (1,44 ± 0,26 ng / mg urine creatinine; 0,22 ± 0,03 ng / mg urine creatinine, respectively ; p<0,01). The content of IL-18 in the urine of term infants with AKI on 3-5th day of life was 2-fold higher (945,55 ± 122,69 pg / mg urine creatinine) than in infants without AKI (420,86 ± 28 02 pg / mg urine creatinine) to 18-21th days of age, this difference was maintained at the same level (p <0, 05). Increase in urine at 3-5th day life NGAL levels ≥ 944,4 ng / mg urine creatinine, and / or a KIM-1 ≥ 2,36 ng / mg urine creatinine, and / or IL-18 ≥ 1060,16 / mg urine creatinine is an early diagnostic marker of AKI and the continued improvement of NGAL in urine for 10-14th days of age ≥ 850 ng / mg urine creatinine indicates poor prognosis.
Conclusions: We were able to derive a mathematical equation to predict the presence of acute kidney injury, depending on the level of NGAL, KIM-1 and IL-18 in the urine of term infants in critical ly ill on the 3-5th day of life (86% diagnostic efficiency, sensitivity 83, 3%, specificity 86.5%) and 10-14th day of life (diagnostic efficiency of 93%, sensitivity 75%, specificity 95.9%). Based on these data has been optimized algorithm for early diagnosis of AKI and tactics of term infants in critically ill, based on the definition of NGAL, KIM-1 and IL-18 in the urine for 3-5 th and 10-14 th days of life, allows to distinguish high risk for AKI and AKI assess prognosis in the case of its development.

P - 5 NEW USES OF RASBURICASE?

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Introduction: Hyperuricemia might be the root of uric acid nephropathy causing acute kidney insufficiency (AKI). It also contributes to a worsening of the renal function when a chronic kidney disease (CKD) is diagnosed. Rasburicase is a recombinant urate oxidase enzyme that oxidazes uric acid into a soluble and inactive metabolite, allantoin. It is used in prevention/treatment of tumour lysis syndrome. Our proposal

states that rasburicase is used to prevent renal damage from worsening, and so not use an continuous renal replacement therapy (CRRT).
Material and methods: 8 patients to whom rasburicase was administered from September-2013 to January-2015 (17months) are described.
Results: Their ages range from 3days old to 20years old (median:4 months; mode:1 month), 75% boys and 25% girls. 75% presented a known primary pathology: 25%kidney transplant; 25% on post-operative care after a complex congenital cardiopathy; and 12%CKD. 100% present a worsening of the basal renal function or AKI (mean:GF 25.6ml/min/1.73). All of them were administered treatment for oliguric AKI (serotherapy and/or diuretics) with no response to it. 25% went through CRRT. All of them presented hyperuricemia (mean:12.2mg/dl) with hyperuricosuria (FEUA>1). Informed consent was given and G6PD deficit was ruled out prior to the administration of rasburicase. It was administered 4 times to one patient. Uric acid levels decreased below 0.5mg/dl in less than 24 hours with an increase of dieresis rhythm and a fall of creatinine/cystatine. There were not any secondary effects detected. Renal function was either normalized or returned to basal for those diagnosed with CKD. One patient died due to a primary disease.
Conclusions: Although the prescription of rasburicase is not approved as a normal procedure in children with AKI, its use has been successful. It has not shown complications and has been an aid in preventing increasing renal damage. We propose its use in such as complex paediatric patients.

P - 6 RADIONUCLIDE EVALUATION OF RENAL THROMBOEMBOLIC EVENT DURING TREATMENT WITH RECOMBINANT ACTIVATED FACTOR VII IN A CHILD WITH HAEMOPHILIA B WITH PLASMA IX INHIBITORS

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Introduction: We present a patient with hemophilia B and high titer inhibitors to coagulation IX (FIX) who was treated with rFVIIa for severe life-threatening hematuria.
Material and methods: A total rFVIIa dose was subsequently increased by administration every three hours, four times in total with each amount of 105 μg/kg. The treatment successfully stabilized red blood count and reduced hematuria. As hematuria, although reduced, continued, for the following two days the child received additional rFVIIa (once daily 285 μg/kg). Clinical and laboratory examinations, several ultrasound (US) examinations, ^{99m}Tc-DTPA , ^{99m}Tc-MAG3 scintigraphy and MSCT (multi-slice computer tomography) renal angiography were performed.
Results: Severe left kidney damage with 3 independent unobstructed arteries; two of them starting regularly and the third beginning caudally at the approximate position of the lower pole of the left kidney were found. The same kidney had 2 veins who communicated with each other. Renographic curve showed obstruction over the third phase of the renogram. According to radionuclide examinations the main site of lesion and clotting event was intrarenal vascular bed, primarily in glomerular region, while tubular region was less affected. Renal damage secondary to pelvicaliceal obstruction is less likely. Nine months later renal scintigraphy was repeated. The finding was normal. Right normal kidney was fully spared.
Conclusions: Such an extremely rare troboembolic event in patients with hemophilia B certainly do not compromise safe administration of rFVIIa. However, caution is necessary if hematuria requires administration of rFVIIa. US color doppler renal imaging before and after drug administration should be sufficient as an early warning.

P - 7 EFFECT OF ALBUMIN ADMINISTRATION ON THE RENAL DYSFUNCTION AFTER EXPERIMENTAL SURGICAL OBSTRUCTIVE JAUNDICE IN MALE RATS

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Introduction: The aim to study the influence of albumin supplementation on the changes of kidney function and structure in cirrhotic rats induced by common bile duct ligation (BDL).
Material and methods: 24 male albino rats weighing 200-250g were divided into Group I, 6 rats were undergone laparotomy alone and bile duct was just dissected from the surrounding tissue. Group II, 6 rats underwent sham operation and received albumin 2% in drinking water. Group III, 6 rats were subjected to bile duct ligation only. Group IV, 6 rats were subjected to bile duct ligation and received a daily albumin 2% in drinking water and then all rats sacrificed after 4 weeks. We measured liver and kidney functions, oxidative stress markers in the renal tissue and histological evaluation of the liver and kidney.
Results: Liver enzymes were decreased, but no significant difference in bilirubin levels in group IV when compared to group III. There was a significant elevation of serum creatinine in group III as compared to groups II and attenuated in group IV. Renal tissue catalase activity, and reduced glutathione as well as Nitric oxide levels were significantly increased in group IV and elevated in group III. Histologically, the liver of group IV showed degeneration and inflammatory cells infiltration with regeneration areas in which normal hepatocytes appeared. Kidney of group IV showed recovery, areas of inflammatory cells infiltration. Some tubules appeared with normal lining epithelium.
Conclusions: In conclusion, the results suggest that albumin partially improves the renal functions and structures after their disturbances in BDL.

P - 8 SERUM NEUTROPHIL GELATINASE ASSOCIATED LIPOCALIN IN INFANTS AND CHILDREN WITH SEPSIS RELATED CONDITIONS WITH OR WITHOUT ACUTE RENAL DYSFUNCTION

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Introduction: Acut kidny injury(AKI) is a common sequel of sepsis, early detection of AKI in sepsis may preserve kidny function. NAGL is apromising marker for kidny damage.
Material and methods: 65 patients diagnosed **as sepsis(**Group I):divided into three subgroups according to the severity of sepsis into: ***Group Ia* (*SIRS*):** 23 patients ,***Group Ib* (*severe sepsis*):** 20 patients ,***Group Ic* (*Sptic shock*):** 22 patients .Twenty patients served as controls**(**GroupII). **All studied patients and control groups were subjected to:**CBC ,CRP , LFT ,Prothrombin time and concentration . Urine collected in a sterile bag in 24hr. Serum creatinine and serum NGAL concentrations were estimated initially within 24 hours of admission and another sample within 72hours.
Results: Serum creatinine and NGAL (1st and 2nd) levels were significantly higher in patients with septic shock than those of SIRS and severe sepsis p-value=0.001, and increase in stepwise pattern in different stages

p-value=0.001.Also, there were significant increased levels of serum NGAL in non-survivors patients compared with survivors p-value=0.001.
Conclusions: Early measurement of serum NGAL level in sepsis can serve as a clinically useful marker for early prediction of evolving AKI and for grading of its severity.

P - 9 CD4+ LYMPHOCYTE ADENOSINE TRIPHOSPHATE MAY BE A POTENTIAL MARKER FOR PREDICTING RENAL PROGNOSIS IN CHILDREN WITH SEPSIS-ASSOCIATED AKI.

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Introduction: Sepsis is an important cause of morbidity and mortality especially among hospitalized children. Currently there are no diagnostic markers that can early predict the prognosis of sepsis associated AKI .The aim of this study was to determine ATP content of CD4+ Tcells (ATP_CD4) as a risk predicator in sepsis associated AKI.
Material and methods: The prospective study was conducted from May 2013-Dec2014 in PICU at faculty of medicine Suez Canal University Hospital.The study attained an approval from the Human Ethics Committee of thefaculty of medicine ,Suez Canal University Patient care and monitoring were performed as part of the hospital's standard protocol, and no specific intervention, other than the collection of umbilical cord blood, was required for this research.A total of 30 children (1-13 yrs.) with septicemia without gross congenital anomaly of genitourinary tract or pre-existing chronic kidney disease were included in the study on the basis of either a positive sepsis screen and/or a positive blood culture. AKI was diagnosed based AKIN criteria. ATP_CD4 was measured at three different time points. Results were related to survival, renal recovery and further clinical and laboratory data.
Results: Patients with complete renal recovery at 48hr after onset of sepsis had lower levels of ATP_CD4. There were no differences between patients with no AKI and those with AKI with different severity.
Conclusions: Lower concentrations of ATP_CD4 at 48hr after onset of sepsis may indicate a chance for complete renal recovery.

P - 10 EFFECT OF ACUTE KIDNEY FAILURE ON OUTCOME IN CHILDREN WITH SEPSIS

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Introduction: The aim of the study – to determine causative agents of bacterial sepsis, the course, outcomes of the disease and frequency of acute renal failure in children with sepsis.
Material and methods: Retrospective analysis of medical records data of 128 children treated for sepsis in during the period 2010-2012 years was made. Causes of sepsis, the course of the disease, renal function, indications for renal replacement therapy, outcomes were evaluated. Patients were divided into 2 groups: I group consisted of patients with sepsis, II – sepsis with multiple organ dysfunction syndrome (MODS).
Results: 108 (84,4%) children had sepsis (I group) and 20 (15,6%) - sepsis with MODS (II group), (p<0,0001). 34 (31,5%) children from the I group and 20 (100 %) – from the II group were treated in pediatric intensive care unit. Causative agents in blood culture were determined in 25 (23,1%) I and in 13 (63,0%) II group patients. The most common causative agents were S. aureus and Str.pneumonia: 20,8% in the I and23,1% - in the II group. Septic shock developed for 2 (1,9%) patients in group I and for 13 (65,0%) patients in group II. Acute renal failure developed for 6 patients (30,0%) in II group. 4 (66,7%) of them needed renal replacement therapy and 2 (33,3%) died. All I group patients recovered. In the II group full recovery was observed in 15 (75,0%), 1 (5,0%) remained hypertensive and 4 (20,0%) patients died (p<0,0001). 4 (3,1%) patients from both groups died.
Conclusions: S. aureus and Str.pneumonia are the main causative agents of septicemia in children. Acute renal failure developed in one third of patients with sepsis with MOD. Patients with sepsis and MODS mortality rate was significantly high (p<0,0001). According to the data of our study, the development of MODS, increases mortality 6.5 times.

P - 11 DETERMINANT FACTORS OF ACUTE RENAL INSUFFICIENCY IN THE COURSE OF GASTROENTERITIS

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Introduction: Acute gastroenteritis (GEA) is one of the main causes of entrance in the emergency unit for the pediatric age population. Practically, all the children at the age of three represent an episode of GEA. The absence of hidration and the secondary hypovolemia are the principal causes of morbidity and mortality and the reduction basis of the glomerural filtration(GF) in the acute phase. However, there are several guidelines linked to pediatric GEA, there is no data in the literature that help the pediatricians to identify the children with a greater risk of renal insufficiency .
Material and methods: We have analyzed 113 children (M=82, F=31, 0, 1-12 years old, average age 2,4±2,4) that have been admitted in the pediatric emergency unit between January 1 2009 till April 30 2009 and have done haematochemical tests. We have studied the statistical correlation among the principal clinic data provided from the anamnesis and clinical visit (the number of vomit episodes, diarrhea episodes, weight loss, diuresis referred from the parents, neurologic condition) divided in three gravity categories prior to the criteria appeared in the literature and the renal glomerular filtration(GFR).
Results: Renal insufficiency was estimated using the cut-off 80 ml/min/m2 where 32% of the subjects represented renal insufficiency. In univariate analysis none of the parameters taken into account has resulted to be correlated in a statistically significant mode with the glomerular filtration. In the multivariate analysis the age of the participants expressed like a continuous variable has resulted the solitary parameter statistically significant (P= 0,04) correlated to GFR. Particularly, the increase of age of the patients goes with the enhancement of 3,8 ml/min/m2 in GFR. Weight loss is not associated significantly to the reduction of the glomerular filtration : the difficulty of collecting anamnestic data and the measurement differences among home and emergency unit are certainly responsible for that.
Conclusions: The small children have a higher risk to develop acute renal insufficiency in the course of gastroenteritis and therefore could benefit from a therapeutic diagnostic approach more aggressive compared to the successive ages.

P - 12 ACUTE TUBULOINTERSTITIAL NEPHRITIS: A CASE SERIES AND LONG-TERM RENAL OUTCOMES

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Introduction: Acute tubulointerstitial nephritis (TIN) is a common cause of acute renal impairment, characterized by the infiltration of inflammatory cells in the interstitium of the kidney.

Material and methods: We retrospectively reviewed the medical records of 19 acute TIN patients attended to our Pediatric Nephrology department between April 1999 and April 2014.
Results: 19 patients (7 boys and 12 girls) were evaluated. The median age was 14 years (range 7-19). Five were diagnosed as TIN histopathologically, fourteen patients were diagnosed as clinically. Six patients were treated with steroids, thirteen patients were treated symptomatically. All patients showed a rapid recovery as longest in one month.
Conclusions: TIN is a common cause of acute renal impairment. Renal biopsy is recommended at persistent cases. Renal outcome is mostly good with symptomatic treatment but steroids could be preferred in severe nephritis however long term follow up showed no differences between the treated and non-treated group.

P - 13 A RARE CAUSE OF ANURIC ACUTE KIDNEY INJURY: BILATERAL URETEROLITHIASIS

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Introduction: Acute kidney injury (AKI) is characterized by abrupt deterioration in kidney function, manifested by an increase in serum creatinine level with or without reduced urine output. The spectrum of injury ranges from mild to advanced, sometimes requiring renal replacement therapy. The causes of AKI are classified as prerenal, renal and postrenal. The treatment of AKI is dependent to stage of AKI and underlying etiology.
Material and methods: Here we report a 10-years old male pateint who presented to our pediatric emergency clinic with the complaint of anuria and dyspnea for three days. In the history of patient, we learned that he was followed by pediatric neurologist with the diagnosis of epilepsy and motor mental retardation for nine years. Physical examination revealed microcephaly, coarse respiratory sounds, spastic tetraparesis, abdominal distention.
Results: Although uretral catheterization, there was no urine output of patient. His laboratory tests revealed that blood creatinine and blood urea nitrogen level were 4.23 mg/dl and 42 mg/dl, respectively. The level of electrolytes and blood gas analysis were normal. There were significant cardiomegaly and pulmonary edema on his telecardiography. The hemodialysis was performed due to pulmoner edema and anuria. After hemodynamic stabilization of patient, ultrasonography and computed tomography was performed respectively revealed bilateral hydroureteronephrosis and nephrolithiasis in the lower end of both ureters. After removal of ureteral stones by ureteroscopy, patients urine output increased and his blood creatinine level decreased to normal level.
Conclusions: We report this rare case to increase the awareness of physician, because prompt diagnosis followed by early relief of obstruction is associated with improvement in renal function in most patients as in our case.

P - 14 A CASE OF PEDIATRIC IDIOPATHIC CAPILLARY LEAK SYNDROME (CLARKSON'S DISEASE)

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Introduction: Capillary leak syndrome (CLS) is a rare disease and pediatric cases are even rarer.
Material and methods: Case report and systematic review.
Results: A 17 month-old boy without familial or personal medical history presented with a hypovolemic shock triggered by a benign adenovirus and picornavirus infection. This episode recurred at 20, 24, 30, and 33 months, caused each time by viral infections such as chicken pox or a respiratory infection. A common clinical sequence was noticed retrospectively: first a mild periorbital oedema followed by a sudden hypovolemic shock with initial hemoconcentration but paradoxically hypoalbuminemia without albuminuria or clear enteric loss and hyponatremia, then an oedema phase lasting a few days, and finally, a polyuria phase before a return to a normal state. Hyponatremia was associated with low plasma osmolality, insufficient urine dilution, normal-high plasma vasopressin and no sodium urinary nor enteric loss. The child presented a severe pericardial effusion during the second phase of the latest attack. The hormonal and metabolic tests performed returned normal results, in terms of adrenal function and the renin angiotensin aldosterone system in particular, and diagnosis of bradykinin-induced angioedema was ruled out.
Conclusions: CLS can be idiopathic (Clarkson's disease), as in the present case, but is most often secondary (malignant hematologic diseases, chemotherapies, other drugs, etc.). Its pathophysiology remains poorly understood. Acute pulmonary oedema, pericarditis, and other fluid overload complications are potentially life threatening. Emergency procedures should be established as soon as a relapse is suspected. Interestingly, hyponatremia as observed here is not usually described in CLS, we hypothesize that syndrome of inappropriate antidiuresis may occur in this rare condition.

P - 15 SAFETY OF PERCUTANEOUS KIDNEY BIOPSIES OF TRANSPLANTED AND NATIVE KIDNEYS IN CHILDREN

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Introduction: To evaluate the safety and complications of percutaneous kidney biopsy in children with native and transplanted kidneys.
Material and methods: We analysed in a retrospective single center study kidney biopsy related complications, both major (macrocopic hematuria requiring transfusion, or arteriovenous fistula requiring arterial embolization) and minor (subcapsular hematoma and hematuria). Three hundred and eighty-nine children underwent percutaneous kidney biopsy using a 16 gauge needle by a senior pediatric nephrologist or a trained junior fellow. Ultrasound was done to exclude structural problems, visualise the location and the depth of the kidney immediately before biopsy. Two fragments were obtained, and all patients had an over night observation period to check for complications mainly persistent macroscopic hematuria requiring further investigations.
Protocol biopsies were done in transplanted patients and in case of suspected rejection; biopsies of native kidneys were done in all cases with persistent proteinuria, hematuria, steroid resistant nephrotic syndrome and unexplained renal failure.
Results: 143 children with kidneys grafts and 246 children with native kidneys underwent kidney biopsy. Age (median, range) at biopsy performance was 13 (1-19). In the report forms 10/389 patients had macroscopic hematuria, only 1/10 required a Foley catheter insertion, and intravenous hydration to prevent blood clots. No blood transfusion was required in any of the 10 patients. Peri-renal capsular hematoma was identified in 60 patients without clinical significance.
Conclusions: It seems that percutaneous kidney biopsy is safe in children, independent of age group, providing that general contraindications are respected.

P - 16 A 28-YEAR RETROSPECTIVE ANALYSIS OF CLINICOPATHOLOGICAL DATA OF CHILDRENS RENAL BIOPSY

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Introduction: To investigate the composition and the alteration of clinical classication and pathological patterns of renal biopsy in children in 1st affiliated hospital of SUMS
Material and methods: A retrospective analysis of pathological and clinical data recruited from children with renal disease undergoing biopsy performed from January 1984 to August 2011 in 1st affiliated hospital of SUMS was done.
Results: The median age of 1313 children undergoing renal biopsy was 4months past 9 years old.There were 824 boys(62.8%) and 489 girls(37.2%). (1)921 children with primary glomerular disease (PGD) accounted for 70.1% in children undergoing renal biopsy and 312 children with secondary glomerular disease (SDG) accounting for 23.8%. (2)The main clinical manifestations of PGD were nephrotic syndrome (NS), isolated hematuria (IH) and acute glomerulonephritis (AGN) accounting for 31.2%, 16.1%, 11.0% respectively while IgAN (27.6%), MCD/GML (24.0%), and MsPGN (16.9%) were the main pathological patterns. (3)The main causes of SGD were LN (40.7%), HSPN (34.3%) and HBV-GN (19.6%). (4) The main diseases of the children undergoing renal biopsy are PGD in the two periods (1984-1997, 1998-2011). There was a trend the ratio of PGD was reducing while the ratio of SGD and other causes of glomerular disease were increasing year by year during the past 28 years. In 1998-2011 period the ratios of IgAN, MCD/GML and FSGS were more, meanwhile renal pathological constituent ratios of MsPGN, IgMN and CreGN were less ($P<0.05$). MsPGN in the pathological pattern of PNS was less ($P<0.05$). HBV-GN was less in the SGD ($P<0.05$). All of the above have statistical significance ($P<0.05$) compared with 1984-1997 periodabove have statistical significance ($P<0.05$) compared with 1984-1997 period.
Conclusions: PGD was the main cause of children undergoing renal biopsy in 1st affiliated hospital of SUMS. IgAN accounted for the commonest pathological pattern. NS was the most frequently clinical manifestation. In recent 28 years, composition of children renal disease changed. Different age interval has different compositions of renal disease. Renal biopsy was important in diagnosis, treatment and prognosis of renal disease in children.

P - 17 ULTRASOUND-GUIDED PERCUTANEOUS RENAL BIOPSY COMPLICATIONS IN CHILDREN: SINGLE CENTER EXPERIENCE

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Introduction: Percutaneous renal biopsy(PRB) is a very important diagnostic tool in the evaluation of renal diseases in children. Aim of this study was to evaluate retrospectively the complication rates of percutaneous kidney biopsies and the role of ultrasound-guidance.
Material and methods: A total number of 95 obtained from patients under18 years of age, within the period from January 2010 to March 2015, were analyzed retrospectively. All PRB were performed by a standardized technique using an automated spring fired biopsy gun, with 18 G disposable needle. Clinically significant hematomas were considered larger than 10 mm.
Results: The mean age of the patients at presentation was 13,5±5,04 years old, and 55,8% of the patients were female. Hematoma were observed in 7 out of 95 cases (7,3%). Of those, only one patient who diagnosed hemolytic uremic syndrome had hematoma which was larger than 10 mm and macroscopic hematuria. The major complication rate was low (1,05%).There was no statistically significance in terms of age, gender, and body mass index, primary renal disease between the patients with hematoma and without.
Conclusions: Percutaneos renal biopsy has been an essential procedure in establishing the histological diagnosis, adequate therapy and prognosis of kidney diseases. The use of real-time imaging and automatedgun biopsy needles, the renal biopsy has become a safe procedure today.

P - 18 ASSESSMENT OF TEN-YEAR-LONG RESULTS OF KIDNEY BIOPSIES PERFORMED ON CHILDREN IN THE THRACE REGION OF TURKEY

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Introduction: The aim of study is to determine incidences of renal diseases that could be diagnosed by biopsy during childhood ages in the Thrace Region, Turkey, and to compare clinical and histopathological findings by assessing all biopsy results in the past ten years.
Material and methods: The patients who underwent kidney biopsy between 2005 and 2015 in the Thrace University, Pediatric Nephrology Clinic were assessed retrospectively.
Results: Biopsies of 101 patients (54 girls, 47 boys) were examined. According to biopsy results, primary glomerulonephritis, which was observed in 49 (48.5%) cases, was the most observed renal disease when major histopathological findings were considered. IgA nephropathy, seen in 12 (11.88%) cases, was the most observed subtype in primary glomerulonephritis groups. Secondary glomerulonephritis was diagnosed in 27 (26.73%) cases. Subtypes of secondary glomerulonephritis were determined as systemic lupus erythematosus in 14 (13.8%) cases, Henoch-Schonlein Purpura in 12 (11.8%) cases, and amyloidosis in 1 (0.99%) case. Acute tubulointerstitial nephritis was diagnosed in two (1.98%) cases and end-stage renal disease in one (0.99%) case. Specific diagnoses could not be made in six (5.94%) cases, and seven (6.93%) cases were evaluated as normal.
Conclusions: IgA nephropathy as primary glomerulonephritis and systemic lupus erythematosus as secondary glomerulonephritis were the most common renal diseases in our region among children. In cases of compatible clinical findings, we may consider these renal diseases as being primarily important, and establishing early diagnosis by performing a renal biopsy may contribute to a positive prognosis.

P - 19 KIDNEY BIOPSIES OVER TWO DECADES IN A SINGLE MEDICAL CENTER: YIELD AND COMPLICATIONS

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Introduction: Kidney biopsy serves as an adjunct for the diagnosis of renal disease, but technical failures (inadequate sample) or non-informative findings may lessen its productivity. The studys aim was to define the rate of kidney biopsies that provide clinically valuable information in native and transplanted kidneys.
Material and methods: The database of the pathology institute was searched for all kidney biopsies performed in 1995-2014. Data were collected on patient characteristics, biopsy indications, technical and histopathological findings, biopsy yield (defines as positive if confirmed diagnosis or contributed valuable information, or negative in cases of technical failure or non-informative), and biopsy complications.
Results: During the study period, biopsies were performed on 216 native kidneys and 85 transplanted kidneys. Rates of positive biopsy yield were high in both groups: 86.6% for native kidneys, 82.1% for transplanted kidneys, with no significant between-group difference. The most common indications for biopsy were steroid-resistant nephrotic syndrome in the native-kidney group and decreased glomerular filtration rate and suspected rejection in the transplanted-kidney group (83% of cases). In the native kidney group, the presence of nephrotic-range proteinuria was directly associated with biopsy yield. Significant differences were found between the groups in patient age at biopsy, gender distribution, and family history and various technical and histopathological parameters. Post-procedural complications occurred in only 3 cases (1.3%) in the native-kidney group and 1 case (1.1%) in the transplanted-kidney group.
Conclusions: Both native and transplanted kidney biopsies are efficient and safe diagnostic procedures.

P - 20 A EUROPEAN RENAL BIOPSY SURVEY IN CHILDREN

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Introduction: Guidelines for Renal biopsy in children (RB) are still lacking. A questionnaire investigating technical aspects and indications was sent to ESPN and ERA-EDTA members in March 2014.
Material and methods: 229 questionnaires from paediatric nephrologists (PN) were received.
Results: 67% of PN are 35-55y.o, 86% working in academic centers, performing variable RB/year (21% >50 RB/yr, 36% 20-50 RB/yr, 43% <20 RB/yr). Transcutaneous ultrasound-guided puncture is the most common; 8.7% surgical in infants. RB is mostly performed by PN, 26% by radiologist, 30.4% by PN helped by radiologist, 7.2% by urologist. 80% choose the prone position, use 16 gauge needle (73%) mostly automatic (64%). 69% take 2 samples, with immediate microscope check. IF is performed in almost all centers, electron microscopy in 62%. RB is read in 65% by pathologists, in 33% by PN with pathologist . 85% of RB are performed in overnight hospitalized children. Platelet function is evaluated by 64%, mostly by bleeding time. Only 20.4% of PN perform RB in children on anti-platelets, the others wait 2-14 days after withdrawal. Desmopressin is used by 15%. Vital signs are always checked over the first 3 hours; 40% prescribe 24h bed rest. Red blood cell count is performed by 58% with different timing (2-24 hours). 69% of children receive ultrasound scan after 12-14hrs; 20% ultrasound scan/doppler after 6 months looking for artero-venous fistula. Significant bleeding requiring angiographic intervention were reported very rarely; nephrectomy is eceptional.
Conclusions: This is the largest survey on RB in children: results will be useful for a position paper from ESPN experts.

P - 21 CLINICAL INDICATIONS FOR RENAL BIOPSY IN CHILDREN AND RESULTS : OUR EXPERIENCE

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Introduction: The retrospective study was conducted in order to analyse the clinical and histopathological findings in the diagnosis of renal diseases in children.
Material and methods: The study included 32 children aged up to 15, who were found to have a renal disease through percutaneous renal biopsy. The research was conducted at our Department of paediatrics in the period between 2000 and 2010. Clinical and laboratory features, as well as indications for renal biopsy and pathohistological findings were analyzed.
Results: The most common indication for renal biopsy was nephrotic syndrome in 18 (56.2%), followed by asymptomatic haematuria with proteinuria and isolated microscopic haematuria each accounted in 3 (9.4%).The most common were glomerular diseases in 24 (75.0%), systemic disease with renal involvement was found in 2 (6.3%), tubulointerstitial nephritis in 1 (3.1%) and congenital renal parenchyma anomalies in 1 (3.1%) of our patients. The biopsy was negative in 4 (12.5%) patients. Among patients with glomerulonephritis, in 22 (68.8%) it was primary, in 4 (12.5%) it was secondary. The most common primary glomerulonephritis was focal segmental glomerulosclerosis (FSGS) in 7 (21.9%), mesangial proliferative glomerulonephritis (MEPGN) was found in 9 (28.1%), membranoproliferative glomerulonephritis (MPGN) in 2 (6.3 %), minimal change disease (MCD) in 3 (9,4%) and rapidly progressive glomerulonephritis (RPGN) in 1 (3,1%) of patients. Among the secondary glomerulonephritis, 1 (3.1%) patient had biopsy-proven lupus nephritis (LN), 1 (3.1%) had Henoch-Schönlein purpura nephritis (HSPN). Hereditary glomerulonephritis Alports syndrome had 1 (3.1%) of our patients.
Conclusions: The most common indication for renal biopsy was nephrotic syndrome. MEPGN and FSGS were the most common biopsy-proven renal diseases in our study.

P - 22 A PROSPECTIVE AUDIT OF 100 PAEDIATRIC RENAL BIOPSY DONE UNDER REAL TIME ULTRASOUND GUIDANCE.

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Introduction: To present a prospective audit of hundred renal biopsies.
Material and methods: All renal biopsies performed at either of the centers between June 2013 and July 2014 was included. Audit criteria were as per BAPN standards.
Results: Mean age was 8.52 years ± 5.08 years (youngest 4 month) with majority male (75%). In 77% two passes yielded the requisite two cores whereas more than three pass was required in only 1 case. Average number of glomerulus obtained were 26± 15 with ≤5 glomerulus in two cases (2%). Adequate tissues were obtained for a definitive diagnosis in all except 1 child. Major complication (gross haematuria requiring interventions) were seen in one case (1 %).
Conclusions: BAPN standards are achieveable even in developing countries.

P - 23 RENAL DAMAGE IN HIV/AIDS ROMANIAN COHORT

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Introduction: As the life expectancy of patients with HIV infection increased due HAART therapy, renal damage associated with this infection has become a real problem.
Our aim was to describe the characteristics of renal diseases in patients with HIV infection.
Material and methods: Between 1991 and 2015, 640 HIV-infected patients were admitted to the Emergency children hospital Timisoara. We focused on 202 HIV-infected patients that presented different forms of renal impairment.
Results: CD4+ level at diagnosis of HIV/AIDS showed that 47.52% can be considered "late presenters" with values below 200 CD4 T lymphocytes. The frequency was: urinary tract infection - 169 patients (83.66%), followed by renal lithiasis in 35 patients (17.32%). We find 3 patients with nephrotic syndrome (1.48%), nephrolithiasis - 16.33% (33 of patients), 8 patients - acute kidney injury (3.96%), 9 patients - chronic renal failure (4.45%), 7 patients - renal and urinary malformations (3.46%), and 5 subjects had enuresis (2.47%).
Conclusions: Most of the patients were born between 1988-1990 (88.61%), and were diagnosed with HIV/AIDS after a period of 6 months to 17 years after the infection. This is the cohort due to which, between 1990 and 2000, Romania had the highest number of HIV infected infants in Europe. 5 cases were diagnosed with HIV in infancy, most of the cases have been diagnosed 6-14 years after infection - 123 cases (60.89%). This approves literature **data** regarding the natural history of HIV/AIDS infection witch progresses silently for 10-12 years. **In patients with UTI, *Escherichia coli*, occurred in 99 cases (61.87%) followed by *Klebsiella pneumoniae* - 34 cases (21.25%). The renal biopsy was performed in 5 patients with glomerular damage.** The renal diseases are constantly present in HIV patients **as an** independent disorder or as a consequence of nephrotoxic HAART therapy.

P - 24 FOLLOW-UP DATA ON 179 DANISH CHILDREN AFTER THEIR FIRST PYELONEPHRITIS

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Introduction: Controversy exists regarding follow-up investigations in children diagnosed with their first pyelonephritis. In our centre children with upper urinary tract infections are subjected to a DMSA or MAG3 scan to assess renal parenchymal damage app. 6 months following the UTI.
We aimed to analyse follow-up data on 179 consecutive Danish children after their first pyelonephritis.
Material and methods: We examined the records of children diagnosed with their first upper UTI confirmed by urine culture during the years 2011-2013. We collected data on the clinical course of the pyelonephritis, the results of the DMSA and MAG3 scans as well as renal ultrasound scans. All children with known congenital renal and urinary tract malformations where excluded from the analysis.
Results: Of the initial population (age 2 months to 14 years), only 9 (5%) children presented with abnormal US scan (3 with bilateral and 6 with unilateral hydronephrosis). Twenty-one children (12%) presented with parenchymal defects in the DMSA/MAG3 scans (17 unilateral, 4 bilateral). Fifteen children (8%) all with scars presented with an uneven renal differential function on renal scans (<40/60). Of these patients, 9 underwent a VCUG and in all reflux was confirmed, 8 unilateral (n=3 grade V, n=3 grade IV, n=1 grade III, n=1 grade II) and 1 bilateral reflux (grade IV). Six of these patients underwent endoscopic reflux treatment.Of the 21 children with DMSA/MAG3 abnormalities only 5 presented with abnormalities in renal ultrasound (2 with bilateral hydronephrosis, 3 with unilateral hydronephrosis).
Conclusions: Renal DMSA/MAG3 scans are important tools when assessing differential renal function and renal parenchymal defects following a pyelonephritis. Whether to perform these investigations already after the first pyelonephritis is still under debate. We find a considerable number of children (12%) with clinically significant abnormalities in DMSA/MAG3 scans following their first pyelonephritis.

P - 25 URINARY TRACT INFECTION IN SMALL CHILDREN: THE PROGRESSION OF RENAL SCARRING OVER TIME

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Introduction: Renal scarring is frequently found in children with urinary tract infection (UTI) and may lead to long-term consequences. However, few studies have described the progression of renal scarring over time and the results are inconsistent. The aim of this study was to analyse the progression of renal lesions in relation to vesicoureteral reflux (VUR) and UTI recurrence.
Material and methods: Retrospective study of a cohort of 995 children under age 2 years, with first time UTI. DMSA scintigraphy >3 months after primary UTI was abnormal in 197 children. Of those 97 children, 46 boys and 51 girls, had additional scans > 2 years after the index UTI and were included in the study. The median follow-up time was 9.1 years, range 2.2 – 17.3 years. Progression of scarring was defined as either an increased up-take defect or decline in split function by >3%.
Results: 22 children, 10 boys and 12 girls, had resolution of renal lesions of which 13 were complete and 9 partial. In 21 children, 10 boys and 11 girls, the renal scarring showed progression; 18 with >3% deterioration of split function. In 54 children, 26 boys and 28 girls, no change was found. 31 (32%) children had recurrent UTI, 14 (14%) had VUR grade I-II and 44 (45%) grade III-V. The frequency of UTI recurrence and VUR grade III-V in the resolution group was 9% and 14%, respectively, compared to and 67% and 76% in the progression group ($p<0.001$). In the unchanged group the corresponding figures were 28% and 47%. There was no difference between the groups concerning gender or age at index UTI.
Conclusions: In children with renal damage the risk of progression is associated with recurrent UTI and high-grad VUR. In the absence of recurrence and dilating VUR progression is uncommon.

P - 26 SWEDISH UTI GUIDELINES

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Introduction: Management of children with UTI has been increasingly diverse during recent years. In 2013 a national working group presented new Swedish UTI guidelines with emphasis on children below 2 years of age. Recommendations were also given regarding UTI in older children, children with VUR and follow-up of children with UTI-related renal damage.
Material and methods: The working group analyzed different aspects of UTI management such as definition of bacteriuria and UTI, epidemiology and risk factors, antibiotic treatment, diagnostic procedures (urine

sampling, analysis and culture, laboratory findings, ultrasound, DMSA-scan, voiding cystourethrography), diagnosis and treatment of VUR and bladder and bowel dysfunction and its impact on UTI recurrences. Algorithms were designed for children <2 years of age, children ≥2 years, management of VUR and UTI-related renal damage.
Results: For children <2 years the new algorithm recommends ultrasound in all children. Investigation is guided by risk factors such as CRP ≥70mg/L or high S-creatinine, non-E. coli infection, abnormal ultrasound and recurrent UTI. Early DMSA-scan is recommended for those with risk factors. VCUG is only done in those with pathological results on DMSA-scan or ultrasound. An alternative algorithm with a late scan was made for centers where DMSA-scan cannot be offered within 4 weeks. In older children DMSA-scan is recommended only in case of recurrent febrile UTI or ultrasound abnormality. In VUR, antibiotic prophylaxis is recommended only in dilating VUR, with longer treatment in girls. Endoscopic injection is recommended after the first recurrence in girls with VUR grade IV, in other cases after a second UTI recurrence. VUR grade V is managed on an individual basis.
Conclusions: The new Swedish guidelines on UTI in children will make the management of these children more uniform and assure an accepted standard of quality. They balance the need for risk factor analysis and simplicity, limiting diagnostic procedures.

P - 27 ANTENATALLY DETECTED URINARY TRACT ABNORMALITIES: IS 7MM BETTER THAN 4MM?

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Introduction: A prospective cohort study was conducted to assess the change in incidence and outcome of antenatally detected urinary tract anomalies (AUTA) in the Nottingham population following a 2010 change in the UK definition of antenatal hydronephrosis. Our findings were compared with a previously published cohort (1999-2003).[1]
[1] Mallik,M; Watson,A Pediatr Nephrol 2008 Jun: 23(6) 897-904
Material and methods: Two new cohorts were identified. The 2007-2009 cohort contained all infants with fetal anteroposterior renal pelvic diameter (APRPD) ≥5mm on the 20 week anomaly scan progressing to APRPD≥7mm in the third trimester *and* all other AUTAs. The 2011-2013 cohort contained all infants with APRPD≥7mm on the 20 week anomaly scan *and* all other AUTAs. Significant APRPD in the 1999-2003 cohort was defined as ≥4mm on 20 week scan progressing to APRPD≥7mm in the third trimester. Incidence of AUTA, postnatal diagnoses and surgical intervention were compared between all groups. The 2007-2009 cohort was analysed to determine pathology missed under the 2010 definition of antenatal hydronephrosis.
Results: Incidence of AUTA was reduced between the 2007-2009 and 2011-2013 cohorts (165 vs. 110 live births) and reduced in comparison with 1999-2003 data (350 live births). The proportion of cases with normal postnatal scans was reduced with the change in definition of antenatal hydronephrosis (2007-2009 33.9% vs. 2011-2013 24.5%). The incidence of all other postnatal diagnoses was broadly similar between all three cohorts. Surgical intervention was less common in the most recent cohort (2007-2009 11.6% vs. 2011-2013 6.4%). 34 patients in the 2007-2009 cohort would not have been reviewed postnatally under new guidance, of whom 9 had persistent pathology requiring further investigation. Two of these patients required surgical intervention.
Conclusions: Changing definition of antenatal hydronephrosis results in reduced incidence of AUTA largely related to reduction in proportion of infants with normal postnatal imaging. Retrospective application of current criteria demonstrated that few cases of significant pathology would have been missed.

P - 28 RESULTS OF ONABOTULINUMTOXIN-A IN CHILDREN WITH THERAPY RESISTANT OVERACTIVE BLADDER: 10-YEAR EXPERIENCE

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Introduction: In this study we present the results and side effects of all non-neuropathic children, which have been treated in our institution between 2004 and 2014 (n=192), in order to define the place of botulinum toxin in the treatment of non-neurogenic OAB.
Material and methods: During the study period, 122 boys and 70 girls with a mean age of 9 years (+- 2,5) were treated with botulinum toxin. All patients received ona-BoNT-A, a standard dose of 100 IU was used. The injection was performed in 15 extratrigonal spots and without including the bladder dome. All patients were true therapy resistant, meaning that all previous therapies, both urotherapy and medical treatment, were unsuccessful. For the definition of success, the ICCS criteria were used, however, for enuresis it was adapted: full success 0 episodes/month, partial success <2 month.
Results: For diurnal incontinence, in 74% the treatment was successful (52% full response and 22% partial response). In patients presenting with enuresis the successrate was lower: 49% (27% full success and 22% partial success). In 15 patients (8%) a UTI was reported as treatment related complication. Retention was not observed. No general side effects or severe adverse events were observed.
Conclusions: OnaBotulinum toxin A is a safe and effective treatment for OAB in non-neuropathic children. It can be a useful treatment option for therapy resistant overactive bladder and/or nonmonosymptomatic enuresis.

P - 29 PATIENTS WITH ENURESIS MAY HAVE BALANCE DISORDERS

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Introduction: Balance is the ability of an individual to maintain body stability, even under disturbance. Balance requires integration of visual, somatosensory and vestibular systems. Children with enuresis have delayed maturation of motor cortex with changes in sensory and motor systems that comprise the basis of balance. Thus, we hypothesized: enuretic patients may have balance disorders.
Material and methods: One hundred eleven kids with enuresis (EG) from 7-16 years old were paired with 60 asymptomatic kids (CG) for gender and body mass. Two age groups were subdivided: A: 7-11 years (EG/A, N=77; CG/A N=38) and B: 12-16 years (EG/B, N=34; CG/B N=22). Balance is assessed using an electronic force plate (60 Hz) measuring the Area and Velocity(VM) of Center of Pressure Displacement, which is the point of application of the resultant of vertical forces acting on the supporting surface. Sensory Integration was measured by a 60-second trial standing in four conditions: (1) open eyes, stable surface; (2) closed eyes, stable surface; (3) open eyes, unstable surface; (4) closed eyes, unstable surface. Postural adjustment was assessed using belt traction with 4% of body weight and unexpected release of it to produce a controlled postural perturbation followed by adjustments observed during 10 seconds.

Results: EG/A group showed greater Area and VM compared to CG/A in all 4 sensorial conditions and greater VM with delayed recover for postural adjustment. EG/B group only showed greater Area compared to CG/B in sensorial conditions 1, 2 and 4.
Conclusions: Enuretic patients showed worse balance compared to control group.

P - 30 ATOMOXETINE AMELIORATES NOCTURNAL ENURESIS IN PATIENTS WITH MILD ADHD

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Introduction: Recent studies showed that incontinence and ADHD coexist and interact each other. However, the treatment for the patients with nocturnal enuresis (NE) and ADHD has not been established.
Material and methods: We treated 265 new patients with NE at Juntendo University Nerima Hospital & Musashi-murayama Hospital (Tokyo, Japan) since May 2013 to October 2014, with ages of 6 – 14 (198 cases with MNE and 67 cases with NMNE). With the routine interviews and physical examinations at the patients' first visits, we had excluded the possibility of comorbid ADHD and its related disorders. Patients with MNE were treated with or desmopressin and/or alarm and those with NMNE were treated with anti-cholinergics and/or alarm. At 12-weeks after the treatments, 52 with MNE and 13 with NMNE were classified as PR or NR. These 65 patients were re-assessed whether they had "subclinical" ADHD, and 24 patients (15 with MNE and 9 with NMNE) met the diagnostic criteria of DSM-IV-TR. They were treated with atomoxetine (ATX) (1.8mg/kg/day) in addition to ongoing therapy for NE.
Results: After 8-weeks ATX therapy, the average wet nights per months were significantly decreased: 17.1 to 2.7 in MNE (P=0.0007) and 23.2 to 11.4 in NMNE (p=0.0117). Overall, ATX treatment was beneficial in 20 of 24 cases (FR:3, R:9, PR:8, NR:4).
Conclusions: We need pay more attentions for the possible comorbid ADHD in refractory cases with NE, and recommend ATX therapy for those patients.

P - 31 SIGNIFICANCE OF EXAMINATION OF CONCENTRATION OF TGF-β IN 24 H URINE FOR EARLY DIAGNOSTIC OF RENAL SCARRING IN PATIENTS WITH VESICOURETERIC REFLUX

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Introduction: The aim of the study was to determine concentration of TGF-β in urine of patients with vesicoureteric reflux (VUR) and reflux nephropathy A (RN A) for early diagnostic of renal scarring .
Material and methods: We examined 60 children with RN A and VUR. All children were comparable on gender and age. All patients underwent ultrasound, X-ray and DMSA scan. We examined concentration of TGF-β in 24 h urine of patients by ELISA. Children were divided into 2 groups: I – with unilateral RN A according to classification of Smellie J. et all, 1975 (n=30); II – with VUR without renal damage (n= 30)
Results: We established that data of concentration of TGF-β in 24 h urine of patients with VUR without renal damage was 7,62±0,25 pg/ml. Concentration of TGF-β in 24 h urine of patients with unilateral RN A was 8,57±0,34 pg/ml. The ranges of concentration of TGF-β in 24 h urine of patients with VUR without renal damage were significant different with concentration of TGF-β in 24 h urine of patients with RN A ($p<0,05$).
Conclusions: So, we determined that concentration of TGF-β in 24 h urine increased in process of renal scarring. That's why data of concentration of TGF-β in 24 h urine can be used for early diagnostic of renal scarring in children with VUR.

P - 32 ORAL ANTIBIOTICS FOR FIRST EPISODE OF ACUTE PYELONEPHRITIS IN DANISH CHILDREN; DETERMINING THE OPTIMAL EMPIRICAL ALTERNATIVE

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Introduction: In Denmark children with acute pyelonephritis are treated by parenteral antibiotics. We wanted to determine safe and effective oral antibiotics for children aged at least 6 months with first episode of uncomplicated pyelonephritis(UTI).
Material and methods: A retrospective analysis of positive urine cultures collected at a Danish general paediatric ward 2010-2013. Cultures from 390 children aged 0-15.9 years, without urological anomalies, treated for UTI were included. The antimicrobial susceptibility was determined for ampicillin, amoxicillin-clavulanate, piv-mecillinam, nitrofurantoin, trimethoprim and cefuroxime.
Results: The most common etiologic agents were 81.6% *Escherichia coli*(*E.coli*), 10.8% *Klebsiella species* and other enterobacteriacea, and 5.6% *enterococci species*. Bacterial resistance were 7.9% for amoxicillin-clavulanate, 8.8% piv-mecillinam, 8.2% nitrofurantoin, 8.9% cefuroxime, 23% trimethoprim and 50% ampicillin. *E.coli* had resistance rates of 1.2% for both amoxicillin-clavulanate and piv-mecillinam, 4.3% for cefuroxime, 18% nitrofurantoin, 27% trimethoprim and 47% ampicillin.
Isolates from boys more seldom than girls showed *E.coli* (69.9% versus 87.5%, $p<0.0001$). Equivalently, isolates from boys were more resistant to ampicillin (61.8% versus 44.4%, p=0.001) and piv-mecillinam (14.7% versus 5.9%, p=0.005) than those from girls. For 251 patients older than 6 months of age the isolate-resistance rates were 6.3% for amoxicillin-clavulanate, 7.4% piv-mecillinam, 7.7% nitrofurantoin, 7.8% cefuroxime, 27.3% trimethoprim and 46.7% ampicillin.
Conclusions: Amoxicillin-clavulanate and piv-mecillinam had lowest bacterial resistance rates of 8% and 9%, respectively (for patients older than 6 months: 6% and 7%, respectively). Our results may guide which oralantibiotics should be recommended for empirical treatment of UTI in Danish children, and populations with similar resistance patterns.

P - 33 USE OF URINE NGAL IN EARLY DIAGNOSIS OF UTI

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Introduction: Urinary Tract Infection is one of the most common infections in pediatric age group. Such infection with non specific symptoms, yet serious sequelae (renal scarring, hypertension and renal failure) needs

early detection and management. Neutrophil Gelatinase Associated Lipocalin(NGAL) is a member of lipocalin superfamily, which is produced from nephrons in response to tubular epithelial damage. Recent studies have shown that plasma NGAL is a novel biomarker for Acute Kidney Injury. However, data reflect the use of urinary NGAL as a biomarker for diagnosing febrile UTI, is still missing

Material and methods: We included all febrile children admitted to KAAUH(age = 0-18 years). Patients with (CKD GFR>60mlm) were excluded. Then Urinary (NGAL) levels were measured using immunoassay. In addition to: urine analysis, urine culture and sensitivity test, C-RP and CBC

Results: The study showed statistically significant difference between NGAL levels in patients with UTI and patients without UTI (p=0.008, mean= -352.44). Roc Curve, showed (60.3%)sensitivity and (60.4%)specificity.

Conclusions: Urinary NGAL is an acceptable early biomarker for febrile UTI.

P - 34 REINTRODUCTION OF ALARM THERAPY IN CHILDREN WITH REFRACTORY MNE

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Introduction: ICCS standardisation advocates as initial treatment in children with MNE alarm, desmopressin or the combination = Level I Grade A recommendation . But little is known in refractory cases

Aim : Succes rate of re-introduction alarm in “alarm therapy “ refractory cases ?

Material and methods: Methods ; retrospective study 2012-2013 Patients receiving alarm therapy : 73 MNE Patients / (719 NMNE files in same period) : Age 8-17 y, Full screening , In children with MNE and ND > 100% Bvage , No daytime symptoms at presence , History of “failed” alarm therapy

Results: Response rate 74%, But 72 % relapse rate Increased response rate associated with Age, Associated desmopressin therapy (n = 49))

No correlation with Gender , Latency , Duration and type of previous therapies, inclusive n alarm therapies

Conclusions: Refractory MNE is a minor population (+/_ 10%) in a tertiary enuresis centre . This study demonstrates that in patients with a history of MNE, refractory to previous treatments, inclusive the alarm, a reintroduction of the alarm has a high response rate, although a relapse rate of 2/3.

P - 35 FACTORS PREDICTING THE LONG-TERM RENAL OUTCOME IN BOYS PRESENTING WITH POSTERIOR URETHRAL VALVES AT TYGERBERG CHILDREN’S HOSPITAL, SOUTH AFRICA

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Introduction: To determine the prognostic value of certain clinical, biochemical and radiological variables in the long-term renal outcome of boys presenting with posterior urethral valves, compared with international findings.

Material and methods: Retrospective, descriptive study of boys diagnosed and treated with posterior urethral valves at Tygerberg Children’s Hospital between 2001 and 2011.

Results: Of 47 cases identified, 13 were excluded, 7(20,6%) were diagnosed antenatally and 27 (79,4%) presented postnatal. Mean age at presentation was 13,9 months. The most common postnatal presentation was urinary tract infection (51,9%). Mean follow-up was 54,2 months (median 47,5; range 12-133). 13 boys (38,2%) developed chronic kidney disease of which 2(6%) required renal replacement therapy. Initial and nadir serum creatinine, poor corticomedullary differentiation and moderate-severe hydronephrosis were significant predictors of final renal outcome (p<0,050). Patient age at presentation, type of primary surgical intervention, increased renal echogenicity, bladder wall thickness, the presence of vesico-ureteric reflux, severe bladder dysfunction and initial or breakthrough urinary tract infection had no significant impact on future renal function. Boys with an initial serum creatinine ≥145μmol/L and a nadir serum creatinine ≥62μmol/L were at highest risk of developing chronic kidney disease (AUC 0,8 and 0,9, respectively).

Conclusions: A third of boys (38,2%) developed chronic kidney disease at the end of follow-up. Our data concur with the high prognostic value of initial and nadir serum creatinine as seen in other centers, although optimal threshold levels for initial and nadir serum creatinine to predict final renal function differed. Similarly, poor corticomedullary differentiation and moderate-severe hydronephrosis on initial kidney ultrasound were significant indicators of poor renal outcome.

P - 36 RESOLUTION OF NOCTURNAL ENURESIS IN CHILDREN WITH SLEEP-DISORDERED BREATHING AFTER ADENOTONSILLECTOMY: THE ROLE OF ANTIDIURETIC HORMONE AND BRAIN NATRIURETIC PEPTIDE

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Introduction: Antidiuretic hormone- (ADH-) and brain natriuretic peptide- (BNP-) induced natriuresis and diuresis have been reported in both sleep disordered breathing (SDB) and nocturnal enuresis (NE). We have previously reported that adenotonsillectomy (T&A) led to complete resolution of NE in about 50% of children. However, the mechanism by which T&A results in resolution of enuresis remains unknown. In this study we assessed (1) the effect of T&A on urinary electrolytes and secretion of ADH and BNP in children with NE and SDB, and (2) whether these changes correlated with NE resolution post T&A.

Material and methods: Prospective study comparing the urinary electrolytes and plasma ADH and BNP levels between (1) children with SDB and NE (study group) pre and 1-month post T&A, and (2) study group and age-matched control group (children with SBD without NE)(ANOVA).

Results: Prior to T&A, study group (N=37, 20 Males, mean age 8.79 +/- 2.41 years) had significantly lower ADH and significantly higher BNP levels than controls (N=31, 17 Males, mean age 8.71 +/- 2.99 years)(p=0.004, p=0.002, respectively). There were no significant differences between the groups post-surgery. Study group showed significantly decreased BNP, UNa/Cr and UCa/Cr post T&A compared to the pre T&A values (Table), with no differences between dry (N=16) and wet children post T&A.

	Study Group (N=37)		P-value
	Pre-T&A	Post-T&A	
ADH (pg/ml)	6.49 ± 7.09	8.84±8.60	0.080
BNP (ng/ml)	46.77 ± 65.04	22.43 ± 31.03	0.030
UCa/Cr*	0.10 ± 0.06	0.07 ± 0.05	0.007
UK/Cr*	3.85 ± 2.01	4.70 ± 2.97	0.133
UNa/Cr*	17.70 ± 8.68	13.08 ± 9.52	0.020

*Urinary ratios (mmol/mmol); Ca-calcium; K-potassium; Na-sodium; Cr-creatinine

Conclusions: The presence of NE alters ADH and BNP levels in children with SDB. T&A led to ADH- and BNP- normalization probably through a calcium- and sodium-dependent mechanism, but this does not correlate with the resolution of NE.

P - 37 COPY-NUMBER VARIATION GENETIC ANALYSIS OF FAMILIAL PAEDIATRIC CASES OF CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT

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Introduction: Congenital anomalies of the kidney and urinary tract (CAKUT) are the main cause of end-stage renal disease in childhood. While most cases are sporadic, familial clustering of CAKUT is common, emphasizing a strong genetic contribution. Recently, mutations in 12/17 autosomal dominant known CAKUT-causing genes were identified, in 6.3% of 650 unrelated families with CAKUT. Copy-number variation (CNV) (submicroscopic chromosomal imbalances) has also been detected in CAKUT patients, where a high incidence of CNV was found in cases with multicystic dysplastic kidney (MCDK) and urethra valves. To identify novel genomic regions associated with CAKUT, we investigated the presence of CNV in familial CAKUT cases.
Material and methods: We screened for CNV seven familial cases of CAKUT using array-CGH (Comparative Genomic Hybridization). Array-CGH was performed using Cytochip ISCA array (BlueGnome-version 1.0) with 180,000 oligos, analyzed using build GRCh37 (hg19). Those were two female twins with duplex collecting system/ bilateral VUR grade III-IV and unilateral renal hypodyspasia (RHD); two brothers with VUR grade III and RHD; 3 second cousins with bilateral VUR grade V and RHD (1 patient), bilateral VUR grade III (1 patient) and ureterovesical junction obstruction (1 patient). The families of the last 3 patients came from a cohort of Gypsies with a high rate of inbreeding (first cousins be married).
Results: Of the seven paediatric patients, five had normal constitution of CNV, one had a duplication of approximately 0.2Mb on the 5q-arm (5q23.3) which is probably unrelated to CAKUT, and one patient with ureterovesical junction obstruction had a deletion approximately 1.4Mb in size on the 17q-arm (17q12) which includes a known CAKUT gene, the HNF1B, and has been previously described in a patient with MCDK.
Conclusions: CNV analysis could reveal novel causative genes or genomic regions in CAKUT patients and further studies in larger cohorts should be performed.

P - 38 TRANSDERMAL DELIVERY OF NITROFURANTOIN

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Introduction: Nitrofurantoin (NFT), is widely used in the prophylaxis of urinary-tract infections (UTI). We aimed to develop and characterize innovative transdermal formulations of NFT to increase the patient compliance and decrease the adverse effects such as nausea and vomiting which are limited the drug use in long-term.

Material and methods: We prepared and characterized microemulsion, gel (hydrogel, lipogel and DMSO gel) and film type formulations for transdermal delivery of NFT. In vitro drug release studies were performed to determine the drug release from formulations. In preliminary in vivo studies, all the formulations were applied to male Wistar rats transdermally to analyse the transition to urine. The presence of NFT was measured by High-Performance Liquid Chromotograpy (HPLC) in urine samples collected periodically. Skin irritation tests (transepidermal water loss, melanin and erythema values) were performed to analyse the irritation on the rat skin.
Results: In the 168th hour, percent NFT releases were nearly 12.8%, 16%, 36%, 37% and 40% in the hydrogel, lipogel, film, microemulsion and DMSO gel formulations respectively in in vitro studies. NFT was passed to urine only in DMSO gel and film type formulations and passage to urine was higher in film type formulation compared to DMSO jel type formulation. Transepidermal water loss was increased compared to basal level in film type formulation ($p<0.05$).
Conclusions: Transition to urine of NFT was high in film type formulation. Increase in transepidermal water loss may assist the permeation of NFT from the skin. The lack of change in the result of erythema and melanin demonstrating that the film type formulations does not cause irritation in the skin. NFT is suitable to be applied transdermal route in film type formulations. Pharmakokinetic studies of transdermal NFT in rats must be performed.

P - 39 PROCALCITONIN AS A PREDICTOR-RENAL SCAR DEVELOPMENT OF URINARY TRACT INFECTION IN CHILDREN

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Introduction: Urinary tract infection (UTI) is a common disease in children. The objective of this study was to correlate elevated serum procalcitonin (PCT) values with renal scarring in children with UTI compared with C-reactive protein (CRP).
Material and methods: We have studied prospective 50 children 1 month to 2 years of age with first episode of febrile UTI. PCT was measured by immunochromatografic assay in serum samples from children with microbiologically documented infection. Severe renal parenchymal involvement was assessed by 99mTcdimercaptosuccinic acid (DMSA) gammagraphy done 6 months after the episode UTI.
Results: Out of 50 children 40 (80%) showed to have renal parenchymal involvement (renal scar) documented by DMSA scintigraphy. Among children with pyelonephritis with scars, elevated serum PCT values >2ng/l was identified among 37 (74%) and CRP>50 mg/l 26 (52%). And among children with pyelonephritis without scars serum PCT values was 0.5ng/l<PCT<2ng/l, and 20mg/l<CRP>50 mg/l 14 (35%). PCT at presentation showed a significant correlation (P <0.0054) with the presence of renal scars in children with UTI. The PCT values were correlated with the degree of renal involvement, whereas the CRP values failed to show such a significant correlation P >0.05 PCT had a sensitivity of 90.47% and a specificity of 88% in predicting renal scar, whereas CRP had sensitivity of 85.71% and a specificity of 48%.
Conclusions: A low PCT value at admission indicates a low risk of long term renal scarring. Increased PCT values at admission correlate with the presence of scars. PCT values have proved to be more specific than CRP for identifying patients who might develop renal damage

P - 40 GENETIC POLYMORPHISMS IN INFLAMMASOME-DEPENDENT INNATE IMMUNITY AMONG PEDIATRIC PATIENTS WITH SEVERE RENAL PARENCHYMAL INFECTIONS

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Introduction: Activation of inflammasome innate immune responses have been demonstrated in various inflammatory diseases and microbial infections. But no studies has examined the inflammasome-dependent pathway among patients with urinary tract infections. Defective or variations in genes associated with innate immunity is believed to alter the host's susceptibility to microbial infections. This investigation is aimed to explore the genetic polymorphisms for genes encoding the inflammasome and subsequent cytokine released among pediatric patients with severe renal parenchymal infections.
Material and methods: Patients diagnosed as acute pyelonephritis (APN) and acute lobar nephronia (ALN) without underlying diseases or structural anomalies, except for vesicoureteral reflux (VUR), were enrolled. Genotyping of the single nucleotide polymoephisms (SNPs) in the genes associated with inflammasome formation and activation (*NLRP3*, *CARD8*), and subsequent IL-1β cytokine generation (*IL-1*β) was performed.
Results: A total of 40 SNPs were selected for initial genotyping. Analysis of 96 normal and 48 patients' samples revealed that only nine SNPs (5 SNPs in *NLRP3*; 3 SNPs in *CARD8*; 1 SNP in *IL-1*β) had heterozygosity rates >0.01. Hardy-Weinberg equilibrium was satisfied for the observed genotype frequencies on these SNPs. After elimination of patients with VUR, a well-known risk factor for severe UTIs, from the analysis, patients with APN and ALN had a lower *NLRP3* (rs4612666) CC genotype frequency than the control. With the correction for multiple-SNP testing, only the no-VUR subgroup of (APN+ALN) combined disease group remained significant difference from the control group ($P<0.0055$).
Conclusions: The inflmammasome-dependent innate immunity pathway is suggested to be associated with the pathogenesis of pediatric severe renal parenchymal infections for the first time. Further investigation is warranted to clarify its pathogenic mechanism.

P - 41 USEFULNESS OF NEUTROPHIL LYMPHOCYTE RATIO IN YOUNG CHILDREN WITH FEBRILE URINARY TRACT INFECTION

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Introduction: Acute pyelonephritis (APN) is the one of serous bacterial infection in children that could cause renal scarring. Early identification of APN in febrile urinary tract infection (UTI) is important as prompt treatment improves outcomes. Neutrophil Lymphocyte ratio (NLR) has been reported to be a prognosis marker of various diseases such as tumor, infectious disease and coronary heart disease. However it has not yet been well-established in UTI. Our goal of this study was to propose NLR as a useful marker to predict APN.
Material and methods: We retrospectively evaluated data of young children ( ) with febrile UTI who had undergone renal ultrasonography (USG), dimercaptosuccinic acid (DMSA), and voiding cystourethrogram (VCUG) fromJanuary 2010 to December 2014. Conventional infection markers (white blood cell [WBC], erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]) and NLR were measured.
Results: A total 298 of UTI patients were included (APN in 54.7%). The NLR, WBC, CRP and ESR were higher in APN than in lower UTI ($p < 0.001$). Multiple logistic regression analyses showed that NLR (odds ratio [OR] 1.063, 95 % confidence interval [CI]: 1.263 – 2.035, $p < 0.001$] were independent predictive factors for positive DMSA defects in UTI patients. The area under the receiver operating characteristic (ROC) curve was also highest for NLR (0.713; 95% CI 0.654-0.771, $p < 0.001$) and CRP (0.726; 95% CI 0.669-0.783, $p < 0.001$) with DMSA defects. NLR demonstrated a significantly the highest area under the ROC curve than those of the inflammation markers for diagnosis of Vesicoureteral reflux (VUR) (0.638; 95 % CI: 0.565–0.711, $p < 0.001$).
Conclusions: This study showed that NLR was significantly associated with APN and outperformed conventional markers for predict of VUR. Our results suggest that NLR could be used as an easily measurable and reliable diagnostic method for distinguishing APN from lower UTI.

P - 42 THE ASSOCIATION BETWEEN SERUM 25-HYDROXY VITAMIN D LEVEL AND URINE CATHELICIDIN IN CHILDREN WITH A URINARY TRACT INFECTION

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Introduction: Cathelicidin is an important antimicrobial peptide in urinary tract. Cathelicidin expression is strongly stimulated by 1,25-dihydroxy vitamin D in epithelial cells, macrophage/monocyte and neutrophils. Vitamin D and cathelicidin status in children with Urinary tract infection (UTI) is unknown. Therefore, we analyzed serum vitamin D and urine cathelicidin levels in children with a UTI.
Material and methods: Thirty six patients with UTI (6 males, mean age 6.8±3.6 years, range: 0.25-12.6 years) and 38 control (10 males, mean age 6.3±2.8 years, range: 0.42-13 years) were investigated. Both study and control subjects underwent serum 25-hydroxy vitamin D and urine cathelicidin level measurement.
Results: There were not significant differences between the study and control groups for urine cathelicidin level ($p>0.05$). Eight (22.2%) patients in the study group and 21 (58.3%) children in the control group have sufficient vitamin D (≥20 ng/ml). Patients with sufficient vitamin D has higher urine cathelicidin level than control with sufficient vitamin D (respectively 262.5±41.1 vs 168±31.6 ng/ml, $p=0.001$).
Conclusions: The children with vitamin D insufficiency may not increase of the urine cathelicidin level during UTI. With the increase in the number of antibiotic-resistant bacteria, there is a need to develop treatment strategies for infections. Our results suggest that adequate vitamin D may benefit the urinary tract during a UTI by inducing cathelicidin expression. There is a need of prospective studies in order to prove a beneficial effect of vitamin D supplementation for the restoration of cathelicidin stimulation and finally the prevention of UTI recurrence.

P - 43 BLADDER AUTOAUGMENTATION: ATTEMPT OR REALITY OF THE NEUROPATHIC BLADDER TREATMENT

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Introduction: Bladder augmentation has proved to be a useful surgical technique in patients with neurogenic bladder, resulting in a compliant reservoir with a good capacity and providing bladder emptying control, either by voluntary voiding or via Mitrofanoff stoma. Complications related to conventional enterocystoplasty and gastrocystoplasty stimulated the development of alternative methods for bladder augmentation. Bladder autoaugmentation with rectus muscle backing has been demonstrated to be an efficient surgical technique for bladder augmentation. We evaluated long-term outcomes to determine the value of this procedure.
Material and methods: Between August 1999 and June 2004, autoaugmentation was performed in 27 patients (18 girls and 9 boys) aged 3 – 14 years (median 8). The indication was neurogenic bladder with small capacity and poor compliance (myelomeningocele in 22, tethered cord in 3 and sacral agenesis in 2 patients). Surgery included detrusorectomy of the upper half of the bladder with creation of the bladder mucosa diverticulum that was hitched to both rectus muscles to prevent its retraction and to offer easier bladder emptying with voluntary muscle contractions.
Results: At the median long term follow-up of 134 months (ranged from 94 to 159), bladder volume continued to be significant compared to median bladder capacity preoperatively and ranged from 296 to 552 mL (median 419 mL). Voluntary voiding was achieved in 17 patients without residual urine while another 10 were not able to empty bladder voluntarily and had to use clean intermittent catheterization.
Conclusions: Bladder autoaugmentation with detrusorectomy and rectus muscle hitch and backing is a minimally invasive, completely extraperitoneal, simple and safe procedure. However, the technique is indicated only in select cases without anterior abdominal wall anomalies.

P - 44 RENAL FUNCTION IN ADULT WOMEN WITH URINARY TRACT INFECTION IN CHILDHOOD

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Introduction: The risk of deterioration of renal function in patients with urinary tract infection (UTI) associated renal damage over several decades is incompletely known but of importance in regard to follow-up.
Material and methods: A population-based cohort of women followed from their first UTI in childhood was studied at median age 27 years and now at 41 years. Renal damage was evaluated by ^{99m}Tc-dimercaptosuccinic acid scan and glomerular filtration rate (GFR) by ^{51}Cr-edetic acid clearance. Extent of individual kidney damage was graded as class 1 to 3.
Results: Eighy-six women completed the investigation, 58 with renal damage and 28 without. Of those with damage, 1 had chronic kidney disease stage 3, 14 stage 2, and 43 stage 1. Women with bilateral damage had lower GFR than those with no or unilateral damage ($p<0.0001$). Women with class 3 damage had numerically but not significantly lower GFR than the others with damage ($p=0.07$). Between the two studies there was significant decrease of GFR in the group with bilateral damage ($p=0.01$).
Conclusions: Women with UTI associated renal damage had remarkably well preserved renal function but those with bilateral or severe individual kidney damage may be considered for regular monitoring of GFR and blood pressure.

P - 45 THE DISTURBANCE OF CELLULAR ENERGY EXCHANGE AND ITS CORRECTION FOR CHILDREN WITH A HYPERACTIVE BLADDER

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Introduction: To determine the condition of a power exchange in children with hyperactive bladders, depending on the severity of the disease and to instill a condition for a cellular power exchange after the performance of energotropic therapy
Material and methods: 35 children with hyperactive bladders aged from 5 till 14 (8±2.5) years old were examined. Patients (pts) with clinical manifestations of hyperactive bladders were divided into three groups, depending on severity of the dysfunctional urination. For diagnostics of violations of cellular power exchange in children with hyperactive bladders determination of activity of succinate dehydrogenase (SDG) in lymphocytes of peripheral blood on the Pears method was carried out to R.P. Nartsisovs modifications, with subsequent visual assessment (initial level, after three months of therapy by a L-carnitine in a dosage of 30-50 mg/kg / 24Hr).
Results: In the assessment of the initial level, the activity of SDG amounted to17,4 ± 2,01 c.u. (norm 18-23), and was reduced in 63% of those examined, with unequivocally a more dramatic decrease in the SDG levels among children from II and III groups of patients. A reverse correlative interrelation was established with the level of SDG ($r = -0,7$; $p<0,05$) depending on the degree of severity of hyperactivity of a bladder. After 3 months of therapy by a L-carnitine the SDG level in lymphocytes of blood was raised above the initial level ($p<0,05$) and made 20,9 ± 1,13 conventional units. Significant increase in the SDG levels was observed in all patients, and in 92% of pts its level was within normal limits. In 75% pts was clinical signification improvement of signs hyperactive bladder.
Conclusions: Thus, in most children with hyperactive bladders, the disruptions in metabolism in the form of the decrease in the level of a succinate dehydrogenase are apparent.

P - 46 SEVERE CONSTIPATION AND LAZY BLADDER DUE TO ABSENCE OF INTERSTITIAL CELLS OF CAJAL

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Case description: A girl born from non-consanguineous parents presented with severe constipation since birth. She passed meconium 24-72 hours after birth. Additional investigations included normal anorectal manometry and rectal biopsy (excluding Hirschsprung disease and achalasia), normal sweat analysis (excluding cystic fibrosis), normal duodenal biopsy (excluding celiac disease), and normal spinal cord MRI (excluding tethered cord). Colon transit time was significantly decreased, proven by pellet studies. Treatment with a cow's milk protein deprived diet,

combination of multiple laxatives, daily enemas and anal infiltration with botulinum toxin A did not have the desired result. At the age of 3 years, a double-looped ileostomy was made, biopsies were taken throughout the colon and terminal ileum. Initial light microscopy showed no abnormalities. Additional immunofluorescence showed a markedly decrease/absence of interstitial cells of Cajal (ICC) throughout the colon, with normal ICC presence in the terminal ileum. The ganglion cells of the plexus of Meissner and Auerbach were normal and there was no inflammation. Since she suffered from recurrent bladder infections persisting after ileostomy, video urodynamics were performed showing a lazy bladder. Subsequent bladder biopsies showed normal examination on initial light microscopy, while immunofluorescence confirmed the absence of ICC.

Conclusions: After stimulation of the muscarinergic (M3) receptor, ICC increase smooth muscle contraction. They are expressed in intestine and bladder, ICC numbers can be reduced after longstanding severe constipation but a total absence is rarely reported. In constipation, ICC numbers can improve after treatment. A total absence of ICC was described in megacystic microcolon hypoperistalsis syndrome (MMHS), but our patient did not have microcolon, no distended, obstructed bladder and a normal functioning small bowel. Thus, this is the first report of severely decreased colon and bladder motility caused by an absence of ICC, not fitting the diagnosis of MMHS.

P - 47 IS THERE ANY RELATION BETWEEN CONNECTIVE TISSUE GROWTH FACTOR AND SCAR TISSUE IN VESICOURETERAL REFLUX?

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Introduction: Vesicoureteral reflux (VUR) is the most common uropathy in childhood which leads to increased frequency of urinary tract infection(UTI) and renal scarring . Connective tissue growth factor(CTGF) plays an important role in the development of glomerular and tubulointerstitial fibrosis in progressive kidney diseases. The aim of this study is to investigate the relation between urinary CTGF and renal damage resulted from VUR.

Material and methods: This cross sectional study included 70 patients with VUR and 62 healthy sex-and age-matched children. Urinary creatinine (mg/dl) and CTFG (pg/ml) concentrations were analysed in all cases and CTFG to creatinine ratio were calculated. The records of radiologic evalatuations of the patients including ultrasound, voiding cystouretrography and 99m-Technetium dimercaptosuccinic acid (DMSA) scintigraphy were obtained retrospectively. The patient group was further divided into two groups according to the existence of renal cortical scarring in DMSA scan. The study consisted of three groups; group 1-control group, group 2-VUR positive-scar negative, group 3-VUR positive-scar positive.

Results: The medians of urinary CTFG to creatinine ratio of the three groups were significantly different (p=0.000). Pairwise group comparisons according to urinary CTGF/creatinine ratio, revealed that group 1 were significantly lower from group 2 and group 3 (p=0.000 and p=0.002). There was no statistically difference between group 2 and group 3 (p=0.052).

Conclusions: Connective tissue growth factor is significantly increased in children with VUR without being dependent on the presence of renal scarring. Increased urinary CTGF could be interpreted as development of glomerular and tubulointerstitial fibrosis in reflux nephropathy and it seems to reasonable to use that biomarker for detection of early renal complications.

P - 48 THERAPEUTIC EFFICACY OF HYDROCHLOROTHIAZIDE IN PRIMARY MONOSYMPTOMATIC NOCTURNAL ENURESIS IN BOYS WITH IDIOPATHIC HYPERCALCIURIA

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Introduction: We assessed therapeutic efficacy of hydrochlorothiazide (HCT) in boys with primary monosymptomatic nocturnal enuresis (PMNE).

Material and methods: This research was a randomized double-blind placebo-controlled clinical trial. Two hundred 6-12 years old boys, who were followed in pediatric nephrology outpatient clinics of referral hospital in Markazi Province of Iran, were recruited. All patients had IHC and PMNE and were randomly divided into two equal groups (intervention and control groups). The control group received conservative measures for PMNE and placebo and the intervention group, in addition to conservative measures, received 1 mg/kg/day hydrochlorothiazide tablet as morning dose. Patients were followed for 4 months for the number of wet-night episodes.

Results: The mean numbers of wet-nights episodes in the first (intervention: 8.34±8.54, control: 9.1±9.3, p=0.3), second (7.1±7.3, 7.9±8.1 p=0.4), third (7.8±8, 7.9±8.1 p=0.1) and fourth (4.9±5.1, 5.9±6, p=0.3) months were not significantly different between the two groups. However, the decrease in the average wet-night episodes during the 4 months of treatment in the intervention group (p = 0.019) was significant in contrast to the control group (p = 0.191). All patients who were treated by hydrochlorothiazide became normocalciuric. However, in 21 patients the dose was increased to 2 mg/kg/day.

Conclusions: HCT can be effective in the treatment of children with PMNE. However, due to the lack of clinical studies and also unknown mechanism of the association between IHC and NE, further studies are recommended.

P - 49 CORRELATION ANALYSIS BETWEEN GLOMERULAR FILTRATION RATE (GFR) AND URINARY LEVELS OF ANGIOTENSIN II (ANG II) IN CHILDREN WITH VESICOURETERAL REFLUX (VUR) AND REFLUX NEPHROPATHY (RN)

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Introduction: Children with urinary tract infection and VUR may lead to RN. GFR is a clinical marker of glomerular hypertension. Ang II – is biologically active peptide of the renin-angiotensin system, which has a profound role synthesis and degradation of the extracellular matrix and has prosclerotic action. The aim of this study is to estimate the correlation between urinary level of of Ang II and GRF according the degree of renal scars in children with VUR.

Material and methods: 94 patients (65 f. 69,1%, χ^2=6.72, p<0.05) aged 5.66±0.38 y. with VUR were involved. All children were divided according to the results of DMSA-scan into 3 groups depending on the degree of renal scars: 12 p. with VUR without renal scars, 51 p. with mild RN (scars 1-3) and 31 p. with severe RN (> 3 scars). 20 healthy children served as controls, aged 6.24 ± 0.31 y. Urinary excretion and ratios over creatinine of Ang II were examined by ELISA.

Results: Urinary level of AngII in VUR patients was higher compared to control (78,94 ±6,9 vs 28,44±2,7, p<0.05). The highest urinary level of AngII was found in patients with severe RN (114,87±13,6) and low level

in group without RN signs (40,84±3,93, p<0.05). The level of GFR in scarring kidneys decreased no significantly to group without RN signs (96,013±2.59 and 88,67±3,58 vs 97,37±5,38 ml/min/1.73 m², p>0.05). A negative correlation was noted between the urinary level of AngII and GFR (r=-0,63).
Conclusions: The increased uric activity of Ang II in children with VUR and RN can be considered as early marker of renal tissue damage and scar formation. Established a direct correlation between the level of urinary excretion of AngII and the severity of RN in patients with VUR demonstrates the feasibility and prospects for it inclusion as a marker before to the development of renal dysfunction.

P - 50 URINE EXOGLYCOSIDASES - MARKERS OF RENAL INJURY IN CHILDREN WITH URETEROPELVIC JUNCTION OBSTRUCTION.

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Introduction: Hydronephrosis (HN) caused by ureteropelvic junction obstruction (UPJO) is an important problem in children and young adults. The aim of our research was to determine urine profiles of the following lysosomal exoglycosidases: N acethyl β hexosaminidase (HEX), its isoenzymes A (HEX A) and B (HEX B), α – fucosidase (FUC), β - galactosidase (GAL), α – mannosidase (MAN), and β - glucuronidase (GLU) as indicators of tubular renal damage in children with UPJO.
Material and methods: We measured HEX, its isoenzymes HEX A, HEX B and FUC, GAL, MAN, GLU urine activities in 32 patients with UPJO subdivided in groups: surgical group (SG) - 16 children with severe HN who required surgery; non-surgical group (NSG) - 16 patients with mild HN, and reference group (RG) - 42 healthy children.
Results: Urine activities of all exoglycosidases (pKat/μg Cr) were significantly higher in UPJO children than in RG (P <0.01). A strong positive correlation was also found between almost all urine exoglycosidases and urine albumin/ creatinine ratio (P <0.01).
Conclusions: The present pilot study has demonstrated that children with UPJO showed increased renal activities of assessed exoglycosidases, which correlated positively with urine albumin/ creatinine ratio. A larger multicenter study is required to confirm the clinical applicability of these observations.

P - 51 THE VALUE OF DMSA SCAN IN PREDICTING THE GRADE OF VESICOURETERAL REFLUX IN CHILDREN

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Introduction: There are controversies about the relationship of the changes in DMSA scan with the presence or absence of VUR or its grade. The present study aimed to assess the relationship between DMSA changes assessing by a new DMSA scoring system and the presence and severity of vesicoureteral reflux (VUR).
Material and methods: This prospective study was performed on 132 consecutive children) and thereafter 264 kidneys) with a first episode of febrile UTI. The changes of DMSA were graded by a new classification method. Renal damages in the DMSA scan were classified as grade 0 (normal kidney); grade 1 (decreased uptake in one pole with intact border); grade 2 (decreased uptake in two poles with intact borders); grade 3 (diffuse decreased uptake with intact border); grade 4 (decreased uptake in one pole with scar); grade 5 (decreased uptake in two poles with scar); grade 6 (multiple scars); grade 7 (diffuse decreased uptake with one pole scar); or grade 8 (diffuse decreased uptake with multiple scars). Grades 0-3 were considered without scars, whereas grades 4-8 were considered with scars.
Results: DMSA scanning had a sensitivity of 66.9 (95%CI: 57.7%-75.1%), a specificity of 41.3% (95%CI: 33.2%-49.8%) and an accuracy of 53.0% (95%CI: 44.1%-59.6%) for detecting VUR. DMSA had a sensitivity of 69.4% (95%CI: 59.8%-77.6%), a specificity of 42.5% (95%CI: 34.6%-50.7%), and an accuracy of 53.8% (95%CI: 46.6%-60.4%) for detection of dilated VUR. Assessing agreement between VCUG and DMSA scanning, the Kappa values for agreement between the two procedures measured 0.117 (p = 0.056), 0.080 (p = 0.170), for detecting VUR and dilated VUR, respectively.
Conclusions: Performing a DMSA scan alone in children with febrile UTI and reserving VCUG for patients with abnormal DMSA misses a significant number of patients with high grade VUR.

P - 52 DEMONSTRATION OF VESICOURETRAL REFLUX IS SOMETIMES MEANINGLESS

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Introduction: Primary vesicoureteral reflux (VUR) is mostly diagnosed in infants (46%) and preschool children (9%) presenting with urinary tract infections (UTI). Traditional approach was performing voiding cystourethrography (VCUG) in children with first time UTI. However, recent guidelines emphasize that detection of VUR do not alter significantly the management of children with UTI. Thus, they do not recommend routine VCUG in these children as it is invazive and leads to radiation exposure.Some infants are erroneously diagnosed as UTI depending on the bag culture results, older children with apparently lower UTI are evaluated by VCUG. We aimed to determine the children evaluated by unnecessary VCUG and found to have VUR not altering the management.
Material and methods: Infants and children presenting to Dokuz Eylül University Medical Faculty Pediatric Nephrology Outpatient Clinic due to a history of UTI and imaging results including USG, VCUG and DMSA scintigraphy performed in other health care facilities were evaluated retrospectively. Patients with significant urinary malformations, abnormal DMSA scan findings and clinical signs of pyelonephritis were excluded. The remaining patients were evaluated for age, gender, follow-up duration, UTI recurrence, VUR grade and course (resolution, persistence, surgical correction), antimicrobial prophylaxis renal ultrasonography and DMSA scintigraphy findings, estimated GFR and proteinuria levels.
Results: There were 29 patients (M/F:15/14, 17±17 months) with normal DMSA findings who were free of UTI during follow up. Except 2 patients, all urine samples had been obtained by urine bag. USG were normal in 22 and showed mild pelvicalyceal dilatation in 7. VUR was bilateral in 18 and unilateral in 11 patients. VUR grades were 1 (n=1), 2 (n=11), 3 (n=13), and 4 (n=4). DMSA were normal in all patients. None of the patients had proven UTI during follow up even after cessation of antimicrobial prophylaxis, and none had undergone for surgical correction.
Conclusions: When evaluating infants for UTI, bag urine samples should not be relied on. Tthe results of these infants implies that VUR may be present without any associated renal anomaly, rather it may be a physiologic finding in this age group.

P - 53 ANTIREFLUX SURGERY DOES NOT PREVENT PROGRESSION OF RENAL DISEASE

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Introduction: Treatment modalities of vesicoureteral reflux (VUR) consist of anti-microbial prophylaxis and antireflux surgery.The ratio of patients undergoing renal transplantation due to reflux nephropathy did not change over years despite these treatment modalities. In this study, we aimed to determine the impact of the surgical versus medical treatment of VUR on long term renal functions in our patients.
Material and methods: Patients with VUR diagnosed during the evaluation for UTI or hydronephrosis between were evaluated retrospectively. Patients with secondary reflux, and with a follow up period of <12 months were excluded. The patients were divided into two groups as solely medically treated (Group 1) and both medically and surgically treated (Group 2). The following parameters were determined: gender, presenting complaint, age at diagnosis, follow up period and DMSA findings along with estimated glomerular filtration rate (eGFR) and urinary protein levels at admission, before surgery and at last visit.
Results: There were 140 patients fulfilling the inclusion criteria. Group 1 and 2 included 82 and 58 patients respectively. There were 14 patients with renal injury before surgery in Group 2, while this number increased to 27 after 74.6±33.5 months of follow up. In Group 2, the number of patients with scar in DMSA was higher than in Group 1 (53/58 vs 28/82 respectively, p<0.001). Similarly, severe renal scar was also higher in Group 1 (16/58 vs 7/82, p=0.003). However, when the patients with postoperative progressive/new renal injury (Group 2a) were compared to the patients with postoperative normal renal functions (Group 2b), total and severe scar rates were not different (25/27 vs 28/31, p=0.759 and 6/27 vs 10/31, p=0.394). However, bilateral renal scar was higher in Group 2a compared to Group 2b (7/27 vs 1/31, p=0.044).
Conclusions: Antireflux surgery does not guarantee the preservation of renal functions in children with renal scars in DMSA scintigraphy. This is true especially in children with bilateral renal scarring.

P - 54 PROGRESSION TO ESRD IN CHILDREN WITH RENAL HYPO/DYSPLASIA WITHOUT POSTERIOR URETHRAL VALVES

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Introduction: Normal renal development is dependent upon the interaction between the ureteric bud and metanephric mesenchyme, the renal malformations arise when this process is disrupted. Renal hypo/dysplasia (RHD) account for 20 percent of end-stage renal disease (ESRD) in children. We evaluated risk factors for progression to ESRD in pediatric patients with RHD.
Material and methods: This study retrospectively analyzed children under two years of age, referred to our department, with a diagnosis of bilateral RHD without posterior urethral valve. Incidence of ESRD was compared with potential risk factors such as serum creatinine (Crs) at onset, low birth weight < 2500 g (LBW), severe bladder dysfunction and bilateral vesicoureteral reflux (VUR), using Kaplan-Meier analysis and log rank tests.
Results: Sixteen patients (male/female=10/6) were included in the analysis. The mean age at last follow-up was 10.3 years of age. Age of onset was under two years of age. Six of sixteen patients progressed to ESRD at a mean age of 7.3 years. Among the risk factors, only a value of serum Creatinine greater than 1.0 mg/dl at the time of diagnosis was a risk factor for progression to ESRD (logrank p < 0.001).
Conclusions: In our study children with RHD and a value of Cr > 1.0 mg/dl at two years of age showed a more severe renal involvement. The total population showed a progression to ESRD before adolescence.

P - 55 DOES THE PRESENCE OF VESICOURETERAL REFLUX AFFECT THE GROWTH RATE OF UROPATHOGENIC ESCHERICHIA COLI?

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Introduction: Vesicoureteral reflux (VUR) is the most common urinary anomaly in children with urinary tract infections (UTI). Uropathogenic Escherichia coli (UPEC), the most frequent cause of UTI, is colonized in perineum, attaches to uroepithelium and invades tissues. Uroepithelial molecules like uroplakins are involved in these stages. Uroplakins also play role in the development of urinary system, and uroplakin disorders are associated with VUR. We hypothesized that urine contents, as well as urinary flow, may change in VUR, and aimed to determine whether UPEC growth is faster in urine samples from the refluxing systems.
Material and methods: Children evaluated by voiding cystourethrography for UTI were enrolled. Groups 1 and 2 included children with and without VUR, respectively. Sterile bag/clean catch urine samples were processed as follows: 0.1 mL UPEC suspension ($2x10^3$ cfu/mL) was added to 0.9 mL urine, incubated for 4 hours, and 0.1 mL of this last suspension ($2x10^2$ cfu/mL) was inoculated to blood and EMB agars, incubated for 24 hours and colony counts were assessed. Both groups were compared for the number of urine samples with any bacterial growth and for colony counts.
Results: 42 sterile urine samples were included in the study (21 in each group). After inoculation of $2x10^2$ cfu UPEC to all samples, this microorganism was cultured in 9 (43%) and 3 (14%) samples in Groups 1 and 2, respectively (p=0.040, OR 4.5). Colony counts were not different in both groups (log x; 2.36±0.25 vs 2.37±0.12, p=0.923).
Conclusions: Inoculation of low number of UPEC ($2x10^2$ cfu) resulted in growth in almost half of the urine samples obtained from refluxing urinary systems, while UPEC growth was inhibited in most urine samples from non-refluxig systems. This finding suggests that the factors facilitating bacterial growth increase or the factors impeding bacterial growth decrease in urine samples obtained from refluxing systems.

P - 56 PRENATAL HYDRONEPHROSIS: POSTNATAL EVALUATION AND FOLLOW UP

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Introduction: Prenatal hydronephrosis (PNH) is a common ultrasound finding, with an incidence of 0.6 to 4.5%. The advantage of prenatal ultrasound is to allow early diagnosis and treatment of renal and urinary tract anomalies, preventing its complications. However, in most cases PNH exhibits spontaneous remission. This study aim is to evaluate the relationship between PNH and its postnatal confirmation, so as its follow-up.
Material and methods: Retrospective study of infants born in the years 2010, 2011 and 2012 in A2 level hospital, who where referenced to renal pathology consultation due to PNH, with collaboration of a tertiary center. It was made a distribution by severity groups: mild (anteroposterior diameter-APD <9 mm), moderate(APD 9-14 mm) and severe(APD≥ 15 mm).
Results: Between 2010 and 2012 we observed 4950 births, of which 127 (2.6%) newborns were referred to nephrology consultation due to PNH, mostly male (75%). The average gestational age at prenatal diagnosis was 31 weeks. It was observed mild PNH in 76(60%), moderate in 39(31%) and severe in 12(9%) cases. In 67 (53%) there was no postnatal ultrasound hydronephrosis confirmation. 70% of them had a correspondent mild

degree of PNH. In those who were identified postnatal hydronephrosis, 25 (40%) patients had complete hydronephrosis resolution in the first year of life. In 15 (25%) cases were found kidney and urinary tract abnormalities. The most common were ureteropelvic junction obstruction (51%) and vesicoureteral reflux(27%). Eight(53%) of those patients underwent surgical intervention. 67% of the cases diagnosed with urinary tract abnormalities were previous evaluated as a severe degree of PNH.

Conclusions: There is a positive correlation between HNPN value and postnatal outcome, which support the recent literature. Although there are several false positives on prenatal diagnosis, this work highlights the importance of early identification of patients at risk of renal impairment for a better counseling and treatment.

P - 57 FLUOROQUINOLONES IN CHILDREN WITH URINARY TRACT INFECTIONS: OLD ENEMY OR NEW FRIEND? A REVIEW OF CURRENT LITTERATURE

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Introduction: Fluoroquinolones (FQs), a class of broad spectrum antibiotics, are labelled for and widely used in adults with urinary tract infections. Pharmacokinetics of FQs are favourable above other antibiotics, as tissue penetration of these antibiotics after oral ingestion is almost similar to intravenous administration. Since juvenile animals who were exposed to FQs turned out to have irreversible cartillage tissue damage, paediatric drug studies in FQs were stopped in an early phase. FQs are subsequently not labelled for children by international drug regulatory authorities. There is a worldwide trend to use FQs off-label in children for a variety of diseases of which urinary tract infections.

Material and methods: We searched in PubMed as well as Embase for English articles about FQs administration in children with urinary tract infections with an emphasis on drug safety studies.We present a preliminary systematic review of our findings here.

Results: FQs are used worldwide mainly to treat complicated urinary tract infections in children, although there are some centers which use FQs as first line treatment for urinary tract infections in children. Growing FQs resistance patterns have been published in different parts of the world. Although muscoloskeletal complaints during FQ treatment have been described, there seems to be little evidence for irreversible cartillage tissue damage as side effect of FQs. We did not find a paediatric case report of Achilles tendon rupture, a feared side effect of FQs in adults. Pharmacokinetic data of FQs in children are scarce.

Conclusions: Fluoroquinolones are useful and probably safe for treatment of urinary tract infections in children, particularly for complicated urinary tract infections. Increasing resistancy patterns for fluoroquinolones (FQs) worldwide are a serious threat. More pharmacokinetic studies are desirable ensuring sufficient bioavailability of FQs and thereby diminish the antibiotic resistance growth.

P - 58 THE ROLE OF DYNAMIC RENAL SCINTIGRAPHY ON CLINICAL DECISION MAKING FOR HYDRONEPHROSIS

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Introduction: We evaluated the contribution of MAG-3 scintigraphy to the clinical decision for surgery in hydronephrosis.

Material and methods: Patients evaluated by MAG-3 for antenatal/postnatal hydronephrosis between 1992-2014 were evaluated for gender, age, hydronephrosis grade, presence of VUR, MAG-3 result (obstructive vs non-obstructive), final diagnosis and need for surgery. Patients with obstructive vs non-obstructive hydronephrosis were compared.

Results: There were 193 patients (age 35.4±54.8 months; M/F=130/63; antenatal hydronephrosis 62.2%). MAG-3 was obstructive in 85 and non-obstructive in 108. Ultimate diagnoses were obstructive dilatation in 8.3% vs 88.2%, VUR in 13.0% vs 3.5%, and non-obstructive dilatation in 78.7% vs 8.2% patients when MAG-3 was non-obstructive vs obstructive, respectively ($p<0.001$). Surgery was performed in 10.2% and 85.9% of patients in non-obstructive and obstructive groups, respectively ($p<0.001$, OR 53.6). M/F ratio was 80/23 vs 50/35 in non-obstructive vs obstructive groups ($p=0.025$, OR 2.0). In 42 patients with AP diameter >20 mm, MAG-3 was obstructive in 27 (64.3%) and surgery was required in all (100.0%) while only 4 (26.7%) of the remaining 15 patients underwent surgery ($p<0.001$, OR Inf). AP diameter >16.5 mm was the best cut off level for predicting obstruction by MAG-3 (sensitivity 66.7%; specifity 65.8%; OR 3.8). Antenatal and postnatal hydronephrosis cases were not different with respect to MAG-3 result (obstructive vs non-obstructive), ultimate diagnosis or surgery requirement.

Conclusions: MAG-3 significantly effects clinical decision for surgery in hydronephrosis. Hydronephrotic girls have twice as much risk for true obstruction. Combining MAG-3 with USG improves the discrimination of true obstruction.

P - 59 CAN NANOTECHNOLOGY ANTIMICROBIAL UNDERPANT PREVENT BACTERIAL CONTAMINATION IN BAG URINE SAMPLES: RESULTS OF A PRELIMINARY STUDY.

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Introduction: Non-invasive method of urine collection for culture in infants is application of perineal bag. However, bag urine samples are prone to bacterial contamination. Many antimicrobial technologies are available for textiles. We aimed to investigate whether underpants with antimicrobials decrease the contamination rate in bag urine samples.

Material and methods: Infants with bag urine culture results compatible with contamination (either low colony counts or growth of >1 bacterial strain) were enrolled. They were divided into two groups. A second (control) bag urine sample was obtained after about 1 hour wearing of nanotechnology antimicrobial underpants (silane quarternary ammonium compound) without any additional cleansing from the infants in Group 1. Infants in Group 2 gave the control urines without wearing antimicrobial underpants. Groups 1 and 2 were compared for the number of sterile versus contaminated control urine samples.

Results: Thirty two infants (M/F=17/15) with contaminated urine samples were enrolled in the study. They were randomly assigned to Group 1 and Group 2 such that each group included 16 patients.Both groups were similar with respect to M/F ratio (9/7 vs 8/8 in Groups 1 and 2, respectively, $p>0.05$). Control urine cultures were sterile in 1 and 6 infants in Groups 1 and 2, respectively (1/15 vs 6/10, $p=0.033$). Among the nonsterile urine cultures, polymicrobial vs single pathogen growth rates were 12/3 vs 5/5 in Groups 1 and 2, respectively ($p=0.115$).

Conclusions: One hour wearing of nanotechnology antimicrobial underpants did not prevent bacterial contamination of bag urine samples in infants.

P - 60 MCUG AUDIT: ARE WE OVER INVESTIGATING?

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Introduction: Investigating Urinary Tract Infection (UTI) in children has remained debated topic. Micturating cysto-urethrography (MCUG) is an invasive test causes anxiety to the children and their families. We believe that MCUG should be limited to selected population that has a high risk of developing UTI complications.
Material and methods: Retrospective data analysis of UTI database at a tertiary paediatric nephrology unit aiming at evaluating the value of MCUG. Data collection were done over 3 years period from 01/06/2008 to 31/05/2011. We have collected age, sex, febrile UTI, urine microscopy and culture. Family history of recurrent UTI, renal scarring. We have included Ultrasound scan results (USS) as well as results of a technetium -99m-dimercatosuccinic acid (DMSA). We have followed these cases clinically from June 2008 for a minimum of 2 years (2-5 years) in regards of recurrent UTI, surgical referral/intervention and further imaging.
Results: 154 MCUG were done for which 116 were reported normal (75%) . 123 has normal USS following first UTI. 87 were males. Out of these 123 normal USS , 15 had abnormal MCUG(12 has vesicoureteric reflux (VUR), and 3 have ? posterior urethral valves(PUVs), but following cystoscopy, non was found to have PUVs. 12 cases showed abnormal DMSA, 10 with scars and 2 with abnormal split function. No child with normal USS was found to have PUVs. 42% of children with scars on DMSA had a family history of recurrent UTIs. All cases referred for cystoscopy has no PUVs. Scarring on DMSA was not associated with vesicoureteric reflux (VUR).
Conclusions: Invasive investigations of UTIs should be spared to high risk cases. USS is a good screening tool. Positive family history of UTIs could be added as high risk of developing renal scar. MCUG standards for imaging in centres with no paediatric radiology input and these cases should be discussed at tertiary centres with paediatric radiology input before proceeding to invasive investigations.

P - 61 AFTER FIRST EPISODE OF PYELONEPHRITIS RENAL ULTRASOUND AND RENOGRAPHY ARE RECOMMENDED UP TO THE AGE OF 2 YEARS, THEREAFTER RENOGRAPHY IS OPTINAL. THEREBY THE PARENTS HAVE THE POSSIBILITY TO DECIDE IF THE CHILD SHALL UNDERGO FURTHER EXAMINATION FOR DETECTED VUR

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Introduction: There are controversies about the optimal investigation-regime after first pyelonephritis in children. Aim of the study was to propose guidelines for such investigations. The result of routine renal ultrasonography and Technetium-99m-mercaptoacetyltriglycine renography(renography) in a cohort of children treated for the first pyelonefritis were evaluated.
Material and methods: Included were consecutive 0-15-year-old children, who in 2007-2013 were treated for culture diagnosed first episode of pyelonephritis at Hvidovre Hospital. All underwent ultrasonography and renography. Excluded were patients with known urological anomalies. If surgery was indicated all patients were admitted to Rigshospitalet. The cohort underwent follow-up until April, 2014.
Results: We identified 537 patients (361 girls, 176 boys).
After first pyelonefritis 108 patients were treated with prophylactic antibiotics and 24 patients underwent surgery; 3 for posterior urethral valves, 13 for VUR, 2 for pelveo-ureteral stricture, 2 for renal duplex-systems, 3 for phimosis and 1 for hypospadias.
After one recurrent episode of pyelonephritis, additionally 6 patients had surgery for VUR, and 4 had foreskin-surgery within the period of follow-up.VUR was the most common diagnosis including 38 patients, whereof 19 had surgery for VUR.Ultrasonography was normal in 45 cases where renography was abnormal. 4 of these cases had VUR, all were less than 2 years of age including 2 cases with surgery for VUR. Treatment of VUR includes prophylactic antibiotics or surgery. The parents must be involved in the decision. In patients up to 2 years of age both ultrasound and renography are important to detect VUR.
Conclusions: In cases the first episode of pyelonephritis, up to 2 years of age, ultrasonography and renography are mandatory. After 2 years of age renography is optional. Thereby the parents have the possibility to decide if the child shall undergo further examination for detected VUR.

P - 62 CYSTOMETRY FINDINGS AMONG CHILDREN IN KOSOVA, DONE AT THE ONLY URODINAMIK CENTER IN KOSOVA DURING 2014

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Introduction: Urodynamic investigations can be helpful to define the prognosis and especialy, when we need to select a therapeutic strategy in very resistant cases.
Material and methods: The study included a number of 30 children with voiding dysfunction symptoms. They were investigated clinically (voiding and defecation history-charts, physical examination) as well as through imaging techniques: renourinary ultrasound, voiding cystourethrography and uroflow and cystometry. Assessing the vesical pressure is very difficult since child moves and this causes a reflex activity of the pelvic floor muscles. Bladder filling is ideally performed by a pump ensuring a sufficiently slow flow rate to avoid modifying bladder behaviour 5ml/min. The following parameters are recorded: baseline detrusor pressure, first desire to void, detrusor activity, bladder capacity and bladder compliance. Measurement of bladder pressure during voiding is used to confirm whether or not the bladder is contractile, assess obstruction in the case of low urine flow rate with high bladder pressure, to detect abdominal straining and residual urine. Main indications: neuropathic bladders, voiding dysfunctions,UTI, anorectal malformations, failure of first-line treatment.
Results: Female vs male presentation was 66%. 39% had complete recommended evaluation before examination. 21% had neurogenic bladder. 33% Overactive bladder. 9% normal cystometry. 91% with residual urine. 9% no residual urine. Small ages were with MMC mostly and with other dysfunctions were above age of 8, spread around 15% of all.
Conclusions: A specific paediatric procedure should be respected when performing uroflowmetry and cystometry in children. The examination must be interpreted manually without taking into account the automated interpretation

P - 63 SERUM PROCALCITONIN LEVEL IS A USEFUL PREDICTOR OF IN VESICOURETERAL REFLUX IN PEDIATRIC URINARY TRACT INFECTION.

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Introduction: Recently, procalcitonin has been proposed as a novel biomarker for prediction of VUR.. Multiple studies performed in recent years show that serum procalcitonin is a sensitive biomarker for differentiation

of upper UTI from noncomplicated lower UTI, and its level increases when renal tissue inflammation is present. Since VUR is the most important risk factor for occurrence of pyelonephritis and renal tissue inflammation, serum procalcitonin level may have a relationship with VUR. However, literature about the relationship between procalcitonin level and VUR. We evaluated the predictive value of serum procalcitonin level in the diagnosis of VUR in children admitted with their first febrile UTI.

Material and methods: We investigated 140 children with the first febrile UTI (2m-10 yrs.). Serum procalcitonin was measured before initiation of antibiotics. Standard voiding cystourethrography (VCUG) was performed in all children as the gold standard for detection of VUR. Sensitivity and specificity of a high procalcitonin level was evaluated using the receiver operating characteristic curve.

Results: Seventy three patients(52%) had no VUR, while 67patients (48%) had VUR at least in one kidney, including grade 1 to 2 in 20 patients (14.3%), grade 3 in 23 (16.4%), and grade 4 to 5 in 24 patients (18.3%). Procalcitonin level ranged from 0.45 ng/mL to 12.7 ng/mL. . Procalcitonin leve l was significantly higher with increasing the grading of reflux. Comparing procalcitonin levels with VCUG results, a sensitivity of 94% and a specificity of 72% was obtained at a procalcitonin level of 0.52 ng/mL for diagnosis of VUR. There was a significant correlation between procalcitonin level and leukocytosis, erythrocyte sedimentation rate, and C-reactive protein.

Conclusions: This study showed that a high procalcitonin level may be used for prediction of all grades of VUR in children with febrile urinary tract infection. A low procalcitonin level may be used for avoidance of unnecessary VCUG in some low-risk .

P - 64 CLINICAL TRIAL OF VITAMIN E AS ADJUVANT TREATMENT FOR URINARY TRACT INFECTIONS IN GIRLS WITH ACUTE PYELONEPHRITIS

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Introduction: The aim of this study was to investigate the effects of vitamins E supplementation in combination with antibiotics for the treatment of girls with acute pyelonephritis.

Material and methods: This double-blind randomized clinical trial was conducted on 152, 5-12 years old girls with a first UTI (acute pyelonephritis based on DMSA scan), who were admitted to pediatric wards of Amir Kabir and Valiasr hospitals, Arak, Iran. The girls were randomized into two treatment groups: 14-day treatment with only antibiotics (control group; n=76) and 14-day treatment with supplements of vitamin E (intervention group; n=76) in addition to antibiotics. Patients' clinical symptoms were monitored for 14 days and urine culture was performed on all girls 3-4 and 7-10 days after the start of the treatment and its completion, respectively. All girls once again underwent DMSA scan 4-6 months after the treatment.

Results: The average frequency of patients with fever (p=0.012), urinary frequency (p=0.001), urgency (p=0.003), dribbling (p=0.001) and urinary incontinence (p=0.006) were significantly lower in the intervention group compared to the control group. There was no significant difference between the results of urine culture 3-4 days after the start of treatment (p=0.156) and 7-10 days after its termination (p=0.37). There was also no significant difference between the results of DMSA scan 4-6 months after the start of treatment (p=0.31).

Conclusions: Vitamin E supplementation has a significant effect in ameliorating sign and symptoms of UTI. However, future study is recommended due to the lack of clinical studies in this field.

P - 65 DIAGNOSTIC SIGNIFICANCY RATE OF NGAL IN URINE IN ACUTE PYELONEPHRITIS AND URINARY TRACT INFECTIONS IN CHILDREN.

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Introduction: To evaluate the level of NGAL (neutrophil gelatinase-associated lipocalin) in childrens urine with acute pyelonephritis and urinary tract infections and the diagnostic contribution of the above marker used for detection.

Material and methods: 30 children age 2 to 16 were examined. The first group involved 15 children with acute pyelonephritis. The second group involved 15 children with urinary tract infections. The level of NGAL in urine was identified in both groups of patients as soon as they were admitted. CRP and the level of leucocytosis were evaluated in blood.

Results: The undertaken study shows that among the examined children with acute pyelonephritis the level of NGAL in urine was 76,5+8,6 ng/ml, in the second group with urinary tract infections was a lot less and was equal to 4,76+1,3ng/ml. The average level of leucocytes in blood in children with urinary tract infections was 8200+720mcL, in the group of children with acute pyelonephritis 13600+1400mcL. The average level of CRP was higher in the group of children with acute pyelonephritis and was equal to 60mg/l, in the group of children with urinary tract infections 1,9mg/l. In 80% of children the level of NGAL in urine exceeded 50ng/ml (reference interval 35-56 ng/ml). In the group of children with acute pyelonephritis, we identified a straight correaltion relationship pf average strength (r=0,63) between the level of NGAL and the levels of leucocytes abd CRP (r=0,68) in blood.

Conclusions: Therefore, the preliminary received data allowed us to detect the elevation of NGAL in urine in all children with acute pyelonephritis, the level of this marker correlates with the level of leucocytes and CRP in blood. This suggests that the identification of NGAL levels in urine in children with urinary tract infections allows the usage of this non-invasive marker for early diagnosis of acute pyelonephritis in children.

P - 66 IS RENALASE A MARKER OF DECLINE IN RENAL FUNCTION IN CHILDREN WITH SOLITARY KIDNEY?

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Introduction: The long-term outcome of patients born with unilateral renal agenesis (URA) and of those who underwent therapeutic unilateral nephrectomy (UN) remains a topic of concern and debate.Children with a solitary functioning kidney (SFK) have an increased risk of developing hypertension, albuminuria and chronic kidney disease in later life.

The purpose of this study was to explore serum and urine renalase levels and their relation to the kidney function parameters in children with solitary functioning kidney (SFK) in comparison to healthy children (RG).

Material and methods: The study cohort consisted of 93 patients, who were divided into two groups: SFK-36 patients, and RG-57 healthy children. Serum and urine renalase levels were measured using the commercial ELISA kit. Glomerular filtration rate was evaluated by updated Schwartz formula.

Results: Serum (μg/mL) and urine (ng/mL) renalase levels were significantly lower in SFK patients in comparison to RG ($p < 0.05$). The urine renalase/ Cr values were found to be negatively related to serum creatinine ($r = -0.35$; $p < 0.05$), and positively correlated with updated Schwartz eGFR ($r = 0.37$; $p < 0.05$). We did not find significant correlations between renalase levels and BP values. Moreover, in SFK the Fisher exact test did not reveal statistically significant difference between the number of

children with decreased urine renalase/cr (below the 50 centile) who were normotensive and hypertensive.
Conclusions: Our data emphasize the importance of monitoring urine renalase excretion in children with SFK to detect early deterioration of kidney functions before hypertension develops in order to prevent end-organ damage later in life.

P - 67 EXTENDED-SPECTRUM - LACTAMASE (ESBL) PRODUCING ENTEROBACTERIACAE IN COMMUNITY ACQUIRED URINARY TRACT INFECTIONS IN CHILDREN: A SINGLE CENTER EXPERIENCE

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Introduction: Extended-spectrum - lactamase producing enterobacteriacae has emerged worldwide as a significant cause of health care associated as well as community acquired urinary tract infections (CA-UTI) in children. However, paediatric data are lacking.
Objective: To study the prevalence and the associated risk factors of ESBL producing enterobacteriacae in CA-UTI in our department
Material and methods: A retrospective study of UTI cases hospitalised in the department of paediatrics of the hospital of Sahloul in Sousse, between January 2007 and December 2013. Clinical and bacteriological data were collected from the medical records.
Results: CA-UTI represented 3.29% of the total number of hospitalisations. Escherichia coli was the most frequently isolated micro-organism, followed by Klebsiella pneumonia and Proteus Mirabilis. ESBL producing enterobacteriacae were found in 30 cases (9.37%). Children with ESBL UTI were younger (OR 0.98 ; IC à 95% de 1 à 1.1), had a higher rate of urinary tract abnormalities (OR 4.2 ; IC à 95% de 1.7 à 10.8), were more on antibioprophylaxis (OR 4.8 ; IC à 95% 1.6 à 14.5), recently received antibiotics (OR10.2;IC à 95% de 4.5 à22.8), and were more frequently hospitalised within the three previous months (OR 23.9 ; IC à 95% de 9.6 à 59.9) compared to those with non ESBL UTI.
Conclusions: Community ESBL UTI are becoming a real burden for public health, that leads to serious difficulties concerning the treatment. It's of a high importance to identify associated risk factors in order to limit the spread of this phenomenon

P - 68 ETIOLOGICAL FEATURES OF THE URINARY TRACT INFECTION IN NEWBORNS AND BABIES OF THE FIRST MONTHS OF LIFE

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Introduction: The objective of this study was to determine the microbiological features of urinary tract infection (UTI) in newborns and babies depending on age, sex, way of childbirth and intestinal microbiota.
Material and methods: The bacteriological analysis of urine has been carried out for 31 babies having age from 3 days to 1 month and 14 babies having age from 1 month to 4 months.
Results: The most often detected microbes have been Enterococcus and Klebsiella (in 1/3 of the cases), E. coli has been detected in 20%, Pseudomonas aeruginosa in 6.7% of cases. Proteus and Staphylococcus have not been detected at all. Klebsiella and E.coli have been found out more often in the babies of the first month of life than in the older babies ($P<0.01$). Boys have had three times more often microbes than girls. In case of a caesarian section the Enterococcus has been detected significantly more often ($P<0.05$), whereas Klebsiella and E.coli have been more rarely than in case of a vaginal delivery. The frequency of Enterococcus and Klebsiella detection has been 41.2% и 31.3% respectively in case of intestinal bacterial overgrowth. However, the bacteriuria caused by Stafilococcus and E.coli has not been observed in cases of these microbes predominance in intestinal microbiota. 1/2 of E. coli strains and 2/3 of Klebsiella strains has produced β-lactamases of a broad spectrum of actions. Klebsiella and E.coli have been more sensitive to cephalosporins (Cefoperazone/Sulbactam, Ceftriaxone) and aminoglycosides (Amicacin, Netilmicin), whereas Enterococcus was more sensitive to Vancomycin, Gentamycin and Furazidin.
Conclusions: The following features of urine spectrum have been detected in babies with UTI: the predominance of Enterococcus (especially in case of cesarean section) and Klebsiella (especially in newborns), the absence of Proteus and Staphylococcus, the correlation of Enterococcus and Klebsiella detection in urine with their intestinal overgrowth, the greatest sensitivity of gram-negative urine microbes to cephalosporins and aminoglycosides.

P - 69 PSYCHIATRIC DISORDERS AND LOWER URINARY TRACT SYMPTOMS (LUTS): IS ATTENTION-DEFICIT/HYPERACTIVITY DISORDER MORE PREVALENT IN CHILDREN WITH OVERACTIVE BLADDER?

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Introduction: The aim of this study is to investigate Attention Deficit Hyperactivity Disorder (ADHD) in children with overactive bladder (OAB) and compare it with healthy children.
Material and methods: Ninety two 5 to 12 year-old children with OAB and 92 healthy children without OAB were included in this case – control study as case and control groups, respectively. ADHD types were diagnosed by Conners Parent Rating Scale – 48 (CPRS-48) and DSM-IV-TR criteria and confirmed by psychologist consult.
Results: Among 184 (100%) children in both groups, 51 children (27.7%) had ADHD types. ADHD types with 33 cases (35.9%) in the OAB group were significantly higher than the control group with 18 cases (19.6%) ($p = 0.021$). ADHD inattentive type was observed in 22 cases (23.9%) with OAB and 9 controls (9.7%) ($P=0.047$). Despite this significant differences, in the case and control groups, 3 (3.2%) and 4 (4.3%) children were affected by ADHD hyperactive-impulsive type ($p = 0.73$), and 8 (8.6%) and 5 (5.4%) children were affected by ADHD mixed type ($p = 0.42$), respectively.
Conclusions: ADHD in children with OAB is significantly more common than healthy children. The observed correlation between ADHD and OAB makes psychological counseling mandatory in children with OAB.

P - 70 ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN WITH PRIMARY MONOSYMPTOMATIC NOCTURNAL ENURESIS: A CASE-CONTROL STUDY

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Introduction: The aim of this study was to investigate ADHD in children with primary monosymptomatic nocturnal enuresis (PMNE) and compare it with healthy children.
Material and methods: 100, 5-16-year-old children with PMNE and 100 healthy children without NE were included in this case – control study as case and control groups, respectively. Subjects were selected from children who were referred to the pediatric clinic of Amir Kabir Hospital of

Arak, Iran, in the form of simple probability and based on inclusion and exclusion criteria. ADHD was diagnosed by Conners Parent Rating Scale – 48 (CPRS-48) and DSM-IV-TR criteria and was confirmed by psychologist consult.
Results: ADHD inattentive type was observed in 16 cases (16%) with PMNE and 5 controls (5%) (P=0.01). Despite this significant differences, in the case and control groups, 25 (25%) and 16 (16%) children were affected by ADHD hyperactive-impulsive type (p = 0.08), and 15 (15%) and 16 (16%) children were affected by ADHD mixed type (p = 0.84), respectively.
Conclusions: ADHD inattentive type in children with PMNE is significantly more common than healthy children. The observed correlation between ADHD inattentive type and PMNE makes psychological counseling mandatory in children with PMNE.

P - 71 CLINICAL VALUE OF THE CONDITION OF THE CARNITINE EXCHANGE IN CHILDREN WITH THE HYPERACTIVE BLADDER

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Introduction: To estimate a carnitine exchange condition at children with a hyperactive bladder depending on the severity of the disease.
Material and methods: The study of blood general, free carnitine (C0) and associated carnitine (acylcarnitines, AK) by gas chromatography-mass spectrometry method (Agilent 6410 QQQ, the USA) and the coefficient was calculated: acylcarnitines / free carnitine (AK / C0).
Results: 30 children with hyperactive bladders aged from 5 till 14 (8±2.8) years old were examined. Patients (pts) with clinical manifestations of hyperactive bladders were divided 3 groups, depending on severity of the dysfunctional urination. In children with hyperactive bladders the level of the general carnitine varied from 31,085 to 83,443 μmol/l (48, 9 ± 15,1 μmol/l, norm of 60-100 μmol/l), and was reduced in 80% of the examined. Values of a C0 fluctuated in normal limits from 19,1 to 42,1 μmol/l (29,9±7,3 μmol/l; norm of 20-60 μmol/l). Relative increase of the maintenance of AC in structure of the general carnitine to 40% (norm of 20-30%) is noted. Level of AC correlated with severity of dysfunctionality of urination (r=0,4; p<0,05). More expressed correlation is received by comparison of severity of dysfunctionality of the bladder and ratio of AC / C0 with (r=0,6; p<0,05). The ratio of AC /C was raised in 72% of cases (0,69 ±0,2 at norm <0,6) in children with dysfunctional bladders.
Conclusions: Thus, the connection of the severity of dysfunctionality of bladders with AC and AC/C page is established. For heavier options of urinary incontinence, the increase in coefficient of AC / C0 is characteristic. That points to relative insufficiency of a free carnitine and proves the need of inclusion in therapy of preparations of a L-carnitine for children with hyperactive bladder.

P - 72 POSTNATAL NEPHRO-UROLOGIC PROGNOSIS OF PATIENTS WITH PRENATAL DIAGNOSIS OF HYDRONEPHROSIS AT THE PABLO TOBÓN URIBE HOSPITAL

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Introduction: Antenatal hydronephrosis in most cases is a transitory ultrasound finding. However, up to 15.4% of the patients will have some kind of urologic anomaly and, currently, the clinical repercussions of prenatal hydronephrosis are not clear. This study aims to assess the imaging features of hydronephrosis patients and to determine whether the renal pelvis value in the prenatal ultrasound correlates with the presence of urologic malformations and the need for surgery.
Material and methods: A retrospective descriptive study.
Results: We analyzed 97 patients, 73 boys and 24 girls, for a total of 135 kidneys. All patients underwent postnatal ultrasound, and no hydronephrosis was found in 17.8%, while 19.3% had mild hydronephrosis, 22.2% moderate and 40.8% severe. Additionally, 85.1% of the patients with pyeloureteral junction stenosis and 90% of those with posterior urethral valves had been prenatally classified as having mild to severe hydronephrosis. Conversely, 41.4% of kidneys with VUR were classified as having mild hydronephrosis, 34.5% moderate and 24.14 severe. Furthermore, 56.3% of the evaluated kidneys needed some type of surgery. It is also worth mentioning that it was necessary to perform surgical procedures on 26% of the kidneys with hydronephrosis. Finally, the analysis of the ROC curve made it possible to find that, when the pelvis has an APD of 10.5 mm, the sensitivity for the detection of nephro-urologic malformations is 67% and the specificity 71.2%. No kidney abnormalities explaining hydronephrosis were found after following up on 31.1% of the kidneys
Conclusions: Prenatal hydronephrosis, regardless of its degree, may be an indication of malformations in the urinary tract. We recommend performing strict follow-ups on the patients to determine the presence of nephro-urologic malformations requiring some kind of intervention in order to avoid renal damage.

P - 73 EARLY TREATMENT OF URINARY TRACT INFECTION TO PREVENT KIDNEY SCARRING

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Introduction: Around 5% of children with first-time urinary tract infection (UTI) will have renal parenchymal defect on imaging. The delayed antibiotic therapy is one of the risk factors for developing post-inflammatory scars.
Material and methods: The aim of the study was to test the influence of delayed antibiotic treatment and therapeutic response time to size of postpylonephritic scars. We enrolled 96 children (64 girls, 32 boys) with first upper uncomplicated UTI. Each patient received 14-day-long antibiotic treatment. All patients underwent a dimercaptosuccinic acid renal scintigraphy 6 months after the UTI. The images of static scintigraphy were semiquantitatively evaluated according to the Hitzel et al. (J.Nucl.Med.2004). The results were statistically evaluated.
Results: Microbiological analyses of the urine detected E. coli in 96 cases. CRP value was between 35 -158 mg/l (mean:81.7, median:58). Ultrasonographic examination did not refer any pathological anomalies. The therapeutic response time was 1-3 days (median: 1.8 days). In 27 cases, the antibiotic treatment was started within 24h, in 47 cases between 24-48h, in 17 children between 48-72h and in 5 cases after a 4-day-long period of temperature. The correlation between the therapeutic response time and the size of scars was not significant (p=0.2), but the intensity of scarring was significantly higher in children with delayed antibiotic therapy (p=0.02).
Conclusions: Our results showed more extensive scars in children with delayed treatment. We suggest that active management in primary care can reduce the size of post-inflammatory scars of the kidney. Effective antibiotic treatment is associated with less post-inflammatory renal scars.

P - 74 PREDICTIVE VALUE OF URINARY OSMOLALITY IN THE EARLY MORNING FOR DESMOPRESSIN RESPONSE IN ENURESIS

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Introduction: Surrogate parameters identifying desmopressin response or resistance would be of extremely importance in individualizing therapy in children with nocturnal enuresis. But they have been an issue for debate and research in the past decades. Urinary osmolality in the morning was proposed by several authors, but without convincing results. The aim of this study was to identify the potential value of urinary osmolality in an early morning sample, in children with monosymptomatic enuresis nocturna.
Material and methods: Methods : retrospective study in 45 patients (12F) with monosymptomatic enuresis nocturna, age 5-16 years, wet at least 5/7 days: registration of a night time diary, including night time enuresis episodes and diuresis- volume. Morning urine was collected at wake up. Patients were subsequent treated with desmopressin 2x200μg tablets in the evening for minimum 6 weeks
Results: Results : 13/45 patients were full responder, 15 patients partial responder. Urinary osmolality-range was 675 to 1023 mosmol/l, but did not correlate with response-rate. Nocturnal diuresis volume < 100% of Hjalmas formule correlated strongly with desmopressin resistance.
Conclusions: Conclusion; Urinary osmolality in the morning has no added value in prediction of desmopressin response.

P - 75 PRIMARY NOCTURNAL ENURESIS: FACTORS INFLUENCING FAILURE TO ENURESIS ALARM TREATMENT IN ASIAN CHILDREN

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Introduction: The study aims to evaluate environmental and clinical characteristics of Asian children with Primary noctunal enuresis and to identify factors influencing treatment failure to enuresis alarms.
Material and methods: Children aged 6 to 16 years seen at KK Women's and Children's Hospital, Singapore with Primary nocturnal enuresis who opted for enuresis alarm treatment, over a 6 year period from 2007-2013, were included. Prospective data was collected on demographics, age at presentation, frequency of nocturnal enuresis per week and per night, on whether child awaken after wetting, the size of the patch, presence of family history and parental perception of why primary enuresis happens.
Results: One hundred and thirty eight children with primary nocturnal enuresis who were treated with enuresis alarm and complete data were included. Mean age at presentation was 9.2 ± 2.0 years and 79 (57.4%) were male. Thirty three children (24%) had a first degree relative with nocturnal enuresis. Caregivers cited deep sleep as the main reason for nocturnal enuresis (103 children, 74.6 %). Eighty seven (63 %) children achieved the targeted 21 dry consecutive dry nights using an enuresis alarm. In the remaining 51 children, treatment failure to enuresis alarms was observed in the presence of daytime symptoms (Odd's Ratio 4.55, 95% CI 1.29-15.2), family history in first degree relatives (OR 3.10 (1.38-6.93)), male gender (OR 2.13 (1.03-4.42)) and history of developmental delay, (OR 3.51 (1.11-11.1)). Factors such as wetting during daytime naps, frequency of enuresis, size of the patch or arousal when wet, were not found to be significant.
Conclusions: Enuresis alarms are effective in Asian children with 63% of patients achieving success. Treatment failure was more likely in boys, those with a family history of enuresis, developmental delay and daytime urinary symptoms.

P - 76 ANTIBIOTIC RESISTANCE IN CHILDREN WITH RECURRENT UTI DURING A PYELONEPHRITIS EPISODE

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Introduction: The increasing rates of antibiotic resistant in children with urinary tract infection (UTI) are a serious health problem. The objective of this study was to determine urinary pathogens responsible for UTIs in children with recurrent UTI during a pyelonephritis episode, frequency of risk factors (RF), and assess the resistance patterns of the isolates to commonly used antibiotics.
Material and methods: 102 urine isolates were obtained from the 102 different children with recurrent UTI during a pyelonephritis episode.
Results: Escherichia coli (73.5%), Klebsiella pneumoniae (8.8%) and Enterococcus spp (7.8%) were main bacterial pathogens in all of the patients. The antibiotic resistance rates were as follows: trimethoprim-sulfamethoxazole 41.2%, ampicillin 28.4% ceftriaxone 22.5%, co-amoxiclav 17.6%, cipro 13.7%, gentamycin 11.8%, nitrofurantoin 6.9%, ertapenem %2, piperacilline tazobactam 11.8, meropenem 3.9% and gentamycin 11.8% in all of the patients. We found 58 (56.9%) RF in the patients. Reflux was found to be the most important RF for recurrent UTI (14.9%). The obtained pathogens were similar in patients with and without RF. Isolates were significantly more resistant to trimethoprim-sulfamethoxazole with RF than without RF (48.4%, 31.8% respectively, $p<0.05$). The 38 (37.2%) patients were treated with a prophylactic antibiotic during the pyelonephritis episode in this study. Prophylactic antibiotic treatment did not change the sort of causative pathogens in our patients. The causative microorganisms were significantly more resistant to ampicillin, ceftriaxone, trimethoprim-sulfamethoxazole, co-amoxiclav, and piperacillin-tazobactam in patients with under prophylaxis than without prophylaxis, respectively (39.5%/21.9%, $p<0.05$), (34.2%/15.6%, $p<0.05$), (60.5%/29.7%, $p<0.01$) (31.6%/9.4%, $p<0.01$) (21.1%/6.3%, $p<0.01$).
Conclusions: The presence of risk factors and prophylactic antibiotics usage may not change the microbes in patients with recurrent UTI. Ertapenem treatment may be initiated empirically in patients with recurrent UTI and pyelonephritis. Nitrofurantoin may be first choice antibiotics for prophylaxis in these patients.

P - 77 DIAGNOSIS OF RECURRENT URINARY TRACT INFECTIONS CAUSED BY CYSTITIS CYSTICA WITH ULTRASOUND BLADDER WALL THICKNESS MEASUREMENT IN PREPUBERTAL GIRLS

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Introduction: Cystitis cystica (CC) is a pathohistological entity characterized by the appearance of pearl, pink, brown or yellowish nodular changes on bladder wall mucosa, frequently associated with recurrent urinary tract infections (UTI). We evaluate urinary bladder wall thickness (BWT) assessed by ultrasound as a diagnostic tool for recurerent UTI caused by CC.
Material and methods: This was a 9-year prospective study comprising 120 prepubertal girls. Sixty subjects of whom half underwent cystoscopy represented cases while the other 60 (those with a single UTI and healthy subjects) represented controls in which cystoscopy were not performed.
Results: Based on receiver operating characteristics (ROC) analysis, BWT discriminated very well between cases and controls with area under the ROC curve close to 1.0. At the optimum cut-off defined at 3.9 mm, negative predictive value was 100% leaving no probability of CC with BWT <3.9 mm. Positive predictive value was also very high (95.2%), indicating only around 4.82% probability of no CC in patients with BWT values_3.9 mm. BWT could also distinguish between healthy subjects and those with a cured single UTI, although discriminatory properties were moderate (area under ROC86.7%, PPV 78.8%, NPV 85.2%).
Conclusions: Ultrasound mucosal BWT measurement is a non-invasive, simple and quite reliable method in diagnosis of CC in prepubertal girls with recurrent UTI.

P - 78 MEAN PLATELET VOLUME IN YOUNG CHILDREN WITH URINARY TRACT INFECTION

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Introduction: Mean platelet volume (MPV) has been reported to be a marker of various infections and inflammations, but it has not yet been well-established in urinary tract infection (UTI). The purpose of the present study was to evaluate the role of MPV as an acute phase reactant in children with urinary tract infection.
Material and methods: Data from 118 young children (< 2 years) with febrile UTI between 2011 and 2012 were grouped as acute pyelonephritis (n = 62) with lower UTI (n = 56) according to the DMSA scan abnormalities. Platelet indices (MPV, platelet distribution width [PDW], platelet count) and other laboratory examinations (white blood cell [WBC] count, erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]) were measured. We also analyzed correlation of MPV with other blood parameters.
Results: WBC were significantly higher in the acute pyelonephritis group than in the lower UTI group. ESR ($p = 0.005$) and CRP levels ($p < 0.001$) were also significantly higher in the acute pyelonephritis group than lower UTI group . There were significant differences between the acute pyelonephritis and lower UTI group in terms of MPV levels ($p = 0.011$), while platelet count($p = 0.742$) and PDW ($p = 0.452$) did not differ between the two groups. Moreover, MPV positively correlated with CRP levels and negatively with platelet count.
Conclusions: Our results suggest that MPV could be used as an acute inflammatory marker in addition to CRP in children at the diagnosis of upper UTI.

P - 79 HOW TO SUCCESSFULLY OPTIMISE THE SEQUENCE OF RENOGRAPHY IN CHILDREN

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Introduction: Before 2010, chloral hydrate was the standard procedure of sedation of children younger than 3 years in nuclear medicine studies. Oral use of chloral hydrate for sedation of children can be associated with adverse side-effects such as arterial desaturation and therefore close surveillance of the children is necessary. We started to give melatonin for sedation in order to optimise renography in children. Melatonin is a native neurohormone that induces sleep without hitherto reported side effects. In particular, melatonin is well tolerated.
Initially, introduction of the use of melatonin resulted in an increased study time consumption and moreover, the fraction of cancelled studies increased. Therefore, we additionally introduced placing the child into a paediatric box at the department of Paediatrics, or at least to arrive in a bed to the examination.
Material and methods: A filled-in-form was elaborated for the registration of data in all paediatric patients admitted for renography. Moreover, we intensified the amount and quality of information given to the parents, which considerably contributed to a successful study.
The filled-in forms were analysed every third month. Hereafter, the results were discussed with the staff of the Department of Paediatrics and necessary adjustments were secured.
Results: A total of 382 children under 3 years were included. The number of successful renographies increased from 78% to 87% ($p=0.21$). The average time consumption decreased from 69 to 56 minutes ($p=0.11$). Out-patient children were discharged after the renography without observation.
Conclusions: Based on more than 350 patient studies, we recommend melatonin and paediatric box in combination. The changed sedation regimen increased the number and quality of successful renographies. Furthermore, this procedure is safer and does not require nurse assistance during the acquisition. Since the results were very positive and clinically significant we implemented the new procedure in our departments as routine.

P - 80 MULTICYSTIC DYSPLASTIC KIDNEY WITH A CONSERVATIVE APPROACH

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Introduction: Our purpose was to characterize MDK cases followed in our Outpatient Clinic of Pediatric Nephrology, evaluate their progress and reflect on the protocol adopted
Material and methods: 27 MDK patients observed between January 2005 and December 2014 were included in this retrospective study and followed-up. In 26 children the diagnosis was known from prenatal ultrasound. All children underwent a systematic protocol, including conservative treatment (no surgery) and periodic clinical, laboratory and ultrasound evaluation. All children underwent a MAG3 renogram and a voiding cystourethrography, only repeated in cases of vesicoureteral reflux (VUR)
Results: Fourteen children (50%) are male. The median age of first visit was four weeks. The median of follow-up was 60 months. The MDK was in the left kidney in 15 children (56%). Contralateral nephro-urologic pathology was identified in 7 cases (26%): five children with VUR (grade ≥ IV in three), one with ureteropelvic junction obstruction (UPJO) and one with mild pelvic dilatation. There was involution of dysplastic kidney in 20 cases (75%), partial in 15 and total infive. The involution rate was higher in the first 24 months. There was a progressive compensatory hypertrophy of the contralateral kidney, with the highest rate in the first two years of life. There was resolution of VUR in three of the five units reflux (after ureteral reimplantation). There was no malignant degeneration and there was not carry out any nephrectomy of dysplastic kidney. Urinary infection occurred in 3 children (11%) which have VUR. There were no cases of hypertension or decreased glomerular filtration rate

Conclusions: We confirm the fairness of a conservative attitude in the approach of children with MDK. This clinical approach is safe, with a minimum incidence of complications, with tendency to involution of dysplasic kidney being the rule

P - 81 RENAL SCARRING AFTER FEBRILE URINARY INFECTION IN CHILDREN: A POPULATION STUDY

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Introduction: The urinary tract infection (UTI) is one of the most common bacterial illness in children. It is known to be associated with an increased risk of permanent renal damage and scarring, which may lead to generation of pathological conditions such as hypertension, renal insufficiency and end-stage kidney disease. The 99mTc-dimercaptosuccinic acid (DMSA) renal scanning is currently the accepted gold standard for diagnosis of renal scarring.
Material and methods: We reviewed the outpatient medical records of a group of children identified with decreased relative renal function or focal scars in DMSA renal scintigraphy performed after the acute phase of a first episode of febrile urinary infection, from January 2002 to December 2004, to assess differences in clinical outcome.
Results: We studied 80 patients of which 52(65%) had reduced function on DMSA (< 40% fixation) and 28(35%) had focal cortical lesions with normal function). No child had hypertension, although some fall between pre-hypertension. The serum creatinine, serum cystatin C, compared microalbumin/creatinine and protein/creatinine ratio showed no increase trend over time. A considerable number of children with decreased relative renal function presented diameter longitudinal ultrasound below percentile P5 in various stages of evaluation (25% at diagnosis, 33% at 2 years and 19% at 10 year follow-up), when compared to children with focal scars without decreased relative renal function ($p<0.05$).
Conclusions: The achievement of DMSA renal scintigraphy, after a first febrile urinary infection, seems to have no benefit in setting medium term prognosis of children with scarring nephropathy in terms of progression to hypertension and renal failure. Surveillance ultrasound seems to have an interest in children with decreased relative renal function on DMSA.

P - 82 LAPAROSCOPIC TRANSPERITONEAL DISMEMBERED PYELOPLASTY BY UTILIZING V-LOC BARBED SUTURE

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Introduction: Laparoscopic pyeloplasty is a trending technique in surgical therapy of ureteropelvic junction obstruction. Preventing this approach from widespread use is the difficulty of intracorporeal suturation. We present you 2 laparoscopic pyeloplasty cases via utilization of v-loc barbed suture.
Material and methods: Laparoscopic transperitoneal dismembered pyeloplasty was performed in 2 male cases, aged 12 and 15. Following 3 port access to peritoneal cavity, ureter and renal pelvis was reached transmesocolically. One case revealed an intrinsic obstruction, while the other had a crossing aberrant vessel. Pelvic junction was transected in both patients. Pyeloplasty was carried out via v-loc suture without pelvic reduction. Following the first suture, needle was passed through the end loop and anastomosis was performed continuously. Two v-loc sutures were used seperately for anterior and posterior portions. A ureteric stent was applied. Anastomosis was completed without any knots. Mesocolon was sutured continuously with v-loc barbed sutur without knots.
Results: Operation times were 90 minutes in both procedures. Hospital stay was 2 days in both cases. Upon observing clear urine, patients were discharged after urethral decatheterisation.
Conclusions: V-loc suture shares the same material as vicryl sutures. It can be used without the need to knot, due to the barbed architecture. V-loc has been used for superficial suturation, tendon reparation, laparoscopy in obstetrics and urology and also experimented in intestinal anostomosis. V-loc suture provides a reliable and time effective anastomosis in pediatric laparoscopic pyeloplasty by removing the need to apply knots.

P - 83 URINARY TRACT INFECTION IN OMANI CHILDREN: ETIOLOGY AND ANTIMICROBIAL RESISTANCE. A COMPARISON BETWEEN FIRST EPISODE AND RECURRENT INFECTION.

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Introduction: Urinary tract infection (UTI) is common in infants and children, and *Escherichia coli* (*EC*) is the leading pathogen. The aims of this study were to compare first episode of UTI with recurrent infection, reveal organisms that cause UTI, uropathogen resistance, and presence of bacteria producing *extended-spectrum β-lactamase* (*ESBL*).
Material and methods: A retrospective study included Omani children with any documented UTI presented to SQUH between September 2008 and August 2012. Comparison was made between both groups using Chi-squared ($\chi 2$) test or student's t-test and Wilcoxon-Mann-Whitney test as appropriate.
Results: The first-UTI group included 175 children. *EC* was the leading pathogen (69%), *Klebsiella pneumonia* (17%; *P<0.001*), and *ESBL* (3%). 230 uropathogens were isolated from patients with recurrent UTI from total 74 patients. The most common isolated pathogen was *EC* 187 (81.3%; *P<0.001*), followed by *K.pneumonia*12 (5.1%), and *ESBL* (7%; *P=0.042*). Overall resistance to IV antibiotics was less evident than oral antibiotics, with least resistance to *Meropenem* and *Imepenem* (1% each). Higher resistance was found in pathogens of recurrent UTI to *Augmentin*, *Cefuroxime*, *Ceftriaxone*, *and Cefotaxime*. Oral*Nitrofurantoin* showed least resistance in first and recurrent UTI, but increased in non-E.Coli uropathogens.
Conclusions: E.coli and ESBL were more common in recurrent UTI, while K.pneumonia were found more in first UTI. *Meropenem*, *Imepenem*, *Amikacin*, and *Piperacillin*/*Tazobactam* can be used as a first line, while*Cefotaxime* and Ceftriaxone cannot be used due to high resistance in both groups. The uropathogens found in this report show high resistance rates to *Ampicillin*, *Cefuroxime*, and *Amoxicillin*/*Clavulanate*. First-generation cephalosporin is not recommended for use as empiric therapy both in first or recurrent UTI. For oral empiric treatment, we recommend the use of *Nitrofurantoin*.

P - 84 THE EFFECT OF GENDER ON CHILDHOOD VESICOURETERAL REFLUX

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Introduction: Vesicoureteral reflux (VUR) is the most frequent anomaly in patients with urinary tract infections (UTI)s. The aim of this study was to assess the effect of gender on VUR in pediatric patients.
Material and methods: Files of patients who had been seen in our department (during routine follow-up visits) between January 2014 and January 2015 were retrospectively evaluated. Chi-Square test and Mann-Whitney U test were used for statistical analysis. P values less than 0.05 were considered significant.
Results: A total of 220 (142 females and 78 males) patients with VUR were enrolled. Forty-eight patients had grade 1-2; 112 grade 3 and 60 had grade 4-5 reflux. Median follow up was similar for both genders (~5 years). Boys were diagnosed at younger ages than girls (2.00 ± 2.59 vs 3.81 ± 3.15 years; $p<0.001$). Although UTI was the leading cause of diagnosis of VUR in both sexes (81% in girls; 59% in boys)antenatal hydronephrosis was significantly more common in boys (25.6%) compared to girls (3.5%) ($p<0.001$). Frequencies of grade 4-5 reflux (43.6% vs 18.3%); abnormal ultrasound (77% vs 54%) and Tc-99^{m} DMSA scintigraphy findings (77% vs 59%) were statistically higher whereas spontaneous resolution of reflux was lower in males (16.7% vs 31%) as compared to females ($p<0.05$). Surgical correction was performed in similar frequency in both sexes (~47%). Urinary tract infections and lower urinary tract dysfunction were more frequently detected in females ($p<0.05$).
Conclusions: Boys had more severe reflux with abnormal ultrasound and scintigraphy findings. Although age at diagnosis was younger than girls and the need of surgical correction was similar in both sexes, spontaneous resolution was lower in boys.

P - 85 CHRONIC KIDNEY DISEASE IN CHILDREN WITH POSTERIOR URETHRAL VALVES

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Introduction: The most common cause of congenital lower urinary tract obstruction in male infants is posterior urethral valves (PUV) with an incidence about one patient in each 5000–8000 infants. Despite successful treatment of the primary obstruction, it can lead towards to chronic kidney disease (CKD). The aim of study was to evaluate the frequency of renal involvement in children with PUV and CKD in the follow-up period.
Material and methods: This study included 43 boys (from I/2007 until XII/2014), diagnosed as having PUV by miction cystourethrogram (MCUG) and the diagnosis confirmed by cystoscopy. Routine investigations (blood and urine tests, ultrasound, nuclear imaging studies) have been done for all patients.
Results: From 357 fetuses with congenital abnormalities of kidney and urinary tract – 25 (7%) had sign of PUV, and later the diagnosis was confirmed. Clinically congenital lower urinary tract obstruction may present with delayed voiding on first day of life or difficulty poor urinary stream. Nine (21%) children was admit with signs of renal insufficiency. All of 43 children with PUV had obstructive uropathies, 31 patient (72, 1%) had bilateral damage: 21 patients (34 ureters) had vesicoureteric reflux (VUR) on the initial MCUG, predominantly (96%) - high grade (IV-V); 17 patients (30 ureters) had megaureters; 5 children (10 ureters) had combined VUR+megaureter. Ultrasound signs of cystic or/and dysplastic kidneys had 14 (32,5%) patients. All patients (100%) treated surgically by transurethral resection of PUV during the first three months of life. The mean follow – up period was 2.7 years (0.5-7 years). Chronic kidney disease stage II was found – 3 patients, stage III – in 2, stage IV - 3 patients, two progressed to the end– stage renal disease. One of these children subsequently underwent a renal transplantation.
Conclusions: All children with congenital infravesical obstruction need not only optimal neonatal urological care, but also nephrological support, because of high risk of CKD development.

P - 86 CLINICAL USEFULNESS OF SERUM PROCALCITONIN AS A BIOMARKER OF ACUTE PYELONEPHRITIS

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Introduction: Urinary tract infection (UTI) are common childhood bacterial infection that may involve acute pyelonephritis (APN) followed by late scarring. We assessed the usefulness of serum procalcitonin (PCT) as a biologic marker in diagnosing APN in children with UTI, and to determine the accuracy of PCT compared with other inflammatory markers.
Material and methods: Infant with first febrile UTI who underwent renal ultrasonography (US), technetium-99m-dimercaptosuccinic acid scan, and voiding cystourethrography were prospectively studied. Serum samples from all patients were tested for PCT, erythrocyte sedimentation rates (ESR), C-reactive protein (CRP) and white blood cell count (WBC) measurement.
Results: There was no significant differences in the mean age, gender, and microorganisms detected between the APN (n=21) and lower UTI groups (n=32)($P>0.05$). In APN groups, the median serum PCT and CRP level was significant higher than in the lower UTI groups (PCT; 5.44 ±10.0 vs 0.99±3.0 μg/L, P=0.022, CRP; 115.5±75.7 vs 31.02±23.4 mg/L, P=0.014) For the prediction of APN, the sensitivity, specificity, positive predictive value and negative predictive value of PCT (Cutoff value=1.0μg/L) were 65.0%, 87.1%, 76.5%, and 79,4%, respectively; ESR (Cutoff value=20 mm/hr) were 47.6%, 71.8%, 52.6%, and 67.6%; CRP (Cutoff value=60 mg/L) were 71.4%, 87.5%, 83.3%, and 82.3%, respectively.
Conclusions: In febrile UTI infant, the serum PCT combined CRP was a helpful marker for the diagnosis of APN. Therefore, serum PCT levels could be accurate marker for the diagnosis of APN

P - 87 IS IT POSSIBLE TO DIAGNOSE A DILATED VESICOURETERAL REFLUX BY DYNAMIC RENAL SCINTIGRAPHY?

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Introduction: Dynamic renal scintigraphy (DRS) was performed for the evaluation of kidney functions. The aim of this study is to investigate the diagnostic potential of DRS for high grade vesicoureteral reflux (VUR).
Material and methods: The patients having both direct radionuclide voiding cystography (dRVS) and DRS were searched from picture archiving and communication system and included in the study. The data concerning DRS was reached retrospectively. Patient motion, injection routes and if present, the diuretic time were noted. If exists, the presence of involuntary urination and the exact time of urination were also noted. The raw images were examined for any bladder activity in the region of interests (ROI). The images were reprocessed and the time activity curves were obtained. Any sudden disturbances in the curve pattern were determined and analyzed.
Results: 30 patients and 45 99mTc-MAG3 DRS studies were evaluated. A sudden upslope in renogram curve during excretion phase, whether bilateral or unilateral was observed in 9 patients. There wasn't any patient motion, diuretic injection, involuntary urination or any bladder activity in the ROI during the upslope in 3 patients (all had severe VUR episodes on dRVS), leaving the presence of VUR episode as the only choice. The upsloping was bilateral in 4, in whom synchronous diuretic injection or

arm/body motions were detected. In 2 patients, the bladder was full enough entering into the ROI resulting in a unilateral upslope. They were accepted as false positives. In 4 patients, unexplained unilateral and bilateral flattening of renogram curves were observed and accepted as suspicious for VUR.
Conclusions: A DRS study, although not aimed for diagnosing VUR episode can help for the diagnosis of severe VUR if inspected cautiously. Any upslope which is synchronous with the increase in renal activity must be accepted as a severe reflux upon excluding reasons for false positivity.

P - 88 UTI IN YOUNG CHILDREN; CAUSING ORGANISMS AND ASSOCIATED RENAL ANOMALIES

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Introduction: To investigate the commonest underlying organisms and associated urological anomalies in children presenting with urinary tract infection (UTI).
Material and methods: Retrospectively all children who had confirmed UTI between October 2013 and February 2014 were evaluated. Electronic files of 279 children presented with UTI, aged less than 5 years of age were reviewed
Results: A total of 153 patients (85 males) with the mean (SD) age of 15 (19.86) months were included in the study. Recurrent UTI was present in 45.1%.. Urine collection in children less than 2 years of age was through trans-urethral catheterization in 69.37%, while midstream urine was the main method in those above 2 years (78.57 %). *Escherichia coli* (E.coli) was the causative organism in 41.2% of first UTI. The second most common organism was *Klebsiella Pneumonia*e seen in 19.6%.. Urological anomalies were found in 28.1% of the overall study population. Ninety percent of those with single UTI did not have anomalies. However urological anomalies were reported in 50.72% of those with recurrent episodes of UTI (p-value <0.005). Non-E coli cases were associated with higher percentage of abnormal renal ultrasonography (p value0.006).
Conclusions: E- coli was the commonest causative organism for UTI and single episode of UTI signified normal urological anatomy.

P - 89 CLINICAL EVALUATION OF CONGENITAL ANOMALIES OF KIDNEY AND URINARY TRACT IN CHILDREN

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Introduction: Congenital anomalies of kidney and urinary tract (CAKUT) are the most common cause of chronic kidney disease in childhood. The aim of this study was to evaluate the demographic, clinical and imaging findings in different types of CAKUT patients.
Material and methods: Two hundred and fifty eight patients (122 male) with CAKUT who had been admitted for the first time or been followed up in our institution between December 2011- July 2012 were enrolled in the study.
Results: The median age at diagnosis of the study group was 31.7 months (IQR 0-184.5). Age at diagnosis was significantly lower in boys (12.6 months, IQR 0-129.8) as compared with girls (42.6 months, IQR 0-184.5) ($p<0.01$). The most common cause of diagnosis was urinary tract infection (UTI) (52%) followed by antenatal hydronephrosis (AHN) (23%). However, boys were most frequently diagnosed because of AHN (74%) and 45% of them had obstructive uropathy, whereas it was UTI in girls (70%) and 73% had vesicoureteral reflux (VUR) ($p<0.01$). Seventy four percent of the patients had at least one UTI. The frequency of UTI was significantly higher in girls (85%) as compared with boys (62%) ($p<0.01$). In addition, UTI rate was higher in patients with VUR compared to patients with other CAKUT ($p<0.01$). Chronic kidney disease developed in 12% of the patients, 68% was boys. The distribution of diagnosis was VUR+ hypodysplasia (48%), posterior uretral valve+/- VUR (26%) and hypodysplasia (16%). Family history of this group revealed 33.3% parental consanguinity whereas it was 23.3% in all CAKUT patients.
Conclusions: CAKUT is a clinically heterogeneous group of diseases with diverse demographic and clinical findings. More efforts should be aimed at improving early diagnosis as well as classification with comprehensive reference to the demographic, clinical and genetic features of the diseases.

P - 90 RENAL ANOMALIES IN TWO CHILDREN WITH TOWNES BROCKS SYNDROME

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Introduction: Townes Brocks syndrome (TBS) is rare autosomal-dominant disease. Phenotypically characterized by anal atresia, malformations of the thumb and ear lobes, sensoreural or conductive hearing loss. About 27% patients have congenital anomalies of the kidneys and urinary tract, and 42% develop end-stage renal failure.
Material and methods: We present case reports of boy and girl aged 7 and 8 years with TBS. Both children had anal atresia in the neonatal period. Boy was reffered to the nephrology clinic at the age of 17 months due to the hyperechoic parenchyma on the kidney ultrasound. Girl was reffered at the age of two due to acute pyelonephritis. Both have ear and tumb abnormalites and sensoneural hearing loss. Ultrasound examination of the kidney in both patients revealed hyperechoic kidneys of the normal size. Girl had a bilateral grade III vesicoureteric reflux. After years of follow up boy has preserved global renal function, while girl is in stage III chronic kidney disease.
Results: The genetic analysis demonstrated SALL 1 mutations in both patients and in girl's mother. Boy was heterozygous for the mutation c.1031T-A. This mutation has not been described in the literature.
Conclusions: In children with suspected Townes Brocks syndrome, it is necessary to conduct a nephrology evaluation and monitor renal function. It is important to inform patients about inheritance and prenatal diagnosis of TBS.

P - 91 THE ROLE OF BREASTFEEDING IN PROTECTION AGAINST ACUTE PYELONEPHRITIS

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Introduction: Exclusive breastfeeding has been found to play a protective role against urinary tract infections (UTIs) in infants. Its protective effect has been suggested to be long lasting even after breastfeeding cessation. The study was to analyze whether breastfeeding or other factors influence the risk of acute pyelonephritis (APN) in children under 2 years of age.
Material and methods: We retrospectively analyzed data files from 72 children (30 boys) under 2 years of age hospitalized due to first-time APN. None of the patients had previously undergone intervention due to congenital anomaly of urinary tract. Gender, birth weight, age, feeding type at the time of admission (breastfeeding, formula feeding, solid food)

and results of pre - and postnatal ultrasound screening were recorded and analyzed.
Results: Boys had higher prevalence of APN during the first 6 months of age, later on the girls prevailed. Postnatal hydronephrosis detected by ultrasound was the most important risk factor for acute pyelonephritis in the first 9 months of age. Overall breastfed vs not breastfed patients ratio at the presentation of APN was 2,4:1. Only in the first month of life there was a significant difference between full breastfeeding at the time of APN onset (50%) and full breastfeeding rates in all children of the same age in Slovakia (88%). Unfortunately, data on feeding were not detailed enough to analyze exclusively breastfed group in our cohort.
Conclusions: Gender at different age and the presence of hydronephrosis are risk factors of UTIs. The detailed history of feeding is frequently an omitted part of patient history. A prospective study with focus on feeding patterns of infants is needed in order to study the influence of exclusive breastfeeding on UTIs.

P - 92 RENAL FUNCTION OF THE BABIES UPON THE DIAGNOSIS OF CONGENITAL URETHRAL STENOSIS

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Introduction: Although congenital urethral stenosis (CUS) is not familiar to many pediatricians, it may cause urinary tract infection in children, and further potentially causes chronic kidney disease (CKD) via inappropriate voiding. Anomalous kidneys and/or refluxing/dilating upper urinary tract are known to cause CKD. However, renal function of the children with CUS is not fully elucidated. Here, initial renal function upon diagnosis was investigated in the pediatric patients with CUS.
Material and methods: Patients who underwent voiding cystourethrography (VCUG) were enrolled. We retrospectively analyzed the findings of VCUG and CKD stage. For the cases of 2 years or older, CKD stage was determined by serum Cr-based eGFR reported by Nagai for Japanese children. For the babies < 2 years of age, CKD stage criteria reported by Ishikura for Japanese children were adopted.
Results: Out of 89 patients enrolled in this study, 20 cases were excluded due to insufficient urethral evaluation. Remaining 51 male and 18 female cases were analyzed. Median age at determination of CKD stage was 1.37 years old. CUS was present in 21 cases, and 9 cases of them required surgical intervention. 13 cases were complicated with vesicoureteral reflux (VUR) or other upper urinary tract abnormalities (UTA), including 3 cases (23.1%) with CKD stage 2. However, the CUS cases without VUR/UTA are all in CKD stage 0 or 1. VUR/UTA was present in 36 cases, including 13 with CUS and 23 without CUS. CKD stage 2 was seen in 3 out of 13 cases with CUS (23.1%), and 5 out of 23 cases without CUS (21.7%), showing little difference.
Conclusions: CUS has little impact on the initial renal function of the babies requiring VCUG, whereas VUR/UTA is more likely linked to renal damage. It is suggested that secondary damage due to CUS is preventable in nature when appropriately diagnosed and treated.

P - 93 CYSTITIS CYSTICA AS A RISK FACTOR FOR RECURRENT URINARY TRACT INFECTIONS IN CHILDREN WITH PRIMARY VESICOURETERAL REFLUX

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Introduction: The research carried into primary vesicoureteral reflux (VUR) to date has still not provided strict guidelines as to which children should be given uroprophylaxis and for how long. Cystitis cystica (CC) has been identified as a risk factor for the recurrent urinary tract infections (UTIs) and affected children should be administered longterm uroprophylaxis.The diagnosis of CC may be confirmed with overall anamnesis and ultrasound findings of bladder wall thickness (BWT).
Material and methods: The prospective study included 102 children with documented primary VUR, taken off prophylactic antibiotics. All patients were submitted to both ultrasound BWT measurement and routine followup urinalysis.
Results: Of 102 patients included in the study, UTI developed in eleven children of whom six had CC confirmed with both ultrasound and cystoscopical findings. Within six months UTI occurred in all six children with CC, so they were treated with antibiotics; four of these patients were hospitalized with pyelonephritis. The other five children belonging to the group in which UTI occurred were diagnosed with cystitis and pyelonephritis (3 and 2, respectively). Of the two patients with pyelonephritis, one developed UTI after voiding cystourethrogram (VCUG), and the other suffered from reflux nephropathy. In the group of children without CC, only the boy with reflux nephropathy was given prophylaxis again. Infecton in this group of patients recurred more than six months after discontinuing uroprophylaxis.
Conclusions: Cystitis cystica is recognised as a risk factor for recurrent UTIs in children with VUR. Ultrasound measurement of BWT is of importance when discontinuing uroprophylaxis. The results of our study suggest that children with primary VUR and CC should receive countinuous antibiotic prophylaxis until CC is resolved.

P - 94 COMPARISON OF LONG-TERM EFFICACY OF DESMOPRESSIN LYOPHILISATE AND ENURETIC ALARM FOR MONOSYMPTOMATIC NOCTURNAL ENURESIS AND ASSESSMENT OF PREDICTIVE FACTORS FOR SUCCESS

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Introduction: We compared the long-term success of desmopressin sublingual lyophilisate formulation and enuretic alarm therapy in children with primary monosymptomatic nocturnal enuresis, and determined predictive factors for treatment success.
Material and methods: A total of 96 children (mean age 7±2 years) with primary monosymptomatic nocturnal enuresis were randomized to receive treatment consisting of desmopressin or enuretic alarm for 6 months. Treatment compliance and response were reviewed monthly in each patient using a 30-day bed-wetting diary.Success rates at 6 and 12 months were compared for desmopressin and enuretic alarm. Possible demographic factors predicting success were investigated by logistic regression analysis.
Results: Overall 4 children (8,3 %) in the desmopressin group and 10 (20, 8%) in the enuretic alarm group withdrew after randomization. Based on patients who completed 6 months of treatment, success (more than 90% reduction in wet nights per month) was achieved in 73.8% and 64.8% of children in the desmopressin and enuretic alarm groups, respectively. At 12 months 76.5% of those receiving desmopressin and 75% of those treated with enuretic alarm had success. However, long-term success rate was significantly higher with desmopressin (68.8% vs 46.2%) if intention to treat population was considered. Multivariate analysis revealed treatment group, severity of enuresis and monthly income as independent predictors of cure at 6 months.
Conclusions: In compliant patients desmopressin lyophilisate and enuretic alarm provided equivalent success at the end of treatment and after extended followup. Compliance is the major problem of alarm therapy . Severe enuresis (more than 5 wet nights weekly) is an important predictive factor for cure after first-line treatment

P - 95 URINARY CALCIUM EXCRETION IN CHILDREN WITH MONOSYMPTOMATIC NOCTURNAL ENURESIS

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Introduction: The aim of our study was to determine the urinary calcium in children with monosymptomatic nocturnal enuresis (MNE)
Material and methods: 96 MNE children and 98 reference group were included (mean age 5±2 years). Urinary calcium excretion (in 24-h collection and per kg of body mass) and Ca/creatinine ratio were estimated
Results: Hypercalciuria in MNE group was diagnosed in 24/96 (25 %) patient. In the reference group hypercalciuria was found in 5/98 children (5,1%). Median urinary calcium excretion (mg/kg/24-h and mmol/24-h) was significantly higher in hypercalciuric enuretic patients, and without any positive correlation with heigh, weight or age
Conclusions: Urinary calcium excretion was significantly disturbed and further studies are needed to assess the role of hypercalciuria in the pathogenesis of MNE

P - 96 OUTCOME OF MULTICYSTIC DYSPLASTIC KIDNEYS IN CHILDREN

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Introduction: Renal cystic diseases are important cause of chronic kidney disease (CKD). We report the pattern of pediatric renal cystic disease in children referred to tertiary teaching hospital and we also evaluate the outcome of children with multicystic dysplastic kidney (MCDK)
Material and methods: Retrospective study of all children with cystic kidney diseases presented to King Abdulaziz University hospital between 2006 and 2014. We studied the outcome of children with MCDK who had been followed up for 6 months or more.
Results: Fifty five children (30 males) diagnosed as renal cystic diseases; 25 children as MCDK, 22 as polycystic kidney disease (PKD), 4 as nephronophthisis and 4 as renal cyst. History of consanguinity between parents was positive in 96.2%. On the last follow up children with MCDK or simple renal cyst had good renal function while children with PKD and nephronophthisis developed renal impairment.
All children with MCKD except one were diagnosed antenatally and 16 of them were followed up for the duration of 3.4 (1.97) years. Their last creatinine was 33.9 (13.5) umol/L. Twenty five percent were in stage I CKD and did not progress. While the other 75% of the cases has regressed to stage I CKD and stage II CKD. 56% had involutes of their kidneys as shown by the US, at mean age of 2.6 (1.3) years.
Conclusions: MCDK is the commonest cystic renal disease and diagnosed antenatally in the majority of cases. It has a good prognosis.

P - 97 THE STUDY OF CLINICAL EFFICACY OF DESMOPRESSIN IN CHILDREN WITH POLYSYMPTOMATIC ENURESIS.

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Introduction: We analyze clinical efficacy of synthetic analog of antidiuretic hormone (desmopressin) in treatment of children with polysymptomatic enuresis (PNE).
Material and methods: We performed clinical investigation of 54 schoolchildren of age 6–11 with enuresis. Most of patients (50 children) have PNE. These patients were randomly divided into primary group (n=26) and comparison group (n=18). Primary group was treated with synthetic analog of antidiuretic hormone (desmopressin) and comparison group was treated with nootropic agent (hopantenic acid).
Results: Study of genealogical anamnesis in both groups revealed significant burdened history on enuresis (84,6% and 38,8%) and urinary tracts diseases (50% and 16,7%). Comparison of clinical efficacy shows positive effect of desmopressin in 88% observations with high (46%) or medium (42%) effectiveness of the medicine for patients with complicated enuresis. Development of long-term effect in younger children (age 6–7) was observed in 77,8% cases and in 46,7% (p=0,446) in elder children (age 8–11). Patients treated with hopantenic acid had no effect of treatment significantly more often (50,1%, p=0,000).
Conclusions: Synthetic analog of antidiuretic hormone (desmopressin) revealed the high efficacy in children with PNE, especially in younger children.

P - 98 CALCIFICATION AT THE SITE OF DEFLUX® - A CASE REPORT

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Introduction: Dextranomer/hyaluronic acid (Dx/HA) copolymer (Deflux®) subureteral injection has proven to be safe and effective treatment for vesicoureteral reflux (VUR). Due its efficacy and low rate of complications, a large number of children are undergoing endoscopic implantation of this material for treatment of VUR. In past few years there is an increasing number of reports on calcification at the site of previous injection, and incidence of calcified Deflux® has been estimated to 2% patients at a minimum of 4 years after injection. These calcifications are usually asymptomatic and benign of nature, but in clinical settings may be perceived as ureteral stones, especially in patients presenting with abdominal pain.
Material and methods: We report a patient with calcifications at the site of Deflux® mimicking ureteral calculi on radiographs.
Results: The patient is a 12 year old girl, who had undergone treatment of bilateral VUR with Deflux® at the age of 7 years.
Now she presented with subrapubic and left lower abdominal pain, fever and dysuria. Since urinalysis showed microhaematuria and leukocyturia, antibiotic treatment was initiated. Due to persistent pain radiologic (X-ray) evaluation was performed and revealed bilateral radio-opaque and hyperechoic density in lower abdomen and child was referred to our Nephrology department as having ureteral calculi.
An ultrasound examination and CT showed radio-opaque and hyperechoic density at the site where previously of Deflux® was injected. After finishing antibiotic treatment the pain ceased and no further evaluation was performed.
Conclusions: Calcification at the site of Deflux® is relatively rare, but considering its progressive nature and a large and continuously increasing number of children treated with Deflux®, we can expect more reported cases in the future.
In order to avoid unnecessary and invasive diagnostics, clinicians should be aware of this benign complication.

P - 99 A PATIENT SEEMING AS ARPKD CLINICALLY AND AS ADPKD GENETICALLY

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Introduction: Polycystic Kidney Disease (PKD) is a genetic disorder that can be autosomal recessive (AR) or dominant (AD) causing end-stage renal disease in most of the patients. Here, we present a child seeming as ARPKD clinically but as ADPKD genetically.
Material and methods: This baby was admitted in the neonatal period as a prenatal ultrasonography (US) showed an increase in renal parenchymal echogenicity of both kidneys. An US performed at the age of three months yielded bilateral milimetric cysts, whereas on US at 6 months old showed five cysts on both kidneys, the largest being 5 mm on the left and 4 mm on the right kidney in addition to increase in renal parenchymal echogenicity. No cysts were observed on US of the parents (mother was 27 and father was 35 years old) renal functions were preserved.
Results: On genetic analysis, a homozygote missense mutation on exon 44 (Ile 4045 Val) and heterozygote sinonimous mutation on exon 45 (Ala 4092 Ala) of PKD 1 gene was detected. Besides, on exon 46 heterozygote Pro4210Pro sinonimous mutation was found, which was not associated with the disease according to Human Gene Mutation Database (HGMD).
Conclusions: A patient had a homozygote missense mutation(likely neutral PKD Mutation Database) of PKD1 gene although she was similar to patients with ARPKD with age of onset, family information and radiologic findings. This mutation or polymorphism of PKD 1 gene may affect clinical findings which is similar to ARPKD.

P - 100 THE PREVALENCE OF CONSTIPATION, ENURESIS AND VOIDING DYSFUNCTION SYMPTOMS IN CHILDREN WITH UNCOMPLICATED RECURRENT URINARY TRACT INFECTION

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Introduction: Urinary tract infections (UTI) are a common clinical problem in the childhood. UTI may lead to long-term consequences, including renal scarring and kidney failure. The aim of this study was to investigate the prevalenve of constipation, enuresis and voiding dysfunction symptoms in children with uncomplicated recurrent urinary tract infections (RUTI).
Material and methods: This study included children, ages 5 to 18 years, with uncomplicated RUTIs. Abdominal ultrasonography and dimercapto-succinic acid scintigraphy were performed for all of the children. The children who had congenital anomalies of the urinary tract were excluded. Detailed voiding and bowel habits of the children were questioned.
Results: A hundred eighty-eight patients were included in this study. The majority of patients were female (n=162, 86.2%). The mean age of the patients was 7.86 ± 2.66 years. Constipation and postponed voidingwere the most prevalent findings [33% (n=62), 33.5% (n=63), respectively]. Prevalence of nocturnal enuresis was 25% (n= 47) and prevalence of voiding dysfunction symptoms (pollakuria, urgency, dripping, holding maneuver) were 19.7% (n=37). Of the 188 patients, 20.7% (n=39) were obese. Voiding dysfunction symptoms were higher in obese children compared with non-obese children [46.1% (n=18), 12.7% (n=19), $p<0.05$]. Prevalence of nocturnal enuresis was higher in patients with constipation compared with patients without constipation [38.7% (n=24), 18.2% (n=23), $p<0.05$]. In addition, it was found that prevalence of nocturnal enüresis was more among obese children according to the non-obese children [43.5% (n=17), 20.1% (n=30), $p<0.05$].
Conclusions: This study supports that voiding and bowel habits should be questioned in children with RUTI. As well as, lower urinary tract dysfunction and nocturnal enüresis should be investigated during the evaluation of obese children with RUTI

P - 101 PELVIS SYNDROME - A CASE-REPORT

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Introduction: PELVIS syndrome is an association between large perineal hemangiomas and congenital anomalies, including anorectal, urinary tract, spine, and external genitalia malformations.
Material and methods: We present male infant with PELVIS syndrome.
Results: The child was followed since early intrauterine age by ultrasound (US) due to left kidney cysts. After birth US showed multicystic dysplastic left kidney with compensatory hypertrophy of the right kidney. DMSA scan confirmed function only of the right kidney. Voiding cystography did not show vesicoureteral reflux and morphology of the bladder and urethra was normal. Clinical examination at birth found large segmental hemangiomas in perineal, gluteal region and left leg. PELVIS syndrome was suspected and child underwent further diagnostic tests which showed: (1) undescended left testis with hypoplastic left scrotum and micropenis, (2) right-sided angulation of the sacrum; spina bifida from S1 to S5; osseous defect covered with fibrous and subcutaneous fat tissue; lipoma of the filum terminale, no signs of tethered cord. MRI finding suggest closed spinal disraphism with lipoma of the filum terminale. During the three-year follow-up there was a spontaneous regression of left kidney cysts; the growth and function of the right kidney were normal and also sphincter contol. There was also significant spontaneous regression of hemangioma. Follow up MRI of lumbosacral spine showed no progression of lipoma.
Conclusions: Large perineal hemangiomas should be recognized as indicators of underlying congenital anomalies including urogenital, anorectal and spine. So additional diagnostic evaluation including ultrasound of abdomen and kidney and spine imaging is necessary.

P - 102 ACUTE FOCAL NEPHRITIS - A RADIOLOGIC FINDING

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Introduction: Acute focal bacterial nephritis is a seldom diagnosed local interstitial infection of the kidney. Presumably it is a preliminary formation of abscesses. The main clinical symptoms are dysuria and side pain. In young children, these symptoms are infrequently and diagnosis can be missed. There is no good evidence, but consistently an antibiotic therapy for 3 weeks is recommended.
Material and methods: We present 7 patients (6 girls and 1 boy) who suffered from acute focal nephritis in the years 2013 and 2014. Data were collected retrospectively.
Results: The median age was 5.12 years (1.54–13.23) and all patients had fever and were in severe distress. Only 2 patients had side pain and 1 patient dysuria. Initial CrP was raised to 131 mg/L on average. Only 2 patients had slight leucocyturia and bacteriuria was found in 6/7 children. In 3 patients ultrasound shared suspicious findings for acute focal nephritis at time of admission. In 4 patients the diagnosis was confirmed by MRI. Altogether, the disease was diagnosed within 5 days after admission, as initial ultrasound was not always conclusive. The average hospitalization amounted to 15 days. The patients received antimicrobial treatment intravenously for 14 days, followed by oral treatment for 7 days. Renal scarring, described by ultrasound, occurred in 2/7 patients after 1 and 3 months, respectively.
Conclusions: In the case of fever of unknown origin and progressive deterioration of health condition acute focal bacterial nephritis should be suspected in spite of normal urinalysis results. Eventually sequential ultrasound or extended radiographic procedures are necessary as typical

symptoms and ultrasound-based diagnostic imaging can be absent in children initially.

P - 103 ACQUIRED NEUROGENIC BLADDER IN A CHILD WITH SPINAL EPIDURAL HEMATOMA

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Introduction: Neurogenic bladder in children is a rare condition and is usually due to birth defects of the spinal cord, or to functional disorders of the bladder (e.g. Hinman syndrome). We hereby describe a case of a child with secondary neurogenic bladder as a result of spinal epidural hematoma (SEH).
Material and methods: A 5-year-old boy that was treated for acute lymphoblastic leukemia and thrombocytopenia, exhibited acute urinary retention along with neurological symptoms located in both lower limbs (paraparesis and decreased sensation) after undergoing therapeutic lumbar puncture. MR scanning revealed the presence of an extensive hematoma in the thoracolumbar region of the spinal column, between T7 and L5 levels, which occupied the entire spinal canal, and compressed the spinal cord and its sac.
The patient was immediately administered platelet and fresh frozen plasma transfusions, the bladder was catheterized, and respective physiotherapy was initiated. Urodynamic studies have shown a neurogenic bladder function.
Results: The boy displayed quick improvement with regards to the neurologic syndrome, and did not require surgical decompression. For the first 45 days the bladder was set in an indwelling urinary catheter, followed by four intermittent self-catheterizations per day for the next month, and concurrent administration of oxybutynin. Now he is still performing self-catheterizations one or two times per day. Six months after the incident the MR imaging showed complete resorption of the hematoma.
Conclusions: In conclusion, prophylactic platelet transfusion prior to lumbar punctures in thrombocytopenic patients is suggested, in order to avoid SEHs and their complications.

P - 104 POSTNATAL EVALUATION AND FOLLOW-UP OF THE CHILDREN DIAGNOSED WITH ANTENATAL HYDRONEPHROSIS

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Introduction: Antenatal hydronephrosis (ANH) is the most commonly detected genitourinary system abnormality with ultrasonography (USG) in the antenatal period. Although it is the most frequent genitourinary system abnormality; there is no consensus about evaluation and follow-ups of these patients in postnatal period. In this study, postnatal follow-ups of the cases diagnosed in antenatal period were retrospectively evaluated.
Material and methods: A total of 364 patients (224 boy, 120 girl) diagnosed with antenatal hydronephrosis during the period between January 2000 and December 2012 were evaluated.
Results: In the first postnatal USG evaluation of the a total of 482 kidney of 364 enrolled patients diagnosed with various degrees of unilateral or bilateral hydronephrosis in prenatal USG evaluation; it was shown that 185, 119 and 86 kidneys had mild, moderate and severe hydronephrosis, respectively; however, remaining 92 kidneys did not have hydronephrosis according to their renal pelvis antero-posterior (AP) diameters. During the follow-ups of kidneys considered normal in the first postnatal USG, kidney abnormality was detected in %29.4 of them. It was found that risk of obstruction increases with increasing degrees of hydronephrosis in postnatal USG. In the end of the study, risk of experiencing UTI among patients with antenatal hydronephrosis was found to be statistically significantly high ($p<0.05$). It was found that antenatal hydronephrosis can cause growth and development retardation and malnutrition due to recurrent UTIs on the basis of scarred renal tissue.
Conclusions: In conclusion, it was found that persistence of ANH can affect growth, development and feeding; persistant hydronephrosis is significantly related with UTIs and the comorbid presence of these three conditions negatively affect feeding, growth and development.

P - 105 COMPLICATED URINARY TRACT INFECTION IN A TWO MONTHS OLD INFANT: WHICH DRUG TO CHOOSE?

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Introduction: Treatment of complicated urinary tract infections in children is challenging. As antimicrobial agents have potential adverse effects, it is sometimes necessary to choose the least worst.
Material and methods: We report the case of a two months old infant who was hospitalized for suspected urosepsis. She was diagnosed antenatally with hydronephrosis due to bilateral vesico-uretral reflux grade 5. For this reason she used long term low dose prophylactic antibiotics which were started shorly after birth. In the current hospitalization she was empirically treated with ampicillin and a third generation cephalosporin without significant clinical improvement. Pseudomonas aeruginosa grew in the blood culture, after which we had to switch the antibiotic therapy.
Results: Aminoglycosids were considered but we feared the nephrotoxic and ototoxic effects. Besides, the vascular access possibilities had become extremely scarce during hospitalization. We therefore decided to continue treatment with ciprofloxacin, a fluoroquinolon, orally. The patient became afebrile after the second dose of ciprofloxacin. She was discharged after 10 days of treatment. No significant adverse effect was observed.
Conclusions: Athough contraindicated in children due to potential cartillage tissue damage, fluoroquinolones have pharmacokinetic and pharmacodynamic characteristics which might be favourable in the treatment of complicated urinary tract infections in children. We will present this case with background information regarding considerations in the antibiotic policy of complicated urinary tract infections.

P - 106 SHORT-TERM POSTNATAL FOLLOW UP OF CHILDREN WITH MILD AND MODERATE ISOLATED ANTENATAL HYDRONEPHROSIS

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Introduction: Antenatal hydronephrosis (AH) is one of the most common anomalies identified on antenatal ultrasound (US). The postnatal management of mild-moderate AH remains controversial. This study was aimed at evaluating the clinical outcome of newborns having mild and moderate isolated AH (MMIAH).
Material and methods: The newborns with MMIAH were included in this study. The inclusion criteria were: 1) Persistent mild-moderate

hydronephrosis on the first US done between seven days and two weeks of age. 2) No other US findings such as ureteral dilatation, duplication anomalies or bladder abnormalities. Hydronephrosis was classified as mild (5-9.9 mm), moderate (10-14.9 mm) by anterior pelvic diameters (APD). Newborns were followed up to 12 months.

Results: Of the 152 patients who were identified, 103 (67,8%) were males. The first US revealed mild hydronephrosis in 62 (40,8%), moderate hydronephrosis in 90 (59,2%). UTI occurred in 21 (13.8%) of the infant.Incidence of UTI was lower in patients with mild hydronephrosis [6.4% (n=4), 18.8% (n=17) respectively, $p<0.05$]. None of the patients with UTI showed renal scarring. During the first year of life, the frequency of spontaneous resolution in patients with mild AHN was significantly higher than patients with moderate HN [95.1% (n=59), 55.5%, (n=50) respectively, $p<0.05$].

Conclusions: This results suggest that risk of UTI increases with increasing grades of HN. Mild hydronephrosis is often a self-limited condition. The degree of hydronephrosis can be used for making decision about further diagnostic imaging and treatment.

P - 107 ASSESSMENT OF PROGNOSTIC FACTORS IN CHILDREN RTA TYPE IV OVERWHELMED BY BILATERAL OBSTRUCTIVE UROPATHY

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Introduction: The aim of this study is to assess of prognostic factors in children RTA type IV overwhelmed by bilateral obstructive uropathy**.**

Material and methods: In this study, we recruited and observed 48 boy patients affected with both bilateral obstructive uropathy at urinary bladder outlet and RTA type IV for two years. In this period, we registered patients' demographic data and also, children growth, sonographic data, renal function and serum electrolytes underwent serial assessment and in case of clinical indication, the patients were treated with drugs like citrate sodium and Kay oxalate. Note-worthy patients death resulted in exclusion from study.

Results: Frequent urinary tract infection ($p=0.0011$), infants and children with abnormal <20 weeks gestational sonography results like bilateral hydronephrosis ($p=0.00001$), birth weight below 2500 gr (LBW) ($p=0.0014$), preterm delivery ($p=0.001$), mothers age at birth below 20 years ($p=0.0018$), pregnancy more than 2 times ($p=0.004$), admission due to respiratory problems during infancy period ($p=0.003$) and gestational diabetes ($P=0.001$) had significantly associated with poor prognosis criteria**.**

Conclusions: Regarding the paper results, it seems logic to consider abortion in case of renal hydronephrosis and dysplasia in gestational age below 20 weeks. More-over, medical care during pregnancy for a term delivery with suitable weight (resulting in better maturation of lung parenchyma and precluding hypoxia related renal injuries) prevents.

P - 108 CAKUT IN NEWBORNS. HEREDITARY, CONGENITAL AND ACQUIRED FACTORS.

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Introduction: The purpose to carry out a structural analysis of CAKUT in fetuses according to autopsy and identify significant risk factors for renal disease.

Material and methods: In retrospect, 2103 was studied history and childrens autopsy protocol for 2001-2010. The analysis of medical records of 110 children with kidney disease-compare with 110 healthy children and a comparative evaluation of fetal abnormalities from women with the disease-139 fetuses, and without kidney disease-378 fetuses. Statistical analysis of the results.

Results: Of the total number of children autopsies CAKUT-2.66%.
In the structure of CAKUT in fetuses: dysplasia renal tissue-28.6%, ureterohydronephrosis-19.6%, polycystic-16.1%, agenesis-16.1%, glomerulonephritis-8.9 % and other diseases-10.7%. In the last 10 years can be traced to the decline in the number of CAKUT. Of the total number of children dying from CAKUT, stillbirths accounted for 44.6%, premature live births-33.9%, full-term live births-21.5%.
Histological examination of the placenta in 98% of cases were identified as inflammatory changes of the placenta and its membranes (villuzit, intervilluzit, chorioamnionitis). Revealed that fetuses of mothers with CAKUT significantly more frequently than from healthy mothers met CAKUT -6.5%+2.1% vs. 1.26 +0.73; $p<0,01$; gastrointestinal tract (GIT) - 17.3+1.94 vs. 1,9+0,70, $p<0,001$; asphyxia-30.9+2.38 versus 19,8+2,05, $p<0,001$; intrauterine infection (IUI) -27.3+2.29 versus 18,3+2,0, $p<0,01$ intrauterine growth retardation (IUGR) -5.8+1.9+1.20 vs. 0.70, $p<0,01$.

Conclusions: In the structure of diagnosed antenatal congenital malformations of the fetus, the CAKUT was 23.4%, and firmly occupy the second place after the pathology of the nervous system.

P - 109 THE ADAPTIVE REACTIONS AND PHYSICO-CHEMICAL PROPERTIES OF URINE IN CHILDREN WITH PYELONEPHRITIS

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Introduction: Now in the development of urinary tract infections in children recognized the role of not only the factors of pathogens, but also the macroorganism defense reactions. The purpose of research wa to study the adaptive response of the organism in the dynamics of complex treatment of pyelonephritis in children for predicting the risk of possible relapse.

Material and methods: The article presents the results of a study adaptive reactions in 236 children with pyelonephritis. Chemiluminescence serum, whole blood and urine tests, evaluation of adaptive responses by leukogram andurine crystallography was used in this study.

Results: The results obtained demonstrate various versions of violations of the childs adaptation to the active phase of microbial inflammation in the urinary system depending on the degree of disease activity. Restructuring adaptive response depending on disease activity decrease was observed. It was found long-term preservation of violations of adaptation in chronic pyelonephritis. The results led us to conclusion that physico-chemical properties of urine characterizes the state of the local adaptive-compensatory mechanisms of the urinary system. The prognostic significance of determining the adaptive capacity of the organism, as well as the physico-chemical properties of the urine was shown.

Conclusions: It was found that a comprehensive evaluation of adaptive responses to general and local levels can predict the nature of the current of pyelonephritis and conduct timely correction of these states for the prevention of a possible relapse.

P - 110 NEW POTTEL ESTIMATING GLOMERULAR FILTRATION RATE EQUATION IN CHILDREN AND ADOLESCENTS

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Introduction: The assessment of glomerular filtration rate (GFR) is an important tool for monitoring renal function, especially during the management of CKD. Inadequate GFR estimations (eGFR) may result in suboptimal medical care. Pottel et al established a height-independent equation. The objective of the present study was to compare the performance of Pottel-equations with other equations to estimation GFR in a cohort of children and adolescents using standardization of plasma creatinine and cystatin C.
Material and methods: Two hundred fifty-nine patients (695 measurements) with a median age of 11.4 years (7.9 - 13.9) were referred for GFR measurement by inulin clearance (mGFR) with concomitant determination of plasma creatinine and cystatin C (standardized method) and blood urea nitrogen (BUN). The patients ages ranged from 2 to 18 years and the measured GFRs from 13 to 201 mL/min/1.73 m^2. Equation performance was assessed using relative bias (median of ratio estimated GFR - measured GFR), precision (limits agrements - LoAs), and accuracy (percentage of estimates 30% higher or lower than the measured GFR - P30).
Results:

Serial measurements (via linear mixed models) (n = 693)

	Relative Bias (%)	Stdev	LOAs	P10	P30
Pottel-Age	-8.5	26.7	[-60.9;43.9]	39.2 [35.1; 43.4]	84.3 [81.0; 87.6]
Pottel-height	-0.8	21.8	[-43.4;41.8]	40.7 [36.7; 44.6]	89.4 [86.8; 92.0]
Schwartz	-10.0	23.7	[-56.5;36.6]	39.3 [35.2; 43.5]	83.1 [79.5; 86.7]
Schwartz-Lyon	-0.7	20.8	[-41.5;40.1]	41.3 [37.2; 45.4]	91.4 [89.0; 93.9]
Filler	-1.1	21.7	[-43.6;41.4]	37.4 [33.6; 41.2]	86.2 [83.6; 88.9]
CkiD	6.4	17.7	[-28.2;41.0]	39.6 [35.5; 43.6]	93.2 [91.3; 95.1]
Pottel-height new	0.7	17.9	[-34.4;35.8]	47.1 [43.1; 51.1]	93.1 [91.1; 95.2]

Conclusions: Pottel-height and Schwartz-Lyon are at least equivalent or even slightly better than Filler. Schwartz is the worst equation of all, together with Pottel-Age for adolescents. But, when PCr is used, it is best to combine it with height, especially for adolescents; this is already something we have seen in previous studies. Combining Scr/Q with Cystatin C seems to be promising in the new Pottel-height equation, although external validation is required.

P - 111 ESTIMATED GLOMERULAR FILTRATION RATE EQUATION IN CHILDREN UP TO ELDERLY IS ACTUAL

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Introduction: Estimating kidney glomerular filtration rate (GFR) is of utmost importance in many clinical conditions. However, very few studies have evaluated the performance of GFR estimating equations over all ages and degrees of kidney impairment.
Material and methods: GFR was measured by urinary inulin or iohexol clearance in 11,707 patients and estimated jointly with several equations to adults and children. The patients ages ranged from 2 to 90 years and the measured GFRs from 3 to 239 mL/min/1.73 m^2. Equation performance was assessed using difference of means of ratio estimated GFR - measured GFR), precision (interquartile range of the ratio), and accuracy (percentage of estimates 10 and 30% higher or lower than the measured GFR).
Results:

Mean bias and accuracies according to CKD groups and equations
GFR=71.88.0 ± 31.7 ml/min/1.73m²) N=11,707

Equation		CKD-EPI	QHA	Schwartz Lyon	Schwartz 2009	QH
eGFR ml/min/1.73m²		98.5 ± 30.8	98.0 ± 31.5	68.5 ± 28.5	73.0 ± 30.8	78.0 ± 32.5
Bias IC 95%		11.5[-3.0;46.0]	11.5 [-4.0;47.0]	-3.0 [-38.0; 31.50]	1.0 [-36.5;38.5]	-6 [-35.0;47.0]
CCC IC 95%		0.83 [0.81;0.85]	0.83 [0.81 - 0.85]	0.84 [0.83 - 0.84]	0.84 [0.82 - 0.86]	0.84[0.82;0.86]
Accuracy	10 %	33.5 [32.5 ;34.5]	33.5 [32.5 ;34.0]	34.0 [33.0;34.5]	34.5[33.5;35.5]	33.0 [32.5;34.0]
IC 95%	30 %	72.0 [71.0;73.0]	72.0 [71.5;73.0]	81.5 [81.0;82.5]	79.0 [78.0;80.0]	74.0[73.0;74.5]

Conclusions: Evaluation of the agreement between these formulas and mGFR (e.g.concordancecorrelation coefficient, Bland–Altman plots, bias, and accuracy) showed that there was a good correlation between mGFR and both pediatric formulas in all age groups, whereas the adult formulas substantially overestimated mGFR. In conclusion, we recommend the use of pediatric equations to estimate GFR from childhood to early adulthood.

P - 112 LONG-TERM OUTCOME OF THE REMNANT KIDNEY IN PATIENTS AFTER NEPHRECTOMY FOR WILMS TUMOR

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Introduction: Wilms tumor (WT) is the second most common abdominal tumor in childhood, with survival rates of 80-95%. The present study

sought to evaluate the function and growth rate of the remnant kidney in children after nephrectomy for unilateral WT and to identify risk factors for renal injury.
Material and methods: Data were retrospectively collected on all patients treated by radical nephrectomy for unilateral "WT" in 1995-2014 at Schneider Children's Medical Center of Israel. Glomerular filtration rate (GFR) was calculated according to the Schwartz formula. Hypertension was defined as systolic blood pressure above the 95th percentile for age, sex, and height. Length of the remnant kidney was expressed in standard deviations (SD) from average for age and size.
Results: Sixty-four children met the inclusion criteria. Median age at presentation was 3.5 years (0.5-14) and the mean follow up period was 7 years. At presentation, mean GFR was 100ml/min/1.73m^2; 22% of patients had a GFR less than 80ml/min/1.73m^2 and 74% had hypertension. At the last visit mean GFR was 103ml/min/1.73m^2; 18% of children had a GFR less than 80ml/min/1.73m^2, and 25% had hypertension. Albuminuria was found in 22%. There was no correlation of chemotherapy type with decreased GFR or increased blood pressure. Radiotherapy was a significant risk factor for protein secretion (p=0.02). Renal length increased significantly, from 0.9SD at presentation to 2.9SD at the last visit (R<0.01). The maximal growth rate was observed during the first post-nephrectomy year.
Conclusions: Although the overall prognosis of children after nephrectomy for WT is guarded, the present cohort had a 20% rate of impaired renal function in the long term. Radiotherapy increased the risk of proteinuria. Close follow-up of this patient population is necessary to monitor the effect of hyperfiltration on the remnant kidney and determine the need for treatment.

P - 113 VITAMIN D STATUS IN CHILDREN WITH CHRONIC KIDNEY DISEASE STAGE 1-5 - INFLUENCE OF SUBSTITUTION, SEASON AND UNDERLYING DISEASE

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Introduction: National and international lstudies show a widespread of vitamin D (25 OHD)deficiency in childhood and adolescence. Vitamin D deficiency is also detected in many disease entities. Because of the role of the kidney in vitamin D metabolism children with chronic kidney disease (CKD) are considered as high-risk group. We investigated whether a particular subgroup of our patients is particularly vulnerable and whether our substitution is appropriate.
Material and methods: We analyzed a cohort of 468 patients who presented in the departments of pediatric nephrology of the university children`s hospitals of Cologne and Bonn with a diagnosis of CKD stage 1-5. We measured blood levels of 25 OHD, parathyroid hormone (PTH), calcium and phosphate and collected data on Vitamin D substitution, underlying disease, age and concomitant medication.
Results: Mean age of patients was 113±61.3 months. 59 percent of subjects were male, 41 percent were female. The median 25 OHD value of all evaluated patients was 21.5 (2.9 to 112) ug/l and thus in suboptimal range (21-29 ug/l) according to German guidelines. The lowest values were found in children with CKD stage 1 (18.4 (2.9-80.4)ug/l) whose eGFR was still within the normal range (> 90 ml/min). The seasonal effect with lower values in winter was confirmed in our analysis.
Conclusions: Low 25 OHD values are already found in early-stages of CKD. In children suffering from advanced chronic renal impairment vitaminD replacement therapy is effective. A seasonal adjustment of therapy, however, should be considered. The supply of vitamin D should be optimized especially in early CKD stages and possibly in certain diseases.

P - 114 IS THERE AN INCREASED RISK OF LINEZOLID-INDUCED THROMBOCYTOPENIA IN PATIENTS WITH RENAL DYSFUNCTION? REPORT OF TWO CASES

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Introduction: Linezolid (LZD) is an oxazolidinone antibiotic, active against gram positive bacteria that are resistant to other antibiotics, including glycopeptides. Thrombocytopenia is a common adverse effect of LZD. Although it is generally considered that the dose adjustment is not required for LZD in patients with renal failure, recent studies have reported that the incidence of LZD-induced thrombocytopenia was higher in patients with renal failure than in patients with normal renal function.
Material and methods: Here we report two children who were under hemodialysis treatment developed thrombocytopenia under LZD therapy.
Results: First patient is a 17 years old male attended to our clinics with the complaint of high fever and respiratory difficulty and diagnosed as pneumonia. Ceftriaxone was started as an empirical therapy. Bacause of blood cultures were positive for staphylococcus aureus (SA) sensitive only to LZD and LZD was started. At 17th day of LZD therapy, platelet counts decreased from 363000/mm^3 to 85000/mm^3. Second patient is a 16 years old female attended to our clinics with the complaint of cough and high fever and diagnosed also as pneumonia. At the 5th day of empirical antibiotic therapy, because of her clinical condition worsened, meropenem and vancomycin were started. At the 1st week of this therapy, radilogical studies showed further worsening of parenchymal consolidation. Because suspicion of SA resistant to vancomycin, LZD was started. At 16th day of LZD therapy, platelet count decreased from 225000/mm3 to 75000/mm3. After LZD therapy was discontinued, the platelet counts recovered to normal levels in both patients.
Conclusions: Although LZD was safe and tolerated well in pediatric patients, Clinicians should be aware of LZD induced-thrombocytopenia in patients with renal insufficiency, because of increased risk of LZD induced thrombocytopenia in these patients. Monitorization of the platelet count is recommended in patients with renal dysfunction who is under LZD therapy as in our cases.

P - 115 EFFECTS OF CRYOPRECIPITATE AND DESMOPRESSIN IN ACHIEVING HAEMOSTASIS AFTER RENAL BIOPSY IN URAEMIC CHILDREN

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Introduction: Renal biopsy, although a very useful diagnostic tool in renal failure, carries a very high risk of haemorrhage. This study aims to describe the experience of our institute of using cryoprecipitate and desmopressin to control bleeding in these children.
Material and methods: Clinical case notes of children whose estimated glomerular filtration rates (eGFR) were <30ml/min/1.73m^2 and who underwent renal biopsy were retrospectively reviewed. All the children had haemoglobin >10mg/dl, haematocrit >30% and normal platelet count and coagulation profile. None had received platelet function altering drugs.
Results: Nine children with a median age of 11 years (range 5 to 12 years) had received either intranasal or intravenous desmopressin before the biopsy. Three of them with severe renal impairment were dialysis dependent and underwent heparin free haemodialysis within 24 hours prior to the procedure. All 3 developed gross haematuria, 15 minutes to 6 hours later with a reduction of haemoglobin by 2.1 to 4mg/dl; 2 of them also had perinephric bleeding. However within 4 to 6 hours of cryoprecipitate infusion, there was marked reduction of haematuria in all 3, with stabilization of haemoglobin levels. Six children with eGFR between 15 to

30ml/min/1.73m^2 had no bleeding manifestations. Post dialysis blood urea levels of those children who bled were comparable with those who did not. The only notable differences in the former group were dialysis dependency and oliguria.

Conclusions: Previous studies suggested favourable outcomes following desmopressin therapy and variable responses to cryoprecipitate. However in this study, all the children with severe renal dysfunction, who did not respond to initial desmopressin therapy, achieved very good haemostasis following a single dose of cryoprecipitate. Pathophysiology of uraemic bleeding is multifaceted; hence these patients need individual management strategies.

P - 116 PAEDIATRIC RENAL DIETETICS IN BELGIUM: THE SEARCH FOR PRACTICAL USE OF NUTRITIONAL GUIDELINES

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Introduction: The paediatric renal Dietitians in Belgium organized a working group in 2014. In Belgium, there are no country specific nutritional guidelines for the treatment of children with kidney disease. The aim of the working group is to review the existing guidelines and translate them into practical advice. The implementation of guidelines is often a big challenge. Children who experience a sudden loss in their renal function often need to make changes to their diet and / or feeding habits and this adaption can be difficult. If the guidelines are to be achieved, many changes need to be implemented, taking into account the possible risk of malnutrition, low calorie intake and refusal of the diet. There is a need for paediatric renal specific products.

Material and methods: We are reviewing literature regarding the nutritional guidelines for paediatric renal disease, pathology of the kidneys and product information. This will enable us to determine if these guidelines are achievable and practical to implement and how best to achieve this. We will then translate every diet prescription into practical advice. The information and practical advice will be collated into a "Pocket Guide".

Results: The first part of our pocket guide which details a summary of various paediatric renal conditions and the specific diet prescriptions has been completed.

Conclusions: The second part, translation of theory into practice will be completed next. After these recommendations, we will check if these guidelines are achievable with patient studies.

P - 117 END STAGE RENAL DISEASE IN A PEDIATRIC PATIENT WITH FABRYS DISEASE

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Introduction: Fabrys disease (FD) is a rare X-linked, lysosomal storage disease leading to accumulation of globotriaoslyceramide (Gb3) and related glycosphingolipids in tissues and organs throughout the body. End stage renal disease (ESRD) in FD is reported to occur in the 3rd decade of life.

Results: We report a male patient aged 15 years, 2nd child of consanguineous parents who started at the age of 10 years to complain of burning pricking pain of both hands and feet of insidious onset and progressive course reaching the whole extremities and not responding to analgesics. The patient developed proteinuria with chronic anemia and progressed to renal impairment. The patient developed hypohidrosis and angiokeratomas together with hypertension. Renal biopsy by electron microscopy showed the characteristic lamellated lipid inclusions (myeloid bodies in podocytes). Alpha-galagtosidase enzyme activity was below the reference range. Molecular genetic analysis for the patient and his parents is pending.

The patient started regular hemodialysis. Enzyme replacement therapy was not given sue to its non-availability. In view of absence of cadaveric renal transplantation in our country, living-related donation is questionable in this case as the mother reported similar burning pain of both hands and feet during adolescence. There are conflicting reports regarding the outcomes of patients with FD after renal transplantation as well as the use of enzyme replacement post-transplantation.

Conclusions: Renal affection could be an early presentation for FD. Screening of family members of the affected patient is important. Diagnosis needs a high index of suspicion for early implementation of therapy and better outcome.

P - 118 CARDIAC EXPRESSION LEVELS OF FIBROBLAST GROWTH FACTOR 23 CORRELATE WITH LEFT VENTRICULAR HYPERTROPHY IN KLOTHO-HYPOMORPHIC MICE

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Introduction: The phosphaturic hormonefibroblast growth factor 23 (FGF23) is expressed and secreted by osteocytes, and recent studies suggest that high circulating levels of FGF23 cause left ventricular hypertrophy (LVH) in patients with chronic kidney disease (CKD). FGF23 signals via FGF receptors (FGFR) in the presence of its cofactor Klotho, but previous studies reveal an Klotho independent pathway of FGF23 in cardiomyocytes to promote cardiac remodeling and LVH. In contrast, Klotho seems to be cardioprotective.

The aim of this study was to investigate the impact of FGF23 on the development of cardiac remodeling and LVH in Klotho-hypomorphic (*kl*/*kl*) mice. The *kl*/*kl* mouse manifests symptoms of premature aging, hyperphosphatemia, and displays high circulating FGF23 levels. Furthermore, we examine the relationship between aKlotho and FGF23 in the activation of FGFRs mediating cardiac remodeling resulting in LVH.

Material and methods: Hearts of 8 week-old wild type (WT) and *kl*/*kl* mice were isolated. The left ventricle was stained with wheat germ agglutinin (WGA) to quantify cardiomyocyte cross-sectional area. Furthermore, cardiac tissue was flashed frozen, homogenized and analyzed by quantitative real-time PCR and by immunoblotting to determine FGF23-mediated activation of calcineurin-NFAT pathway mediating LVH.

Results: Relative heart weight and cardiomyocyte cross-sectional area were markedly increased in *kl*/*kl* mice compared with WT indicating LVH. mRNA and protein levels of cardiac Fgf23 in myocardial tissue were significantly induced in*kl*/*kl* mice. Interestingly, expression of *Fgfr1*, known to be essential for FGF23-Klotho signaling, was unaffected in *kl*/*kl* mice, but *Fgfr4* levels were significantly induced. The calcineurin-NFAT

protein complex inducing genes involved in pathological cardiac remodeling and the development of LVH was activated in *kl/kl* mice.
Conclusions: Our data suggest that cardiac FGF23 might contribute to myocardial remodeling and LVH in Klotho-hypomorphic mice in a paracrine manner indicating a direct impact of FGF23 signaling on cardiovascular disease beyond CKD.

P - 119 VITAMIN D TREATMENT AMELIORATES FIBROBLAST GROWTH FACTOR 23 DRIVEN LEFT VENTRICULAR HYPERTROPHY IN EXPERIMENTAL UREMIA

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Introduction: Vitamin D deficiency and excess of circulating fibroblast growth factor 23 (FGF23) are significant contributors to cardiovascular (CV) morbidity and mortality in patients with chronic kidney disease (CKD). *In vivo*, vitamin D metabolites were shown to downregulate genes involved in the development of left ventricular hypertrophy (LVH). However, vitamin D is a known stimulator of FGF23 synthesis. Thus, vitamin D treatment may have paradoxical effects on the CV phenotype in CKD. Here, we investigated the effects of vitamin D treatment on FGF23 signaling cascade mediated LVH in experimental uremia.
Material and methods: 5/6 nephrectomized rats (Nx) were treated with various doses of vitamin D for 4 and 10 weeks and compared with controls. Heart tissue was determined for gene and protein expression of Fgf23, Fgf receptors (Fgfr) 1 and 4, calcineurin-NFAT, and markers for cardiac remodeling and hypertrophy. The cardiomyocyte cross-sectional area was quantified by immunofluorescence microscopy of wheat germ agglutinin stained myocardial tissue sections.
Results: LVH was increased in 5/6Nx animals compared with controls. Cardiac Fgf23 mRNA and protein levels, and expression of *Fgfr1* and *Fgfr4* were induced in uremic rats. The calcineurin-NFAT signaling pathway was activated in uremia demonstrated by enhanced calcineurin protein accompanied by a strong reduction of phosphorylated NFAT. Genes characteristic for pathological cardiac remodeling were significantly increased in myocardial tissue of 5/6Nx rats. In general, vitamin D treatment of 5/6Nx rats resulted in reduced cardiomyocyte cross-sectional area. Although, cardiac Fgf23 gene and protein expression, and *Fgfr4* mRNA levels were further stimulated by vitamin D, vitamin D treated 5/6Nx rats showed reduced activation of NFAT ameliorating cardiac remodeling processes and LVH.
Conclusions: Cardiac FGF23 expression is enhanced and associated with the development of LVH in experimental uremia. Vitamin D treatment enhances NFAT phosphorylation and thereby blocks pathological remodeling process induced by FGF23.

P - 120 IMPAIRED LONGITUDINAL DEFORMATION MEASURED BY SPECKLE TRACKING ECHOCARDIOGRAPHY IN CHILDREN WITH END-STAGE RENAL DISEASE

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Introduction: End-stage renal disease (ESRD) can cause left ventricular (LV) dysfunction. In adults this is associated with poor prognosis. In children with ESRD LV function generally seems better preserved but limited data are available on the effect of renal disease on early myocardial changes. The aim of this study was to evaluate LV function in pediatric patients with ESRD and trying to identify changes in myocardial mechanics prior to changes in ejection fraction.
Material and methods: 17 Children on dialysis, 17 transplant recipients and 33 age matched healthy controls, were included. Echocardiographic data, including M-mode, Tissue Doppler and Speckle Tracking Echocardiography (STE) measurements, were acquired in the Academic Medical Center in Amsterdam and University Medical Center Utrecht. Longitudinal strain (LS), Radial strain (RS) and Circumferential strain (CS) measurements were performed from the apical four-chamber and the short axis view, respectively. Statistical analysis were performed with SPSS 22 .0 (IBM Corp., Armonk, NY, USA).
Results: No differences were found in systolic function measured by M-mode and TDI (e.g. shortening fraction and LV S') between ESRD patients and healthy children. Using STE, the dialysis and transplant patients had an impaired mean LS compared to controls (mean difference [95%CI] 1.5 [0.8-2.2] and 2.6 [1.1-4.1], respectively, both $p<0.001$). There were no differences found for radial and circumferential strain. Impaired LS was diagnosed in 27 (79%) children with ESRD.
Conclusions: Impaired longitudinal deformation was diagnosed by STE in more than three quarters of children with ESRD who had preserved systolic function measured by M-Mode echocardiography and TDI. Prospective follow-up studies are necessary to evaluate the predictive value of decreased longitudinal myocardial function with ESRD.

P - 121 CAN THE HEIGHT-INDEPENDENT GFR PREDICTING EQUATION BE USED AS AN AUTOMATIC REPORTING OF EGFR IN CHILDREN?

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Introduction: Despite KDOQI recommendations, determination of plasma creatinine in children is rarely associated to an estimation of glomerular filtration rate (eGFR) due to the lack of height information in clinical laboratory databases. Pottel et al. established a height-independent equation, eGFR=107.3/(Pcr/Q) where Q is the median of Pcr (Pottel-Belgium). The aims were to 1) determine a local height-independent equation (Pottel-Lyon) 2) evaluate the performance of these equations compared to the Schwartz-2009 3) evaluate the height-independent equations in laboratory routine.

Material and methods: Therefore 1) all first pediatric Pcr determination (from 12/2009 to 06/2011) were collected and median of Pcr was determined for each one-year-age-interval (Q-Lyon) 2) GFR was measured (mGFR, inulin or iohexol clearances) in 359 children (438 measures) and compared to eGFR 3) all first Pcr determination (from 01/2012 to 06/2013) were used to calculate eGFR with the Pottel-Lyon and the Pottel-Belgium equations. Pcr was determined by an IDMS-standardized enzymatic assay.
Results: In the population with a mGFR, the Pottel-Lyon showed the best performance (bias, P10 and P30). However the performance in identifying patients with a mGFR<75ml/min/1.73m^2 was similar for all the studied equations.
Conclusions: The performance of the height-independent and dependent equations to identify mild renal dysfunction is similar. The height-independent Pottel equation (original or locally-adapted) could be proposed as an automatic reporting of eGFR when Scr measurement is required in children and when height information is not available.

P - 122 EXAMINING THE EFFECTS OF VITAMIN D RECEPTOR ACTIVATORS (VDRAS) ON VASCULAR SMOOTH MUSCLE CELL (VSMC) CALCIFICATION USING INTACT VESSELS FROM CHILDREN WITH CKD

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Introduction: CKD patients are at high risk of vascular calcification due to abnormal mineral metabolism, and potentially their treatment with VDRAs, which is not fully understood. We compare physiological doses of different VDRAs (calcitriol and alfacalcidol) on VSMC calcification in intact vessel rings from children in predialysis CKD stage 4-5 and on dialysis.
Material and methods: Inferior epigastric arteries were harvested during routine renal transplant and vessel rings cultured in normal or raised P&Ca media with VDRAs. Ca load and ALP activity were quantified. Gene expression in VSMCs explanted from non-renal control and dialysis vessels, treated with calcitriol were compared. Data expressed as fold change to vehicle ±SE.
Results: Calcitriol increased calcium load in predialysis 3.20±0.89 and dialysis 6.12±1.5 vessels (n=10). Alfacalcidol had a similar but less marked effect on VSMC calcification: 2.86±0.45 in predialysis and dialysis vessels 3.89±0.71 (n=6). ALP activity in dialysis vessels was upregulated 2.05±0.2 (n=7) by calcitriol, but not by alfacalcidol 0.97±0.02 (n=3). In VSMCs dose dependent responses were observed with x10^{-7}M calcitriol eliciting the greatest up regulation in vitamin D dependent gene expression: the vitamin D receptor increased 1.4±0.1 in control and 2.5±0.5 in dialysis (n=3 each), vitamin D inactivating 24 hydroxylase enzyme was also increased more so in dialysis VSMCs compared to controls.
Conclusions: Alfacalcidol and to a greater extent calcitriol increased calcification particularly in dialysis vessels, where calcitriol also increased ALP activity. Dialysis VSMCs were more responsive than controls to calcitriol regulated gene expression and may have an exaggerated response to VDRAs.

P - 123 SERUM BIOMARKERS OF CARDIOVASCULAR STRESS IN CHILDREN WITH CHRONIC KIDNEY DISEASE: FINDINGS FROM THE CARDIOVASCULAR COMORBIDITY IN CHILDREN WITH CHRONIC KIDNEY DISEASE (4C) STUDY

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Introduction: Children with chronic kidney disease (CKD) are at high risk of developing early cardiovascular disease (CVD). The 4C Study investigates the diagnostic and prognostic usefulness of circulating biomarkers of cardiovascular dysfunction. Here, we report preliminary findings of four established and novel biomarkers of cardiovascular stress.
Material and methods: Serum levels of cTnT, BNP, ST2, and GDF15 were measured in 120 CKD stage 3-5 patients, of whom 110 had follow-up measurements while changing treatment modality (53 CKD->Dialysis, 42 CKD->Tx, 15 CKD->Dialysis->Tx) with a total of 205 observations. Cross-sectional and longitudinal analyses were performed to detect (i) the determinants of biomarker serum levels and (ii) the predictive value of biomarkers for cardiovascular endpoints including left ventricle mass index (LVMI), carotid intima media thickness (cIMT), and pulse wave velocity (PWV).
Results: Levels of all biomarkers except ST2 increased significantly with declining eGFR (GDF15 β=-0.58, p<0.0001; BNP β=-0.31, p=0.0009; cTnT β=-0.31, p=0.001; ST2 β=-0.003, p=0.48). GDF15, BNP and cTNT increased 7.5-, 1.8- and 1.3-fold after start of dialysis, and decreased markedly (by 42%, 79% and 27 %, respectively) following transplantation (all p<0.0001). BNP and cTnT were significantly associated with LVMI (β=0.28, p=0.003 and β=0.25, p=0.008) in CKD and with standardized PWV (β=0.41, p=0.003 and β=0.35, p=0.012) in patients on dialysis. In the transplantation group, BNP and GDF15 were significantly associated with LVMI (β=0.37, p = 0.01 and β=0.32, p=0.02).
Conclusions: GDF15, BNP and cTNT show significant associations with GFR and measures of cardiac morphology and arterial function, and change over time commensurate with changes in renal function. Ongoing further analysis will elucidate the specificity of the biomarkers in predicting subclinical cardiac and vascular dysfunction in children with CKD.

P - 124 THEEFFECT OF DIALYSIS INITIATION TIMING ON LEFT VENTRICULAR HYPERTROPHY AND INFLAMMATION IN PEDIATRIC PATIENTS

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Introduction: The association between glomerular filtration rate (eGFR) and outcome parameters weren't evaluated to date in children. We aimed to evaluate the impact of dialysis timing on left ventricular morphology and inflammation as outcome parameters in pediatric peritoneal dialysis (PD) and hemodialysis (HD) patients.
Material and methods: We retrospectively reviewed medical records of dialysis patients followed-up in nine pediatric nephrology centers in Turkey between 2008 and 2013. Besides demographic findings, data on dialysis modalities; biochemical parameters, as well as CRP and albumin levels and echocardiographic data (LVH/LVMI), and frequency and causes of hospitalizations were recorded.
Results: 245 dialysis patients aged 12.3+/-5.1 years (53% male) were enrolled in this study. 180 patients were undergoing PD and 65 on HD. Twenty-five PD patients had been transferred to HD for different reasons.Patients with obstructive uropathy comprised 38.4% of the study population. 153 patients received antihypertensive drugs. 19 patients were died during follow up period. The most frequent reason of death was congestive heart failure (n=7). The most frequent reason for hospitalization was peritonitis. As expectedly, patients with LVH had significantly higher LVMI compared to those without LVH (75±30g/$m^{2.7}$, n=81 patients vs 34±6g/$m^{2.7}$, n=56 patients) (p=0.000). There were 50 early starters (52% male, mean age 10.9 years) who were initiated on dialysis with a eGFR> 10 ml/min/1.73m^2 and 98 late starters (51% male, mean age 13.0 years) who were initiated on dialysis when eGFR≤ 7ml/min/1.73m^2. Early versus late dialysis did not make any effect on LVMI, LVH and hospitalization frequency (p>0.05). Serum albumin level was significantly higher (3.3±0.7 vs 3.1±0.7 g/dl, p<0.05) whereas CRP level was lower (1.5±2.7 vs 10.2±21.5 mg/dl, p<0.05) in early dialysis group compared with late one.
Conclusions: Our results show that early initiation of dialysis is protective against inflammation, but did not improve all clinical outcomes including hospitalization and LVH.

P - 125 MOLECULAR FINDINGS POTENTIALLY LINKED TO THE INCREASED HEIGHT OF GROWTH PLATE CHONDROCYTES INDUCED BY GROWTH HORMONE (GH) TREATMENT IN UREMIA.

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Introduction: The present study aimed to shed light on the mechanisms by which GH administration increases the height of the growth plate terminal chondrocytes, an effect associated with the GH-induced acceleration of longitudinal growth velocity, in an animal model of chronic renal failure.
Material and methods: Weaning female rats classified (day 0, n=9/group) in control diet (C), 0.5% adenine diet (CKD), 0.5% adenine diet + 3.3 mg/Kg/day of GH from days 14 to 21 (CKDGH); control diet pair fed with CKD (PF). On day 21 of the protocol, rats were sacrificed and the following was analyzed: body growth, serum urea nitrogen (SUN) and creatinine (Cr), femur osseous front advance (OFA), growth plate histomorphometry and expression of aquaporin 1 (AQP1), Na-K-Cl cotransporter (NKCC1), insulin like growth factor-1 (IGF-1) and IGF-1 receptor (IGF-1R) by inmunohistochemistry and western blot (WB).
Results: SUN and Cr were similarly elevated in CKD (70±6 and 0.6±0.1 mg/dl) and CKDGH (59±8 and 0.6±0.1 mg/dl) groups. GH treatment improved weight gain and OFA, an index of longitudinal growth rate, (293±16, 141±13, 257±18, and 251±10 μm/day in C, CKD, CKDGH and PF rats, respectively) and increased the height of the terminal chondrocytes (26.2±1.9, 21.7±2.3, 25.3±2.2, 23.9±1.3μm in C, CKD, CKDGH and PF groups, respectively). Immunohistochemical signal of AQP1, NKCC1, IGF-1 and IGF-1R was located in the hypertrophic zone of the 4 groups of animals. In the uremic rats (CKDGH group), GH treatment enhanced the expression of AQP1, IGF-1 and IGF-1R when analyzed by WB.
Conclusions: The results confirm that acceleration of growth velocity by GH administration in experimental CKD is associated with a greater enlargement of the growth plate's mature chondrocytes and suggest that this positive effect might be linked to an increased local expression of AQP1, IGF-1 and IGF-1R induced by GH.

P - 126 APELIN SERUM LEVEL IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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Introduction: The adipose tissue is the source of several biologically active substances called adipokines, apelin among them. Apelin plays the role in the regulation of cardiovascular and gastrointestinal system, and influences the immune functions, bone metabolism as well as fluid homeostasis. Apelin expressed locally may play a role in renal pathology through stimulation of glomerular endothelial cells proliferation.
Material and methods: Apelin serum concentration was measured in the group of 28 children and young adults (16 females and 12 males) at mean age 13.5±5.5 years, with CKD stage 5 (17 on peritoneal dialysis, 10 on hemodialysis, 1 on conservative treatment) and compared with results obtained in 20 healthy age-, sex- and body size-matched controls. Serum apelin was determined using the immunoenzymatic method.
Results: The mean serum level of apelin in the study group was 99.0±8,0 pg/ml, which was significantly higher than in controls (82.1±11.2 ng/ml; p<0.0001). The difference remained significant after adjustment for BMI and BSA. The results did not differ significantly in regard to sex and RRT method. The correlation analysis revealed positive correlation between apelin concentration and age (r=0.41; p<0.05), but apelin/BSA ratio correlated negatively with age (r=-0.69; p<0.0001). Apelin/BMI ratio correlated negatively with hemoglobin concentration (r=-0.53; p<0.01) and apelin/BSA ratio correlated positively with cholesterol and triglyceride levels (r=0.45; p<0.05 and r=0.70; p<0.0001, respectively). In controls the only significant (negative) dependence was found between apelin/BSA ratio and age (r=-0.87; p<0.0001).
Conclusions: Regarding the physiological role of apelin, its elevated level in CKD children may have protective role to bone tissue status. On the other hand; its higher concentration could be the result of progression of endothelial dysfunction/inflammation in CKD patients. However, the clinical utility and prognostic value of apelin measurements in CKD have to be established in longitudinal studies evaluating long-term outcome of children on renal replacement therapy.

P - 127 RENAL FALUIRE IN GIRL WITH CHRONIC ADIPSIC HYPOVOLEMIA

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Introduction: Deficit of thirst sensation can result in the life threatening profound volume contraction and renal failure. It is uncommon clinical condition in adult patients and very rare in children. The epidemiology, treatment approach and prognosis of patient with chronic adipsic hypovolemia and renal impairment remain unknown.

Material and methods: We review the clinical case of renal damage as result of chronic adipsic hypovolemia.
Results: Nine-year-old Caucasian girl was admitted to our Department because of unclear renal failure. At age 5 yo (after virus infection) she presented growth retardation, rapid-onset obesity, adipsia, oliguria, hypernatriemia 165 mmol/l, creatinemia 110 μmol/l. Admission laboratory examination revealed: hemoglobin 120 g/l, hemotocrit 49%, plasma sodium 169 mmol/l, plasma osmolarity 347 mOsm/kg, serum creatinine 115 μmol/l, eGFR 51 ml/min/1,73m^2, urea 9,3 mmol/l, urine osmolarity 557 mOsm/kg. Calculated water balance parameters demonstrated hypovolemia with preserved renal concentration ability: water deficit was 2,6 l, excretory fraction of sodium was 0,59%, osmotic clearance - 1,56 mOsm/min, clearance of osmotic free water was negative (-1,35ml/min). She had small hyperechoic kidneys. Evaluation of pituitary function revealed low serum level of thyroid stimulation hormone, low STH with positive response to growth hormone, high levels of prolactin and cortisol with positive dexamethasone suppression test. There were no any signs of sella/pituitary damage on MRI. Renal failure due to chronic adipsic hypovolemia as a result of hypothalamic dysfunction (ROHHAD syndrome?) was suggested. Forced drinking led to decreasing of serum creatinine (88 μmol/l) and sodium (149 mmol/l) levels in patient.
Conclusions: Chronic adipsic hypovolemia is a very rare cause of renal failure in pediatric patients. Some conditions (hypothalamic dysfunction of different genesis, long-term parenteral nutrition, changes in mental status of patients) can lead to the development of chronic intravascular volume contraction and renal impairment. The careful control of the water balance and its correction will avoid kidney damage in these patients.

P - 128 SKELETAL IMPAIRMENT IN PIERSON SYNDROME

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Introduction: Pierson syndrome is caused by a mutation of *LAMB2*, encoding for laminin beta2. Clinical phenotype is variable but usually associates congenital nephrotic syndrome (CNS) and ocular abnormalities.
Material and methods: We report on a 14-year old girl, suffering from Pierson Syndrome, who developed severe bone deformations during puberty.
Results: This patient presented with CNS and microcoria, leading to the clinical diagnosis of Pierson syndrome. Genetic analysis found a truncating mutation and a splice site mutation of *LAMB2*. The patient received a renal transplantation (R-Tx) at the age of 3. After R-Tx, renal evolution was simple without major complications, the patient receiving low-dose corticosteroids, tacrolimus and mycophenolate mofetil. At the age of twelve, bone deformations progressively appeared. At the time of bone impairment, renal function was normal (glomerular filtration rate using iohexol clearance 50 mL/min/1.73m²), and parameters of calcium/phosphate metabolism were normal (calcium 2.45 mmol/L, phosphorus 1.30 mmol/L, PTH 81 ng/L, ALP 334 U/L, 25OH-D 73 mmol/L). Radiographs showed major deformations such as scoliosis, genu varum and diffuse epiphyseal abnormalities. A high resolution scanner (HR-pQCT) was performed: trabecular et cortical volumetric densities were close from reference values in healthy volunteers, but major radial and cubital deformations were observed.
Conclusions: This is the first case of skeletal impairment ever described in Pierson syndrome, even though scoliosis has already been reported in a 12-year old patient. This observation raises the question of a potential role for laminin beta 2 in bone physiology, since integrins alpha3 beta1 are found both in podocytes and in osteoblasts.

P - 129 BONE METABOLISM AND ARTERIAL STIFFNESS AFTER RENAL TRANSPLANTATION

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Introduction: The aim of the present study was to assess the relationship between bone and vascular disease and its changes over time after renal transplantation. Metabolic bone disease (MBD) is common in chronic kidney disease (CKD) and is associated with cardiovascular (CV) disease. Following transplantation (Tx), improvement in CV disease has been reported; however, data regarding changes in bone disease remain controversial.
Material and methods: Forty-seven transplanted patients (aged 15.5 (4.6) years, 32 males) were examined. The time spent on dialysis prior to Tx was 11 (0-61) months. Bone turnover and arterial stiffness (pulse wave velocity (PWV)) were assessed in Tx patients (38 (3-191) months after Tx).
Results: Bone alkaline phosphatase (BALP), osteocalcin (OC) and beta-crosslaps were significantly higher in Tx patients, and decreased significantly after one year. There was a negative correlation between BALP, OC and steroid administered (r=-0.35;r=-0.36 respectively). PWV increased in the Tx group (1.15 SD). In patients with a follow up of <24 months, PWV was correlated with BALP and beta–crosslaps (r=0.53; r=0.69 respectively) while in the ≥24 months group, PWV was correlated with cholesterol (r=0.38).
Conclusions: Increased bone turnover and arterial stiffness are present following kidney transplantation. While bone turnover decreases with time, arterial stiffness correlates initially with bone turnover, after which the influence of cholesterol becomes significant. Non-invasive estimation of bone metabolism and arterial stiffness may help to assess CKD-MBD following renal transplantation. Supported by OTKA 100909, MTA (HAS) postdoctoral fellowship (E.K.)

P - 130 FACTORS REGULATING 1,25- DIHYDROXYVITAMIN D3 CONCENTRATIONS IN LIVER TRANSPLANT RECIPIENTS

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Introduction: Following liver transplantation, the concentrations of 25-hydroxyvitamin D3 (25(OH)D3) and vitamin D binding protein increase whereas the 1,25- dihydroxyvitamin D3 (1,25(OH)2D3) levels remain unchanged. Possible explanations are impaired 1,25(OH)2D3 synthesis in the kidney or enhanced catabolism. The aim of this study was to identify the factors regulating 1,25(OH)2D3 concentrations at baseline and up to 3 months in adult liver transplant recipients.
Material and methods: Serum 25(OH)D3, 1,25(OH)2D3 and 24, 25(OH)2D3 were measured in 41 patients before, at 2 weeks and 3 months after transplantation. Dose-adjusted tacrolimus concentration calculated at month 3 was used as a "marker" of CYP3A4 activity. Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI formula. Regulators of 1,25(OH)2D3 levels were identified using multivariate linear regression analysis.
Results: The median 25(OH)D3 increased from 18 (range 4-110) ng/ml at baseline to 26 (6-74) ng/ml at 3 months (P= 0.03), whereas the median

1,25(OH)2D3 levels remained stable: 55 (7.5- 182) pg/ml vs. 46 (7.5-118) pg/ml (P= 0.36) despite an increase in serum albumin (34 g/l to 41 g/l, P= 0.02) and comparable eGFR at baseline and month 3 (94 ml/min and 92 ml/min, respectively, P= 0.15). At 3 months 19% had 1, 25(OH)2D3 < 25 pg/ml. Patients with 24,25(OH)2D3 > 1 ng/ml had high 25(OH)D3 at baseline and 3 months and 1,25(OH)2D3 at baseline. The eGFR at 3 months, pre-transplantation Model for end-stage liver disease score, 1,25(OH)2D3 at 2 weeks and the dose-adjusted tacrolimus concentration were the 1,25(OH)2D3 predictors at 3 months.

Conclusions: Liver transplant recipients are at risk of 1,25(OH)2D3 deficiency despite restored 25(OH)D3. Patients with impaired renal function or high tacrolimus clearance might require supplementation with activated vitamin D analogues.

P - 131 URINE β2-MICROGLOBULIN AS A SENSITIVE DIAGNOSTIC MARKER IN CHILDREN WITH CKD STAGE 3-5

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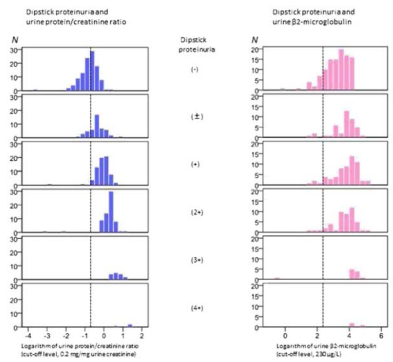
Introduction: In 2010, we conducted a nationwide epidemiologic survey and prospective cohort study of children (3 months to 15 years old) with pre-dialytic CKD (stage 3-5) in Japan, and 447 children (mean age 8.7 years, 271 male) participated in our cohort (Ishikura et al. NDT 2013, Ishikura et al. NDT 2014). Among them, in contrast to adults, 91% had non-glomerular disease, mostly congenital anomalies of the kidney and urinary tract. To detect non-glomerular disease, routine dipstick urinalysis is not necessarily sensitive enough due to dilution and non-proteinuric property of urine.

Material and methods: The results of urinalyses, including dipstick protein, quantification of protein, creatinine, and β2-microgloburin (β2M), in children in our cohort were analyzed. Results of dipstick proteinuria (cut off level, ±) were compared to β2M (cut off level, 230 μg/L, specificity in healthy subjects is 95%), β2M/creatinine (β2M/C) ratio (cut off level, 0.3 μg/mg urine creatinine), and protein/creatinine (P/C) ratio (cut off level, 0.2 mg/mg urine creatinine).

Results: All available data (n=346, age 1.3-17.6 years) for 447 children with CKD were analyzed. Sensitivity (%) of dipstick proteinuria, β2M, β2M/C, and P/C is 58.1, 89.3, 92.2, and 74.2, respectively. Relationship between dipstick proteinuria and β2M or P/C ratio is shown in Figures 1. In children with negative dipstick proteinuria, 85.2% showed positive β2M and 90.2% showed positive β2M/C, but only 43.2% showed positive P/C ratio (p<0.001 for both β2M vs P/C and β2M/C vs P/C).

Figure 1 Dipstick proteinuria and urine protein/creatinine ratio and urine β2-microglobulin



Conclusions: This study revealed that sensitivity of dipstick proteinuria is low in children with CKD, and even P/C ratio is not sufficient. β2M (230 μg/L) and β2M/C (0.3μg/mg urine creatinine) have higher sensitivity than P/C (0.2 mg/mg urine creatinine), exceeding 85%. In addition to routine urinalysis, urine β2M should be analyzed in all children with symptoms attributable to CKD, including urinary tract infection, urogenital malformations, and failure to thrive, to improve sensitivity of diagnosi

P - 132 SERUM KLOTHO: RELATION TO FIBROBLAST GROWTH FACTOR-23 AND OTHER REGULATORS OF PHOSPHATE METABOLISM IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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Introduction: FGF23 and Klotho synergize to regulate phosphate homeostasis by promoting renal phosphate excretion. Chronic kidney disease may be viewed as a state of FGF23 resistance caused by Klotho deficiency. This viewpoint explains several observations on phosphate metabolism in chronic kidney disease that lack mechanistic insights. Our objectives were to correlate serum klotho and FGF-23 with other variables which regulate phosphate metabolism

Material and methods: We studied 40 patients with chronic kidney disease on conservative treatment (group A), 44 patients with end-stage renal disease on regular hemodialysis (group B), 40 kidney transplant recipients (group C) and 40 healthy controls for measurements of serum klotho and FGF-23. Blood samples were withdrawn for measurement of serum Calcium (Ca), Phosphorus (P), alkaline phosphatase (ALP), 1,25 (OH)2 D3, intact parathyroid hormone (PTH), FGF-23 and α klotho

Results: The mean levels of FGF-23 and α klotho in control group were 225.78 ± 111.05 pg/ml (range: 102.4, 418.5) and 6.78 ± 1.90 ng/ml (range: 4, 11), respectively. The mean levels of FGF-23 in the 3 studied groups were 1034.2 ± 84.6, 1288.7 ± 131.4 and1008.7 ± 117.6 pg/ml, respectively. The median levels of s-klotho in the 3 studied groups were 3.15, 2.3 and 2.95, respectively. It was found that FGF-23 was significantly increased and α klotho was significantly decreased in all patients when compared with the control group (p <0.001, < 0.001 respectively). We found that there was a significant inverse correlation between serum Ca and α klotho in the studied groups. There was no significant correlation between FGF-23 and α klotho in the studied groups (p > 0.05).

Conclusions: We have shown that circulating s-klotho was not related to FGF-23 in CKD, dialysis and KTR patients. Also, we have demonstrated a novel association between serum Ca and s-klotho that needs to be further studied.

P - 133 SERUM VITAMIN D, PARATHYROID (PTH) LEVELS AND LEFT VENTRICULAR GEOMETRY IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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Introduction: Nutritional Vitamin D deficiency, serum parathyroid (PTH) level and left ventricular hypertrophy (LVH) are known to be associated with chronic kidney disease (CKD). We conducted this study to investigate the relationship between the above three variables in children with CKD.

Material and methods: Children <18 years of age with CKD (Stage III-VD) attending the Nephrology OPD were included in the study. Serum Vitamin D, PTH and Hemoglobin (Hb) levels were measured in enrolled patients. 2D Echocardiography was done to assess LV geometry. Serum 25(OH) D levels > 30, 10-30 and <10 ng/dL were classified as vitamin D

sufficiency, insufficiency and deficiency, respectively. Serum PTH level > 150 pg/ml was considered as hyperparathyroidism at all stages of CKD.
Results: Out of 30 children evaluated in this study, mean Hb level was 9.2 g/dL, 16 (53.33%) had Vitamin D insufficiency and 8 (26.67%) had Vitamin D deficiency. Hyperparathyroidism was observed in 22(73.33%) children with CKD. LVH was observed in 18(60.0%) children. No significant association was found between Vitamin D sufficiency, insufficiency or deficiency with serum PTH levels or left ventricular hypertrophy, independent of the hemoglobin status. Presence of hyperparathyroidism was significantly associated with LVH.
Conclusions: Vitamin D nutrition may not be an important determinant for development of hyperparathyroidism and LVH. Increased PTH level may be a contributory factor in the evolution of LVH in children with CKD and targeted during therapy.

P - 134 URINARY EXCRETION OF POLYOLS AND SUGARS IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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Introduction: Urinary concentration of sugars and polyols is used for diagnosing inborn errors of metabolism and renal tubular disorders. Reference values are age-related and depend on the method of detection. In this study we examined urinary excretion of sugars and polyols in children with various degrees of chronic kidney disease (CKD) having no known metabolic or renal tubular disorders.
Material and methods: In 28 patients with CKD stage 1-5 urinary concentrations of sugars and polyols (allose, arabinose, arabitol, erythritol, fructose, fucose, galactitol, galactose, glucose , lactose, mannitol, myoinositol, ribitol, sorbitol, sucrose, treitol, xylitol and xylose) were measured by liquid chromatography-tandem mass spectrometry in urinary samples and were compared with age-related reference values. Serum creatinine was measured at the time of urine sample, and the height-independent estimated glomerular filtration rate (eGFR-Pottel) was calculated.
Results: Urinary excretions in CKD were above the reference values for allose – in 68%, arabinose – 75%, arabitol – 64%, erythritol – 86%, fructose – 36%, fucose – 79%, galactitol – 57%, galactose – 41%, glucose - 89%, lactose – 41%, mannitol – 54%, myoinositol – 61%, ribitol – 64%, sorbitol – 52%, sucrose – 26%, treitol – 61%, and xylose 11% of the patients. The significant difference between CKD stage 1-2 compared to CKD stage 3-5 was found for allose, arabitol, galactitol and sorbitol, ($p<0.05$) and for arabinose, fucose, myoinositol, ribitol, xylitol and xylose ($p<0.01$).
Conclusions: We show that the excretion of polyols and sugars depends on eGFR which warrants a cautious interpretation of the results in patients with CKD and indicates the need of further studies for establishing GFR-dependent reference values.

P - 135 ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN WITH EARLY STAGES OF CHRONIC KIDNEY DISEASE

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Introduction: The aim of this study was to investigate ADHD in children with early stages of chronic kidney disease (CKD) and to compare it with healthy children.
Material and methods: Seventy five 5-16-year-old children with early stages of CKD (stage 1, 2 and 3) and 75 healthy children without CKD were included in this case – control study as case and control groups, respectively. The participants were selected from those children who were referred to the pediatric clinic of Amir Kabir Hospital of
Arak (Iran) in the form of simple probability and based on inclusion and exclusion criteria. ADHD was diagnosed
using Conners Parent Rating Scale – 48 (CPRS-48) and DSM-IV criteria and was confirmed by a psychologist
consultant.
Results: ADHD inattentive type was observed in 8 cases (10.6%) with CKD and 2 controls (2.6%) ($p= 0.109$). Moreover, in the case and control groups, 7 (9.3%) and 6 (8%) children were affected by ADHD hyperactiveimpulsive type ($p= 0.997$), and 9 (12%) and 12 (16%) children were affected by ADHD mixed type ($p= 0.664$), respectively.
Conclusions: No differences were found between the prevalence of ADHD in the children with early stages of CKD and the control group. However, due to the importance of the relationships between different types of psychiatric disorders and CKD and lack of enough evidence concerning the relationship between ADHD and different stages of CKD in children, conducting further studies in this field is recommended.

P - 136 THE CLUSTER OF CARDIOVASCULAR RISK FACTORS AND LEFT VENTRICULAR HYPERTROPHY IN CHILDREN WITH CHRONIC KIDNEY DISEASE.

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Introduction: Cardiovascular diseases are the most common cause of morbidity and mortality among patients with chronic kidney disease (CKD). The study aimed to identify risk factors that contribute to the development of left ventricular hypertrophy (LVH) in children with CKD.
Material and methods: The study was conducted in a group of 71 children (27 girls and 44 boys) with CKD stage 1 to 5. The patients' mean age was 11 years and mean GFR was 32 ml/min/1.73m2. Serum cystatin C levels and lipids profiles were measured. Ambulatory blood pressure measurements (ABPM) were performed. Echocardiography examinations were carried out with a HP 5500 device. The 95th percentile of LV mass index relative to height age was used to define LVH.
Results: LVH was detected in 34 out of 71 children. In children with LVH significantly higher values of BP were observed in 24-hour measurements: systolic (119 vs. 109 mm Hg; $p=0.002$), diastolic BP (73 vs. 65 mm Hg; $p=0.009$) and MAP (89 vs. 81 mm Hg, $p=0.004$). Increased level of cholesterol (>5,2 mmol/l) was found in 25 children (35,7%), LDL > 3,4 mmol/l in 12 children, TGL > 1,7 mmol/l in 28, and a decreased HDL level was observed in 20 children. In children with LVH (N=34) significantly higher BMI values (18.6 vs. 16.7 kg/m2;$p=0.039$) were found. LVH group was characterised by significantly lower HDL levels (1.14 vs. 1.5 mmol/l; $p=0.001$). Obesity and low HDL levels were independent LVH risk factors in the multivariate analysis. The results indicated a significant 3-fold increase in the risk of left ventricular hypertrophy in children with hypertension (OR 3.18, 95% CI:1.02-10.1, $p=0.045$), rising up to a 6-fold increase when 2-3 risk factors were present (OR 6, 95% CI:1.3-31, $p=0.015$). HDL levels <10 pc. were associated with a non-significant increase in LVH risk (OR 3.96, 95% CI: 0.85-20, $p=0.059$).

Conclusions: The cluster of cardiovascular risk factors significantly increases the development of left ventricular hypertrophy in children with chronic kidney disease.

P - 137 ALTERATIONS IN CARDIAC AND VASCULAR GEOMETRY IN CHILDREN WITH CKD

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Introduction: Cardiovascular disease (CVD) is the most important risck factor for morbidity and mortality in patients with chronic kidney disease (CKD).
Aim of the study was to evaluate cardiac and vascular geometry in children with CKD in stages 2, 3 and 4.
Material and methods: Twenty-seven patients (18 males and 9 females) mean age 10.9 +/- 5.4 years with CKD and 30 children (control group) comparable for age and sex were enroled. Weight, height, systolic and diastolic blood pressure were obtained. We analyzed biochemical assessments and proteinuria also. We performed echocardiography with Philips iE33 and pulse wave velocity (PWV) with Vicorder PWS system.
Results: We documented significantly higher level of left ventricular mass index (LVMI) (30.3 +/- 7.6 g/m$^{2.7}$) and PWV (4.7 +/- 1.6 m/sec) in CKD patients. Left ventiricular hypertrophy (LVH) was present in 12 % and concentric remodelling in 36 % of our patients. PWV values were significantly correlated with interventricular septal thickness ($p<0.01$) and with LVMI ($p<0.05$).
Conclusions: In this study we documented the alterations of cardiac and vascular geometry since the early stages of CKD. PWV and echocardiography measurements must be considered to assess cardiovascular risck in children with CKD in stages 2-4.

P - 138 RELATIONSHIP BETWEEN VITAMIN D DEFICIENCY AND DIABETIC NEPHROPATHY IN CHILDREN WITH TYPE 1 DIABETES

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Introduction: According to the World Health Organization there are more than one billion people who have vitamin D (VD) deficiency. Animal studies suggested that serum VD (sVD)deficiency may be associated with urine loss due to kidney damage. The aim was to evaluate the relationship between VD deficiency and diabetic nephropathy (DN) in children.
Material and methods: 42 children aged 6 to 17 years with type 1 diabetes (T1D) were examined, among them 24 nornoalbuminuric patients (1st group) and 18 with DN (2nd group). 15 healthy children were included in controls. DN was defined as urinary albumin-to-creatinine ratio > or =30 mg/g in a random spot urine sample. Serum 25 (OH) D levels were measured by 25(OH) vitamin D ELISA assay kit (Eagle Biosciences, Inc, USA). sVD levels were characterized as <20 ng/ml - VD deficiency, 20 to 29 ng/ml -VD insufficiency, and > or =30 ng/ml - normal VD level. Statistical analyses were performed with StatSoft STATISTICA Version 8. Pearsons coefficient for an *R*x*C* contingency table (C) was used to evaluate the association degree between risk factor and outcome.
Results: sVD levels were significantly decreased in the patients of the 1st and 2nd groups ((22.03 (17.23; 24.44) and 14.42 (12.02; 19.63), compared with control group 30.65 (28.45; 35.05) ng/ml) ($p<0.001$)). Higher proportions of DN patients have VD deficiency than individuals without DN (77.8% vs 41.7%; $p=0.0244$). T1D children with VD deficiency have higher the risk of DN development than T1D patients without VD deficiency (relative risk (RR) 2,625 (95% confidence interval [CI] [1, 048; 6,640], $p < 0,05$)). Theassociation degree between risk factor and outcome was seen as relatively strong (C = 0.48).
Conclusions: The results demonstrate decrease sVD in T1D children. To conclude the results support an association between VD deficiency or insufficiency and the DN.

P - 139 LEVEL OF ERYTHROPOIETIN (EPO), HYPOXIA INDUCIBLE FACTOR-1α (HIF-1α) IN CHILDREN WITH ANEMIA IN CHRONIC KIDNEY DISEASE (CKD)

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Introduction: To investigate the relationships between EPO, HIF-1α in 41 children with anemia in CKD.
Material and methods: 41 patients with anemia in CKD were divided into three groups: Group I - 7 predialysis stage, which were treated with iron and erythropoietin stimulating agents (ESA), Group II - 17 predialysis stage without therapy; Group III - 17 dialysis patients, 12 of them on hemodialysis (HD), 5 on peritoneal dialysis (PD), receiving therapy with iron and ESA. We measured levels of EPO and HIF-1α using specific ELISA kits.
Results: In Group I (n=7) CKD stage 5 was in 1 (14%), CKD stage 4 was in 2 (28%), CKD stage 3 was in 4 (58%). In Group II (n=17) CKD stage 5 was in 1 (5%), CKD stage 4 was in 3 (17,5%), CKD stage 3 in 3 (35%), CKD stage 2 was in 10 (60%). In Group III (n=17) CKD stage 5 was in 11 (65%), CKD stage 4 in 6 (35%). Group I excluded from comparing of HIF-1α and EPO. During comparing HIF-1α (0,058±0,01 pg/ml) in 17 patients in Group II and HIF-1α (0,025 ± 0,064 pg/ml) in 17 patients in Group III was revealed lower HIF-1α in children on dialysis ($p <0.05$). While comparing the levels of EPO (27,89 ± 4,7 mIU/ml) in 17 patients in Group II and EPO (55,03±12,08 mIU/ml) in 17 children in Group II was revealed higher level of EPO in children on dialysis ($p<0.05$).
Conclusions: We realized that levels of EPO were higher, and HIF-1α levels were lower in children with CKD on dialysis receiving therapy with ESA and iron than in patients with predialysis CKD without therapy.

P - 140 FGF23 AND SDMA LEVELS CORRELATION IN CHILDREN WITH CKD INDICATE CARDIOVASCULAR INVOLVEMENT BEYOND MINERAL DISTURBANCES

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Introduction: Children with chronic kidney disease (CKD) are exposed to lifelong cardiovascular disease (CVD) risk factors that determine patient outcome. FGF-23 is a key regulator of mineral metabolism and one of most promising CVD biomarker in CKD. Symmetric dymethylarginine (SDMA) is associated with endothelial and CV involvement in CKD too. Despite CVD begins early in the course of CKD few data are available in children without renal replacement therapy.
Material and methods: Aim: to analyze the relationship between FGF-23 plasma levels with traditional (anemia, hypertension, proteinuria) and non-traditional CVD risk factors (plasma P, PTH, symmetric dymethylarginine –SDMA-, high-sensitive C reactive protein –CRP-), and carotid intima-media thickness (cIMT), in a group of children

according to CKD severity Design: cross-sectional study. Population: 40 children (22 boys) of 10.5±4.8 y old with CKD, 92% caucasian. Renal disease: CAKUT 30%, glomerular 20%, tubular 15%, vascular 12%, other 13%. Clasification: CKD stages 2 + 3 (24/40 patients), stages 4 + 5 (16/40 patients). 6 patients were on dialysis and 9 had received a kidney transplant before. 52.5% of patients were hypertensive.
Results: We did not find significant differences in Hb, plasma P, Ca P product, homocystein or CRP levels between CKD 2+3 vs CKD 4+5 patients. However we did observed significant differences regarding PTH (76.3±51.9 vs 307.8±407.4 pg/mL; p=0.012), Uprot/Cr (0.56 ±0.79 vs 7.41±14.2 mg/mg; p<0.001), FGF23 (106.92±54.6 vs 1095.6 ±1042.4 RU/mL; p=0.003) and SDMA (23.16±11.98 vs 7.93±5.68 uM; p<0.001) levels between both subgroups. Those parameters were similar comparing hypertensive vs. normotensive children and those with glomerular vs. non-glomerular renal disease. Interestingly in our study FGF23 levels correlated directly with plasma P (p<0.001), Ca P product (p<0.0001), and proteinuria (p<0.007), and inversely with eGFR (p<0.0001) and SDMA (p<0.0001), whereas did not correlate with the presence of hypertension, homocystein, CRP or PTH levels or cIMT. Multivariate regression demonstrated that FGF23 levels correlated directly with plasma P (p=0.004), Ca P product (p=0.03), and inversely with SDMA levels (p<0.0001).
Conclusions: FGF23 and SDMA levels correlation in a group of children with CKD suggested cardiovascular involvement beyond mineral disturbances.

P - 141 CAROTID INTIMA-MEDIA THICKNESS IN CHILDREN WITH END-STAGE RENAL DISEASE - SINGLE CENTER EXPERIENCE

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Introduction: Chronic kidney disease promotes the development of arterial wall lesions by modifications of calcium and phosphorus metabolism, chronic inflammation, volume overload, hypertension and dialysis stress. The aim of the study was to evaluate changes in the carotid wall in children with End Stage Renal Disease.
Material and methods: We included 23 patients on Dialysis, 12 on Hemodialysis (HD) and 11 on Peritoneal Dialysis (PD), 9 girls and 14 boys with a median age of 15±2.12 years. The control group had 25 patients, 10 girls, 15 boys, median age 14.76±2.14 years. All patients underwent carotid artery ultrasound examination to evaluate Intima-Media Thickness (IMT). We used a 6-12-MHz probe on a GE Logiq C5P ultrasound device. IMT measurements were performed six times on the walls of both common carotid arteries, 1 cm down of bifurcation, and we calculated the average of these twelve measurements as the IMT value. Bivariate Pearson Coefficient and Independent Sample T test were used for statistical analysis.
Results: The two groups were not statistically different regarding the size, age or gender distribution. Mean IMT value for Dialysis patients was 0.587 ±0.074 mm, significantly higher than in controls, 0.443±0.038 mm (p<0.0005, CI=95%). When the dialysis group was divided, mean IMT value for HD patients (0.619±0.079 mm) was significantly higher than in PD patients (0.552±0.051 mm), (p<0.026, CI=95%). In this group there was a positive correlation between IMT and dialysis vintage, but not statistical significant. There was a weak positive correlation between IMT and age (p<0.021, CI=95%) and no correlation with sex.
Conclusions: Dialysis modality is an important factor for Intima-media thickening and can have a major impact in the morality and morbidity of these patients due to cardiovascular complications that may arise.
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P - 142 POTENTIALLY REVERSIBLE ENCEPHALOPATHY IN CHILDREN WITH CHRONIC RENAL FAILURE

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Introduction: Potentially reversible encephalopathy syndrome (PRES) is a clinico-radiological syndrome characterized by headache, nausea, vomiting, altered state of consciousness, visual field defects, convulsions, as well as cortical and subcortical bilateral, symmetrical involvement often in the parietal and occipital lobes, as revealed by brain MRI scans.
Material and methods: A total of 21 patients diagnosed with PRES, followed-up at Baskent University Faculty of Medicine, Adana Teaching and Research Hospital for chronic renal failure between 2000 and 2015, were retrospectively evaluated in terms of their demographic characteristics, clinical, and radiological findings.
Results: The mean age of the patients (10 female, 11 male) was 12.48 ± 3.5 years (ranging from 4 to 18 years). 11 patients had primary VUR (vesicoureteral reflux), 4 nephritic syndrome, 2 Alport syndrome, 1 tubulointerstitial nephritis, 1 nephronophthisis, 1 renal dysplasia and 1 osteopetrosis. In 18 of the patients, hypertension was responsible for the etiology of PRES, and the mean systolic and diastolic blood pressure values were 182.9 ± 36.7 and 115.9 ± 21.7 mmHg, respectively. Three renal transplant patients had a convulsion while using tacrolimus in the first week of transplantation, and they were diagnosed with PRES. These patients had normal blood pressure, therefore tacrolimus therapy was considered to cause the development of PRES. The common clinical symptoms observed in patients were convulsions, altered state of consciousness, headache, and loss of vision in one patient, respectively. As for the radiological findings, the most common regions showing involvement in the brain MRI scans and computed tomography were bilateral parieto-occipital, frontal, temporal, cerebellum, brain stem and basal ganglia. A neurological improvement was achieved within 24 to 48 hours on average after the control of hypertension and replacement of the immunosuppressive therapy. One patient died of intracranial hemorrhage.
Conclusions: Early diagnosis and treatment of potentially reversible encephalopathy is very important. Clinical and radiological findings provide sufficient data for the diagnosis of PRES. Delays in the diagnosis and treatment of patients may result in persistent neurological defects, intracranial hemorrhage, irreversible cerebral infarction, coma and even death. Given the numerous possible risk factors that might lead to the development of PRES in the course of chronic kidney disease, patients presenting with loss of consciousness, convulsions, headache and visual field defects should be evaluated for PRES, as early diagnosis and treatment are known to improve the prognosis.

P - 143 CINACALCET FOR SECONDARY HYPERPARATHYROIDISM IN PEDIATRIC DIALYSIS PATIENTS

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Introduction: Secondary hyperparathyroidism (SHPT) is a major complication in children with end-stage renal disease. SHPT is manifested by elevated PTH levels causing metabolic bone disease. Conventional therapy includes treatment with active vitamin-D metabolites and phosphate binders although some patients continue to exhibit high PTH levels.
Objetive: We report the results of four pediatric patients (three peritoneal dialysis patients and one hemodialisys patient) with uncontrolled hyperparathyroidism despite conventional management who were treated with Cinacalcet.
Material and methods: The indication for the use of Cinacalcet was an elevation in PTH levels despite optimization of serum calcium and phosphate levels. Patients received daily treatment with Cinacalcet at a initial dose of 0.25-0.28mg/kg/day. Doses were increased according to serum PTH to a maximum of 0.5-0.85-mg/kg/day. Patients were admitted for the first 48 hours of therapy to monitor adverse events. Assessment of total and ionized serum calcium, phosphorus, alkaline phosphatase and PTH levels were regularly checked for three months prior treatment and at 24, 48 hours, 7 days after initiation, and monthly during Cinacalcet treatment. Effectiveness was assessed as the difference of PTH levels at the end of treatment, compared to those prior initiation.
Results: Patients' ages ranged from 3.9 to 7 years. Duration of treatment varied from 4 to 15 months and was clinically well tolerated, with no symptoms of hypocalcemia. Three patients out of four discontinued treatment after successful renal transplant and one is still taking Cinacalcet. One patient failed to exhibit a decline in PTH levels (3-months prior: 654 ng/L; 3-months after initiation: 613 ng/L; at this time the patient was transplanted). In the other three patients we observed an overall reduction in PTH level of 79%. Although serum calcium decreased a medium of 0,4 mg/dL, it was not significant (p=0,141).
Conclusions: Cinacalcet is an effective treatment in dialysis patients who have uncontrolled SHPT.

P - 144 RELATIVE CARNITINE DEFICIENCY IN HEMODIALYSIS AND CHRONIC PERITONEAL DIALYSIS SUBJECTS

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Introduction: Carnitine deficiency commonly seen in dialysis patients. We assessed correlation between dialysis and patients' characteristics with plasma carnitines levels and also differences in carnitines levels with considering the modality of dialysis and gender.
Material and methods: plasma carnitine concentrations were measured by tandem mass spectrometry in 46 dialysis cases. Total L-carnitine, free L-carnitine, L-acyl carnitines levels ≤ 40, <7 and <15 μmol/L were defined low and acyl carnitines / free L-carnitine (AC/FC) concentration ratio>0.4 was considered as relative carnitine deficiency. Correlation between carnitines levels and AC/FC ratio with age, duration since onset of dialysis, characteristics of dialysis, serum BUN and albumin concentrations were analyzed by Pearson correlation test. Patients with mild to moderate and those with severe relative carnitines deficiency were compared by considering the mentioned variables .Chi square and independent T tests were used for univariate analysis. P-values ≤0.05 considered as statistically significant differences.
Results: Free . All patients had relative carnitine deficiency .Mean ±SD concentrations of L-acyl carnitines, total and free L- carnitines and AC/FC ratio were not significantly different based on modality of dialysis (P>0.05 for all).More severe relative carnitine deficiency was found in cases with lower serum BUN levels and CAPD cases (P=0.042 and 0.495 respectively).No linear correlation between carnitines levels and AC/FC ratio with patients' characterestics were noted (P>0,05,r>0,01 for all).
Conclusions: relative carnitine deficiency was common and it was more severe in those with lower serum BUN levels and CAPD patients. No correlation between patients'chracterestics, modality of dialysis and characteristics of dialysis with carnitines levels were noted.
Key words: free L- carnitines, L-acyl carnitines, relative carnitine deficiency, hemodialysis, chronic peritoneal dialysis

P - 145 PREDICTORS OF RENAL REPLACEMENT THERAPY AND MORTALITY IN CHILDREN WITH CHRONIC KIDNEY DISEASE.

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Introduction: To study the epidemiology of chronic kidney disease (CKD) in children, and to look for risk factors to predict renal replacement therapy (RRT) and mortality.
Material and methods: This is a retrospective cohort study conducted at King Abdulaziz University Hospital, Jeddah, Saudi Arabia between 2006 and 2014, where the files of 1,000 children with CKD were reviewed.
Results: The mean±standard deviation age at presentation was 4.9±4.3 years. The median duration of follow up was 1.5 (interquartile range [IQR]: 0.4-4.0) years. Only 9.7% of children received RRT, and 8.3% died. The underlying etiology for CKD was congenital in 537 children. The congenital CKD group presented at a younger age group (3.5±4.0 versus 6.6±3.9 years, p<0.0001), had more advanced stages of CKD (p<0.0001), higher rates of consanguinity (75.4% versus 47.1%, p<0.0001), and RRT (p<0.004) than children with non-congenital CKD. Risk factors for RRT among children with CKD include being a Saudi indigene (relative risk [RR]=1.49, 95% confidence interval (CI): 1.01-2.21), and hypertensive (RR=5.29, 95% CI: 3.54-7.91). The risk factor for mortality was hypertension (RR=2.46, 95% CI: 1.66-3.65).
Conclusions: Congenital causes of CKD represent the main etiology of CKD in children living in the western province of Saudi Arabia. Significant risk factors for RRT include congenital CKD, Saudi nationality, and hypertension. Hypertension is also a predictor of mortality in children with CKD

P - 146 BENEFICIAL EFFECTS OF TONSILLECTOMY FOR CLINICOPATHOLOGICAL FINDING AND CLINICAL OUTCOME OF CHILDHOOD IGA NEPHROPATY (IGAN) IN JAPAN.

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Introduction: The mechanism leading from tonsillar abnormality to IgA deposition in the kidney in IgAN is believed to involve impairment by bacterial infection of signal transmission between the tonsillar crypt epithelium and underlying lymphocytes. Tonsillectomy, alone or in combination with pulse steroid therapy, has been studied as treatment for adult IgAN. ; both clinical and histological improvements have been reported. However, pediatric concerns such as possible impaired acquisition of normal immunity and increased infections have limited consideration of tonsillectomy as treatment for pediatric IgAN.
Material and methods: We investigated efficacy and therapeutic mechanisms of tonsillectomy for intractable childhood IgAN. Among 25 patients, 19 patients were able to evaluate histological findings before and

after surgery. Patients with poor (n =7) or relatively poor (n =18) histologically determined prognosis and an age of at least 7 years, together with proteinuria of at least 0.3g/day or severe persisting despite ongoing drug treatment, are candidates for surgery. Patients were grouped by interval between diagnosis of IgAN and tonsillectomy (within 3 years; early group vs 3 years or later; later group). Patients underwent kidney biopsy shortly before and 1 to 2 years after tonsillectomy.

Results: Proteinuria was reduced after tonsillectomy over 2 years of follow-up in both early and later groups compared with proteinuria in the 6 months preceding surgery. Complete remission was achieved in 10 patients, most often among those having surgery within 3 years, while patients refusing surgery failed. The activity index score decreased in both groups, significantly when surgery was early ($P<0.01$). Complement component C3 deposition and activated macrophages (MRP-8+ cells) in glomeruli decreased after tonsillectomy, especially with early surgery ($P<0.01$).

Conclusions: Tonsillectomy improved clinicopathological features in relatively severe paediatric IgA nephropathy, especially with the early-surgery group. Therapeutic mechanisms may include inhibition of complement activity in glomeruli and glomerular infiltration by activated macrophages.

P - 147 INFLUENCE OF STEROID MEDICATION ON BONE MINERAL DENSITY IN CHILDREN WITH NEPHROTIC SYNDROME

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Introduction: Glucocorticoid induced osteoporosis is caused by decreased bone formation and increased bone resorption (Canalis et al., 2002). The combination of decreased bone formation and increase bone resorption leads to extremely rapid bone loss (Lukert et al, 1990). So, in our study we evaluated the effects of long and high dose corticosteroid (CS) therapy on bones in children with nephrotic syndrome.

Material and methods: We performed dual-energy Xray absorptiometry (DEXA) of the spine in 37 children and adolescents with nephrotic syndrome(NS) and correlate the result of dexa with duration of steroid, age of onset, type of NS, laboratory data,

Results: Bone mineral density (BMD) was measured in 37 children with NS with mean age (8.6 ± 3.3) years, 23 males and 14 females, according to their response to steroid, they were classified as steroid responsive (S resp) group which includes 25 patients (67.6%) and the steroid resistant (SR) group which includes 12 patients (32.4%) , the steroid responsive group is subdivided into frequent relapsers (FR) 8 patients (21.6%) and steroid dependent (SD) 17 patients (46%). The mean age of onset were (4.9 ± 2.8) years, mean duration of steroids (3.6 ± 2) years, as regards laboratory data including : albumin / creatinine ratio, total protein, albumin, cholesterol, creatinine, calcium, phosphorus, alkaline phosphatase, intact parathormone all were within normal ranges. As regard BMD patients were divided into 3 groups: Mild osteopenic group (48.7%), severe osteopenic group (18.9%) and the remaining group are normal (32.4%). By comparison of this 3 groups the severe osteopenic group have older age of onset ($P = 0.003$) and 85.7% of this group are steroid resistant., Z-score shows –ve correlation with age of the patients ($r = -0.501$) and +ve correlation with serum albumin and alkaline phosphatase, $r = 0.408$, $r = 0.427$ respectively.

Conclusions: So, we can conclude that patients with nephrotic syndrome, on long and high dose of steroid have decrease bone density, especially the steroid resistant group during relapse and with older age onset.

P - 148 CALCIUM-PHOSPHORUS METABOLISM AND SERUM INTACT PTH IN PEDIATRIC CHRONIC KIDNEY DISEASE

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Introduction: To observe the calcium, phosphate and intact parathyroid hormone (iPTH) at different stages of chronic kidney disease (CKD), increase the awareness of early detection and intervention, prevent the development of renal osteodystrophy.

Material and methods: 138 patients were selected who were admitted to Beijing Childrens Hospital with CKD from Jan 2008 to Dec 2013. The mean age was 10.41±3.51 years. Common information of age, gender and height were collected, serum creatinine, calcium,phosphate and iPTH levels were analyzed. Estimated glomerular filtration rate(eGFR) was calculated using modified Schwartz formula. The stages of CKD were defined according to K/DOQI Clinical Practice Guidelines by National Kidney Foundation.

Results: There were 2 patients in CKD stage II, 19 in stage III, 24 in stage IV, and 93 in stage V. One patient (1/2) in stage II had hyperphosphatemia. There was no significant difference in either serum calcium or phosphate between stage III and IV, but showed significant difference as compared with stage V respectively ($p<0.000$). The incidence of hyperphosphatemia and hypocalcaemia (see in table 2) were in accordance with the above. There was no difference in iPTH between stage IV and V ($p=0.180$), but significant as compared with stage III respectively. Significant difference was seen between stage IV and V in ALP ($p<0.01$), but there was no difference as compared with stage III respectively. Serum calcium was negatively correlated with Ipth

Conclusions: Hyperphosphatemia was observed in CKD stage II. Patients suffered from obvious calcium-phosphorus metabolic disorder since stage III. Monitoring the levels of serum calcium, phosphate and iPTH should be started from CKD stage II, to prevent the development of renal osteodystrophy

P - 149 CKD: FACTORS OF INITIATION AND PROGRESSING

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Introduction: The object of research: to determine the major factors of initiation and progression of tubulointerstitial renal damage in children with congenital malformations (CMF) of the urinary system (US) to optimize early diagnosis of chronic kidney disease (CKD).

Material and methods: The study in the dynamics of 300 children aged from 1 year to 17 years, including 70 children with CMF of the US with no signs of tubulointerstitial renal disease (TIRD), 180 patients with obstructive (100) and non-obstructive (80) pyelonephritis and 50 apparently healthy children. All children underwent complex clinical and paraclinical, nephrology, urology, immunological and bacteriological examination.

Results: The leading risk factors CMF US: genetic, complex perinatal, the influence of infection, on drugs, smoking, alcoholism, occupational hazards in the parents, exposure to heavy metals.

Proved different pathogenetic factors contribute to the formation and progression of TIKD: immunological, proteinuria, hypertension, hypoxia, disturbances of renal hemodynamics, bacterial action, urodynamics and degree of intrarenal reflux. An algorithm for the early diagnosis of children with TIRD CMF US is developed.

Conclusions: The leading factors in the formation and progression of tubulointerstitial renal damage of children with CMF of the US are immunological with the development of the immune imbalance and a combination of the impact of complex non-immune factors.

P - 150 THE GLOBAL REQUIREMENT OF RESOURCES FOR PATIENT EDUCATION: STRATEGIES FROM THE IPNA COUNCIL.

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Introduction: Providing patient and parental/carer education (PPE) is a vital component of health care delivery particularly in Pediatric Nephrology where risks of serious illness are high and much of the care can be delivered at home. We aimed to assess existing PPE resources on an international scale and propose strategies for optimization through the IPNA platform.
Material and methods: A questionnaire was sent to all regional and national representatives on the IPNA council. Lists of resources provided by responders were compiled and 57 online sites or contact details of service providers for children's kidney diseases worldwide were reviewed. Results were presented at the IPNA council meeting in New Delhi, in December 2014.
Results: Twenty four replies were received from 21 countries. The 4 commonest diseases prevalent were reported to be Nephrotic Syndrome (by 83% responders), CAKUT (79%), glomerulonephritis (58%), and UTI (50%). Only 6 (25%) responders expressed complete satisfaction with existing resources for PPE. Common concerns expressed were (1) lack of child oriented disease information and support (2) lack of adequate brochures and printed materials (3) PPE programs restricted only to world kidney day celebrations which were also primarily adult-centric. Amongst existing disease-information websites, the UK site InfoKID was the most comprehensive.
IPNA council members proposed that the IPNA website contain links to (a) Regional support services referenced according to country and (b) Specific disease information sites referenced according to disease. Efforts were initiated to collaborate with InfoKID to provide a more international perspective. As a first step towards encouraging PPE workshops and programs, an initiative has started to support one child oriented PPE activity per year globally, on world kidney day.
Conclusions: The majority of representative pediatric nephrologists from different countries of the world recognise a lack of existing resources for PPE. IPNA is committed to develop and support PPE resources.

P - 151 NEPHRO-UROLOGICAL FINDINGS IN THE BECKWITH-WIEDEMANN SYNDROME: CASES REPORT

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Introduction: Beckwith-Wiedemann Syndrome (BWS) is the most common overgrowth syndrome in infancy characterized by the following main symptoms: macrosomia, macroglossia, omphalocele, hemihyperplasia, visceromegalia, hypoglycemia, kidney abnormalities and an increase oncological risk. Genetic anomalies are found in 75 % of cases. We describe the clinical, genetic anomalies and nephrourological manifestations in patients with diagnosis of BWS.
Material and methods: This is a retrospective descriptive study of patients previously diagnosed with BWS according to Weksberg criteria and by genetic study, during the period between 1989 and 2012 in a tertiary hospital.
Results: We included 15 patients, ages ranging from 2 to 25 years old (median 7 years), 4 males and 11 females. In 8 cases (53%) the diagnoses was made by prenatal disorders, and in the remaining cases were in the first year of life. Two cases (13.3%) were in-vitro pregnancies. Ten cases (66.7%) were premature births, and eight cases (53.3%) were large for gestational age newborn. Two cases (13.3%) had a history of polyhydramnios. Genetic studies found abnormal methylation patterns in the imprinting center 2 in twelve cases (80.0%), uniparental disomy of chromosome 11 in two (13,3%) and the remaining case showed not abnormalities. The most frequent clinical symptoms were macroglossia (100%), omphalocele (53.3%), hypoglycemia (46.1%) and nephron-urological manifestations (40%): medullary renal dysplasia (MRD) (13.3%), renal cysts (13.3%), hypospadias (13.3%) and one patient developed Wilms tumor (6.7%).(Table 1).

Table 1: Nephro-urological manifestations

Patient	Renal findings	Age at diagnosis
1	Wilms Tumor	3 years
2	MRD, hypospadias	Newborn
3	Renal cyst	15 years
4	Renal cyst	2 years
5	DMR	Prenatal
6	Hypospadias	Newborn

Conclusions:
Early diagnosis is important in neonatal period due to high incidence of nephrourological anomalies, risk of malignant tumors and complications associated during the first years of life. Monitoring of patients is recommended in adulthood by the occurrence of late renal abnormalities.

P - 152 HYPOPHOSPHATEMIA, RICKETS AND SECONDARY CRANIOSTENOSIS IN A PRETERM INFANT RECEIVING AN AMINO-ACID FORMULA.

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Introduction: Hypophosphatemic rickets may result of low phosphate intake, digestive absorption defect, or excessive phosphaturia. Poor phosphate intake is a rare condition, even in preterm infants, since modern nutritional management.
Material and methods: We report a case of phosphate depletion, with rickets and secondary craniostenosis in a preterm infant receiving an amino-acid formula.
Results: A 5-month-old white boy was admitted because of feeding difficulties, dyspnea and pain. Rickets was diagnosed with multiple fractures and pneumonia. He was born at 31+5 weeks of gestation, with low birth weight (1040g). He was receiving an amino-acid formula (Neocate®, Nutricia, France), after an episode of mild enteocolitis, and daily 1200 UI of vitamin D.
Laboratory evaluation at diagnosis showed hypophosphatemia (0.67 mmol/L), without phosphaturia (TRP 98%), normal calcemia and calciuria, low PTH and high 1,25(OH)2D, consistent with phosphate depletion.

At diagnosis, an abnormal head shape was noted and computed tomographic scan showed abnormal fusion of sagittal and metopic sutures, and partial fusion of coronal and squamous sutures.
He received mineral and vitamin supplements, with global improvement and supplements were discontinued after 4 months. Unfortunatly, with rickets' correction, craniostenosis progressed, with secondary hydrocephaly. Decompression craniectomy was required at 11 months. No mutations causing craniostenosis (FGFR2, FGFR3, TWIST) were found.
Conclusions: Metabolic bone disease is a common problem in premature infants of low birth weight. Amino-acid formula contains as much phosphate as other preterm formulae, but mineral absorption might be decreased. In this population, phosphate intake and bone mineral markers should be closely monitored.
Craniostenosis is documented in genetic hypophosphatemic rickets. Synostosis could result of FGF-23 binding on FGFR2 on osteoblasts. Craniostenosis has also been reported associated to non-FGF23-mediated hypophosphatemic rickets, such as phosphate depletion due to anti-acid chelation. Mechanisms remain unknown. Craniostenosis should be looked for in patients with rickets, at diagnosis and during treatment.

P - 153 HEMOLYTIC ANEMIA AND ACUTE KIDNEY INJURY CONSECUTIVE TO ACCIDENTAL ALBENDAZOLE SYRUP INJECTION IN A 2 YEARS-OLD CHILD

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Case description: Girl aged of 21 months, without any medical history and treated for a severe ascariasis infection, received an intravenous injection of Albendazole syrup by mistake.
She was referred to our center for management of an acute kidney injury associated with hemolytic anemia
She developed within hours hemolytic anemia (haemoglobin 5.9g/dL with schizocytes) requiring blood transfusion, liver dysfunction (SGOT 1662 UI/L, SGPT 350 UI/L), low serum albumin (13.6 g/dl) and anuric kidney injury (serum creatinine 316μmol/L, urea 24.9mmol/L) treated by renal replacement therapy (RRT) in emergency. The period of anuria and RRT were 16 and 19 days respectively. Moreover, three months after the disease onset, she presented a chronic kidney disease Stage 5 with an estimated GFR of 13.5 mL/min/1.73m^2 (Schwartz 2012) and a proteinuria of 0.35 g/mmol of creatinine. Kidney ultrasound and MRI were highly suggestive of bilateral cortical necrosis. A cerebral MRI was also performed because of the occurrence of intermittent action-related shaking found bilateral hypersignal Flair and T2 in the posterior paraventricular white matter, the semioval centers, fronto-parietal and occipital subcortical regions compatible with ischemic lesions in the small vessels. Ophthalmologic examination found ischemics lesions on the left retina with papillary and retinal pallor, macular irregularity and abnormal pigmentation.
Conclusions: No kidney impairment has been described with Albendazole. However, Albenzole syrup contains a high proportion of glycerol, and injection of glycerol is used as a model of kidney failure in rats (myoglobinuria, tubular necrosis, enhanced renal vasoconstriction and endothelial oxidative stress). In our patient, the clinical course and radiological exams werealso highly suggestive of systemic vascular lesions affecting the small vessels. To our knowledge, this is the first report assessing the effect of intravenous injection of glycerol-based syrup in children. Moreover, it also enlights the physiopathology of glycerol-induced renal failure and underlines the potential injuries in multiple organs.

P - 154 SEVERE VARICELLA IN A BOY TREATED WITH ECULIZUMAB FOR SHIGA TOXIN-ASSOCIATED HEMOLYTIC UREMIC SYNDROME

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Introduction: Shiga-toxin-associated Hemolytic Uremic Syndrome (STEC-HUS) mainly affects children younger than 5 years old. The course of the disease can be severe with up to 50% of affected children requiring dialysis and 20% with neurological involvement during the acute phase. Mortality rates can reach 5%. Apart from supportive care, no specific treatment has proven its efficacy in this life-threatening disease. Recently, eculizumab (EC), an anti-C5 monoclonal antibody was used in severe forms of STEC-HUS with conflicting results.
Case description: We report the case of a 3-year-old boy treated with EC for STEC-HUS who developed a severe disseminated varicella with cutaneous, pulmonary and neurological involvement. After recovery, no constitutional immune deficiency was found in this child.
Recent in vitro and in vivo studies have highlighted the role of complement in adaptive immune response, mainly through a crosstalk between complement and antigen presenting cells - and how it could regulate T-cell activation. We postulate that our patient may have developed this severe infection because of the EC treatment.
Conclusions: There is little data on complement-blocker treatment in children. New insights on complement action, especially in the field of adaptive immune responses, emphasize the need of great care with such treatments in vulnerable patients.

P - 155 NATIVE KIDNEY BK VIRUS NEPHROPATHY AFTER HEMATOPOEITIC STEM CELL TRANSPLANTATION (HSCT)

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Introduction: BK virus is an increasingly identified cause of pathology in immunocompromised transplant recipients. BK virus associated nephropathy (BKAN) is a well-known cause of graft dysfunction after renal transplant. In HSCT patients, BK virus is a commun cause of hemorrhagic cystitis, but only very few cases of BKAN have been reported.
Case description: We report a case of BK virus nephropathy after pediatric HSCT.
A 6-year-old boy was diagnosed with acute lymphocytic leukemia. He received Total Body Irradiation, etoposide and anti-thymocyte before bone marrow transplant, and again 2-months later a second conditioning treatment with cyclophosphamide, fludarabine, and anti-thymocyte before cord blood transplantation. He received also a GVH prophylaxis by cyclosporine and MMF. Serum creatinine was at 35μmol/l at D0.
Urinary BK virus was detected from D8. He developed hemorrhagic cystitis, with clinical improvement under leflunomide. Immunosuppressive drugs were discontinued, but BK virus detection remained highly positive in urine (PCR >9log) and blood (PCR >6log). At D40, creatinine started to rise, up to 200μmol/l at M4, despite nephrotoxics withdrawal. Renal biopsy showed major tubulo-interstitial

injuries, with a positive BK virus antibody hybridation on tubular epithelial cells nuclei.
Treatment associated Cidofovir 1mg/kg, leflunomide and immunoglobuline substitution. After 4 weekly perfusion of cidofovir, creatinine stabilised around 180 μmol/l. One month later, because of persistant viremia, a second course of Cidofovir was performed. Viremia became negative and viruria persisted > 5log. At M11, creatinine was at 170 μmol/l (GFR 28ml/min/1.73m^2), he was still receiving leflunomide and substitutive immunoglobulins. Renal biopsy showed chronic injuries with interstitial fibrosis > 50%, 25% of destructed glomeruli and no more BK virus staining.
Conclusions: BK virus nephropathy is a rare but severe complication after HSCT. It is probably underdiagnosed and should be considered as a differential diagnosis of acute kidney injury in HSCT and furthermore any immunocompromisedpatient.

P - 156 AN UNCOMMON CAUSE OF BLADDER OUTLET OBSTRUCTION: "WHEN THE ANSWER LIES WITHIN THE SKIN"

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Case description: We would like to report the case of an eight month old male infant who was referred for bilateral moderate hydronephrosis.
Our patient had pyloric atresia diagnosed at birth. Neonatal ultrasonography of the kidney ureter bladder which demonstrated bilateral moderate hydronephrosis. Cystoscopy examination at 5 months of age showed tight foreskin adhering to the glans with a trabeculated bladder. Posterior urethral valve was ruled out. he also had minimal blistering over areas covered by adhesive surgical tape. At 7 months of life, he was still straining during micturition. A repeat ultrasound showed worsening of the bilateral hydronephrosis with bilateral tortuous hydroureters till the point of insertion into the urinary bladder. Immunohistochemistry analysis of his skin biopsy demonstrated changes in Integrin beta 4. Junctional epidermolysis bullosa-pyloric atresia syndrome is now a recognized to be associated with genitourinary abnormalities. . Those cases reported were associated with extensive skin blistering. In our patient, his gastrointestinal and genitourinary manifestation were more profound in relation to his minimal skin blisteringDiagnosis could be easily missed.
Conclusions: This case illustrated a rare cause of bladder outlet obstruction. An understanding of the primary skin diagnosis is vital to decide on best method to relieve the congested urinary system. Unaddressed, this condition may lead to early renal insufficiency.

P - 157 AN EVOLVING CASE OF ANCA ASSOCIATED VASCULITIS

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Case description: A 5 year old boy presented with subacute nephritis. The progression of disease from a renal limited microscopic polyangiitis (MPA) to eosinophilic granulomatosis with polyangiitis (EGPA) is a unique evolution between rare childhood diseases.
The child initially presented with 2 months of macroscopic haematuria. He had nephrotic range proteinuria, but normal blood pressure and creatinine. ANCA was positive with reactivity to myeloperoxidase. There were no other signs of systemic disease. Renal biopsy demonstrated pauci-immune crescentic glomerulonephritis. The boy was treated with corticosteroids and 6 x monthly cyclophosphamide. At 7 months he was commenced on azathioprine and continued on low dose prednisolone. Proteinuria improved, although microscopic haematuria remained. At 12 months, following 1 month of nasal congestion and wheeze, he presented with new findings of arthritis and significant eosinophilia on blood count. Further evaluation demonstrated bronchoalveolar lavage eosinophilia, sinusitis on CT scan, and abnormal diffusion capacity on spirometry. Although renal parameters were unchanged, a second renal biopsy was performed which demonstrated dense interstitial eosinophilic infiltrate with tubulitis. There were no crescents, or glomerular inflammation although 8/15 glomeruli were sclerosed. The presentation fulfilled the diagnostic criteria for EGPA. Prednisolone was increased to 1mg/kg/day and azathioprine continued. Chest, joint and nasal symptoms, and eosinophilia, resolved over 1 month. Prednisolone therapy was weaned to 0.15mg/kg/day over 6 months. A dose of Rituximab was given 5 months following the EGPA diagnosis, given medication compliance concerns & low grade eosinophilia associated with wheeze. Now, 18 months following EGPA diagnosis, this patient is well, and is maintained on azathioprine and 0.15mg/kg/day prednisolone.
Conclusions: EGPA is extremely rare in childhood. The young age of this child and associated renal disease make this case notable. Even more unqiue, and to our knowledge previously unreported, is the disease evolution from initial renal limited MPA, to EGPA.

P - 158 REFRACTORY OSTEODISTROPHY IN A BOY WITH PERITONEAL DIALYSIS - RISK FACTOR FOR FATAL EVOLUTION OF CALCIFIC UREMIC ARTERIOPATHY

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Introduction: Calciphylaxis (calcific uremic arteriolopathy) is a rare, but important cause of morbidity and mortality in patients with end stage renal disease (ESRD). With an incidence of 1% to 4% of adults with ESRD, was described only in few cases in children.
Case description: A 4 years old boy was in evidence of our clinic from 2 years, when he was diagnosed with ESRD, caused by an posterior urethra valve, late diagnosed. In the evolution child developedsevere osteodystrophy (phosphorus >10mg / dl, Ca x P product > 70), despite calcium carbonate therapy as phosphate-binder. The child associated constant an inflammatory syndrome (CRP positive), considered in context of recurrent urinary tract infections. In 08.2014 returns for monthly evaluation with dry caught, itching, scratching lesions on facies, limbs and trunk, and irritability. We suspected anallergic pathology (elevated IgE, with pruritic skin lesions, persistent dry caugh), and initiated therapy with Montelkast. From September to november observed marked deterioration of nutritional status (albumin levels < 30g/l), heart failure, and progressive respiratory failure. After an apparent improvement of the general state child suddenly develop cardio-respiratory arrest refractory to resuscitation anddie.
The histopathological examination reveals diffuse dermal, lung, brain calcifications, diffuse dystrophic calcifications at left-heart level, mainly subendocardial, renal calcification and diffuse large califications in arteries, subendothelial, including in the coronary arteries, that suggest a calciphylaxis. Retrospectiv evaluation show us the association of predisposants factors like refractary osteodystrophy,hypoalbuminemia, chronic inflammatory syndrome, skin lesions secondary of metastatic deposits of calcium.
Conclusions: This case illustrates a rare, but typical case of calciphylaxis in a boy with end ESRD. The literature suggests a higher incidence in male with ESRD, secondary hyperparathyroidism, extremity and visceral

organ involvement, worse prognosis. Recognition of this syndrome is mandatory, because the treatment must to be early initiated.

P - 159 APRT DEFICIENCY DIAGNOSED AFTER RENAL ALLOGRAFT DYSFUNCTION IN A 4-YEAR OLD CHILD

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Introduction: Adenine phosphoribosyltransferase (APRT) deficiency is a rare autosomal recessive disorder, manifesting by 2-8 dihydroxyadénine (DHA) urolithiasis and possibly chronic kidney disease, secondary to crystal precipitation into renal parenchyma. It may be diagnosed during childhood, because of recurrent urinary tract infections or stones, but is frequently underrecognized and sometimes diagnosed in adults, after renal allograft dysfunction secondary to recurrent crystalline nephropathy.
Case description: We report the case of a 4-year old girl, born from consanguineous parents, and first diagnosed with Congenital Nephrotic Syndrome (CNS) due to a homozygote mutation of NPHS1. She presented two episodes of urinary tract infection (UTI) during the first year of life. Binephrectomy was performed at 15 months, because of infectious complications of nephrotic syndrome. Renal histology showed yellow-brownish microcrystals thought to be oxalate crystals. She received renal transplantation at 3 years old. At M3, serum creatinine was 30μmol/l and protocolar biopsy was normal. She presented several UTI, with no urological underlying condition. At M12, creatinine raised to 100μmol/l.
Renal biopsy showed tubulo-interstitial injuries with major birefringent crystals deposits. Spectroscopy of renal tissue and crystalluria confirmed the detection of 2-8 DHA. Under increase water intake, purine-low diet, and allopurinol (5mg/kg), allograft function recovered. Nul APRT activity and genetic analysis confirmed APRT deficiency.
Conclusions: 2-8 DHA nephropathy is a rare, underdiagnosed but preventable disorder. It has never been reported in the pediatric population. A few cases of recurrence after renal transplantation have been reported in adults, and crystalline nephropathy can lead within a few weeks or months to allograft dysfunction and graft loss. The presence of crystals in the renal parenchyma or urine sediment should never be overlooked.

P - 160 ALCOHOL SCLEROTHERAPY TREATMENT FOR RECURRING RENAL CYSTS IN THE CONTEXT OF CYSTIC DYSPLASIA, ECTODERMAL DYSPLASIA AND CONGENITAL HEART DISEASE

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Case description: We report a 5 year old girl with complex congenital heart disease (complete atrioventricular septal defect and pulmonary stenosis) and ectodermal dysplasia. She has non-consanguinous parents. Her chromosome array and P63 mutation screen was normal. She presented with abdominal pain, vomiting and hypertension. On presentation she was hypertensive and had palpable abdominal mass. MRI showed bilateral renal cysts with a large encapsulated multiloculated cyst displacing and distorting the kidney and stretching the renal vessels. (Image 1)
A percutaneous drain was inserted into the cyst with immediate symptomatic relief and rapid correction of blood pressure. Drain fluid analysis was suggestive of plasma rather than urine. Repeat renal ultrasound post-drain removal showed re-accumulation of fluid requiring alcohol sclerotherapy. Repeat MRI post sclerotherapy showed recollection of fluid in the cyst. The child remained asymptomatic and therefore was managed conservatively. The patient re-presented 6 months later with a similar history of abdominal pain – this time on the right side. Ultrasound showed right sided septated cyst. The cyst was percutaneously drained but again re-accumulated post drain removal requiring alcohol sclerotherapy. A follow up ultrasound showed recollection of cyst but again was managed conservatively 1 year post 2nd intervention, the child remains well. She is monitored on a regular basis with serial ultrasound scans.
Conclusions: In summary, we report a 5 year old girl with background of complex congenital heart disease, ectodermal dysplasia and bilateral renal cystic disease who presented with large bilateral symptomatic cysts requiring percutaneous drainage and alcohol scerotherapy with quick refilling of the cysts post sclerotherapy

P - 161 ONE PILL CAN KILL - A CASE REPORT OF A PATIENT WHO SURVIVED A POTENTIALLY LETHAL DOSE OF PMMA

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Introduction: Paramethoxymethamphetamine (PMMA) is sold on the illicit market as a substitute for ecstacy and has been linked to several fatalities.
Case description: We describe a case of near-fatal intoxication with PMMA in a 17-year old boy.
Approximately 24 hours after taking two tablets of "Superman" ecstacy, the patient presented with status epilepticus and malignant hyperthermia. Large doses of diazepam, midazolam and ultimately sedation, intubation and phosphenytoin were required to render him clinically seizure-free. Cooling, plasma exchange and continuous veno-venous hemodiafiltration (CVVHDF) were quickly initiated. At first, severe but transient cardio-respiratory failure dominated the clinical picture, however, the patient soon developed oliguric acute kidney injury. Blood tests revealed extremely high levels of creatine kinase, myoglobin and troponin T. Additionally, acute fulminant liver failure with severe coagulopathy ensued. The patient was evaluated for urgent liver transplantation and treated with N-acetylcysteine and artificial liver support (Molecular Adsorbent Recirculating System, MARS) with improvement of liver function. However, rhabdomyolysis persisted, causing a rebound in serum levels of creatinine and transaminases. Due to persisting intermittent fever, shivering and confusion consistent with serotonergic syndrome, treatment with cyproheptadine (a non-selective serotonin-antagonist) was initiated.
Gradually, urinary output increased to polyuria with nephrotic proteinuria. Intermittent hemodialysis replaced CVVHDF after two weeks and was successfully discontinued 19 days after admission. Upon discharge after 33 days, renal and hepatic functions were nearly normalized.
Analysis of another "Superman" tablet, presumably from the same batch, revealed a PMMA-content approximately twice as high as in previously analyzed tablets.
Conclusions: To our knowledge, there are neither any previous reports of individuals surviving PMMA-doses this high, nor has PMMA been known to cause such prolonged serotonergic syndrome or rhabdomyolysis. We conclude that despite the potentially lethal PMMA-dose, the patient's life could be saved as a result of combined aggressive treatment with cooling, anticonvulsants, dialysis, detoxification and cyproheptadine.

P – 162 RITUXIMAB USE IN A CHILD WITH RECURRENT FOCAL SEGMENTAL GLOMERULOSCLEROSIS POST KIDNEY TRANSPLANTATION

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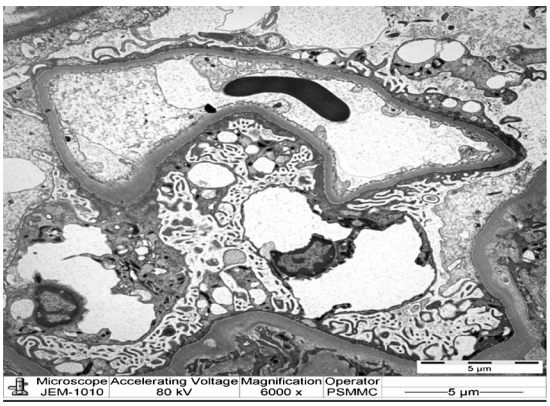
Introduction: Post Transplantation Recurrence Focal Segmental Glomerulosclerosis (FSGS) has an incidence up to 30% with great effect in graft survival if not detected and treated early. There is no known single treatment protocol for such cases and their response is quite unpredicted.
Case description: An 11 year old girl with FSGS diagnosed at two year, she progressed to chronic renal failure with Peritoneal dialysis at 9 year. She underwent a deceased kidney transplantation from a pediatric donor with negative crossmatching. She was induced with Antithymocyte globulin and she started to pass urine immediately with serum creatinine decreased untill it reached 105 micromol/l by day 3. She was maintained on Tacrolimus, Mycophenolate and Prednisone . She was noticed to have proteinuria with protein/creatinine ratio of 2500-4000 mg/mmol and generalized oedema. Serum creainine increased to 324 micromol/l, allograft biopsy done and electron microscopy showed diffuse Foot Processes Effacement with no light microscopy changes. Plasmapheresis(PP) started with albumin/Fresh Frozen Plasma as replacement fluid for initial intensive 12 sessions. Renal function recovered, oedema resolved and creatinine dropped to 95 but she continued to show heavy proteinuria so 4 doses Rituximab (375 mg/m2) given every other week without complication. Both enalapril and candesartan were added. She had complete remission six week later with Protein/Creatinine Ratio <25 mg/mmol, her allograft functioning adequately with Serum Cr of 48 micromol/l. Plasmapheresis was discontinued. She had one episode of relapse with heavy proteinuria which responded well to one dose of Rituximab. She is currently 18 months post Transplant with a stable allograft function and patient status. there was no infectious or noninfectious complications post Rituximab.



Conclusions:
Early use of Rituximab together with PP can dramatically reverse recurrence FSGS and improved graft and patient survival.

P - 163 SUCCESSFUL ENDOVASCULAR EMBOLIZATION OF ARTERIO-CALYCEAL FISTULA AFTER PERCUTANEOUS RENAL BIOPSY IN A 1-YEAR OLD BOY

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Introduction: Percutaneous renal biopsy (PRB), although generally considered as mini-invasive procedure, may lead to serious complications. Arterio-calyceal fistula is one of them.
Case description: In the current report authors present the history of infant, who revealed symptoms of arterio-calyceal fistula after renal biopsy and underwent a successful treatment of that complication. Case report: 1-year old boy (weight 7,5kg) underwent PRB in order to establish the reason for recurrent episodes of renal function impairment. Five months earlier he presented with symptoms of hemolytic uremic syndrome (HUS) developed during zoster infection, with extremely heavy course of the disease (anuria for three weeks). After several procedures of therapeutic plasma exchange he achieved the remission of HUS but persistent proteinuria and recurring AKI episodes not related to HUS were observed.
PRB was performed with single use, semi-automatic biopsy device and monitored by sonography. Massive hematuria was observed immediately during the procedure (seen in catheter placed in urinary bladder). Colour Doppler imaging performed after PRB revealed features of locally enhanced blood flow velocity in the biopsy track, which was interpreted as arterio-venous fistula. Hematuria resolved completely within four consecutive days, but after next 3 days periodic recurrence of massive haemorrhage from urinary tract was observed. After 2 days of ineffective attempts of conservative treatment the patient was referred for renal angiography, which identified the presence of arterio-calyceal fistula. During the same procedure the arterial vessel creating the fistula was selectively catheterized with micro-catheter and embolization with tissue glue was performed. Second injection of contrast confirmed effective obliteration of the vessel. No further recurrences of hematuria were observed.
Conclusions: Highly selective endovascular embolization of arterio-calyceal fistula with the utilization of micro-vascular catheter is an effective way of treatment of this serious post-biopsy complication and prevents even the smallest patients from the necessity of nephrectomy.

P - 164 ATYPICAL HEMOLYTIC-UREMIC SYNDROME IN A CHILD CARRIER OF GENE POLYMORPHISMS OF HEMOSTASIS (CLINICAL OBSERVATION)

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Introduction: To present a clinical case of Atypical Hemolytic-Uremic Syndrome (aHUS) with multiple gene polymorphisms hemostasis.
Case description: The prospective follow-up for 12 months and analysis of medical documentation of patient B.
The disease started acutely in one week after vaccination against influenza with fever, catarrhal symptoms in the throat, icteric skin, rash, vomiting, abdominal pain, macrohematuria, oliguria, hypertension. Thrombotic microangiopathy with clinical and laboratory findings was diagnosed. According to the study: ADAMTS 13 (99%), anti-CFH (9000%), flow cytometry detection of Shiga toxins of types 1 and 2 in the blood (Neg.). Biochemical blood test: urea - 43,32mmol/L, creatinine - 428 mmol/L, LDH-12170 U/L, AST - 121 U/L, ALT - 211 U/L, Coombs test direct and indirect – Neg., Hb - 64 g/l, RBC – 2,2 T/L, PLT 79,0 G/L, shizotsitoz. Urinalysis: protein – 3,87 g/l, leukocytes 26 Leu/µl, gross hematuria. Doppler US of the kidneys - the lack of blood flow in the renal cortex. The diagnosis was Autoimmune aHUS. Acute kidney injury (V stage for Rifle). Pathogenetic treatment - Eculizumab (by the scheme), plasma, peritoneal dialysis (PD). The general condition of the patient has improved, laboratory parameters characterizing the aHUS were

normalized, but preserved renal failure (anuria, hypertension, azotemia). By PCR-mass spectrometry and PCR-restriction analysis were investigated genetic markers of thrombophilia. It was detected next polymorphisms of hemostasis: homozygous carrier- GPIa, PAI-1-4G(-675)5G; heterozygous carrier- F7G10976A, FGBG455A, MTHFRGlu429Ala, MTRRA66G, MTRAsp919Gly. Additionally, appointed a low-molecular-weight heparin (LMWH). Presently the patients condition is stable (urine-400 ml), she receives Eculizumab 300 mg 1 time in two weeks, antihypertensives, LMWH, PD.

Conclusions: Thus, the difficulty of diagnosis and treatment of patient B. with aHUS is a combination of two mechanisms of microcirculatory thrombus formation. In this case, inherited thrombophilia isn't a factor providing its induction, but determines predisposition to hypercoagulation, complicating the course of the underlying disease.

P - 165 A RARE CAUSE OF URETHRAL OBSTRUCTION IN A NEWBORN: ANTERIOR URETHRAL VALVE WITH DIVERTICULUM

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Introduction: Congenital anterior urethral valve (AUV), is quite rare and occurs 15–30 times less frequently than posterior urethral valves, can be difficult to diagnose. Although they are referred to as valves, they often occur in the form of a diverticulum. We present a case of AUV with diverticula herein.

Case description: A term, 2880 gr in weight male baby was born with a history of antenatal hydroureteronephrosis His physical examination was unremarkable except a palpable mass measuring 1.5 cm under the penis and a vesical globe. The infant developed acute kidney injury with increased serum BUN and creatinine, decreased urine output, and urinary tract infection. He was seen by nephrology. A renal ultrasound verified antenatal diagnosis with bladder distension and bilateral hydroureteronephrosis. Urethral catheter could be placed with difficulty and antibiotic was started. A retrograde urethrogram yielded the diagnosis of AUV and diverticula. Suprapubic catheterization (Cystofix) was done and VSUG was performed by this way. Bilateral grade 5 reflux, anterior urethral valve and diverticulum were determined. Suprapubic catheterization resulted in a rapid and complete resolution of the kidney function test.

AUV are congenital mucosal folds constituting a severe obstruction of the urine. The etiology is still controversial, it can be located anywhere in urethra. In our case, it was in penile urethra. Prenatally, it usually present with bilateral hydronephrosis likewise our patient and oligohydramnios. The clinical presentation of AUV is highly variable, our patient had poor urinary stream, a vesical globe, also swelling at the penile urethra, and kidney injury.

Conclusions: AUV can lead to acute kidney injury and urosepsis so it should be kept in mind the differential diagnosis of the causing of antenatal hydronephrosis.

P - 166 MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS ASSOCIATED WITH A MUTATION IN WILMS' TUMOUR SUPPRESSOR GENE 1, A CASE REPORT

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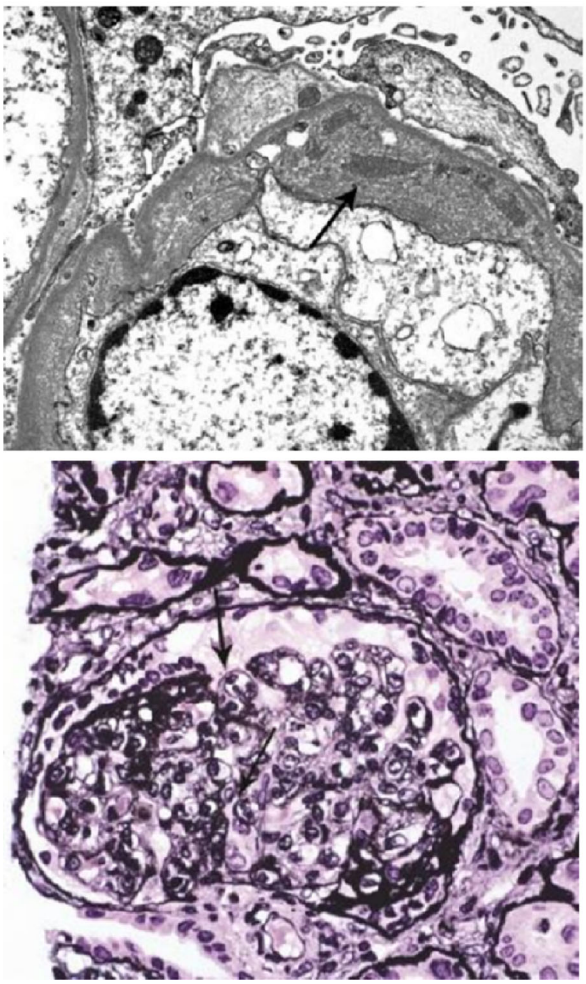
Introduction: Wilms tumour supressor gene 1 (WT1) is linked to diffuse mesengial sclerosis and focal segmental glomerulosclerosis. we described here a rare association between this gene mutation and infantile Membranoproliferative glomerulonephritis (MPGN).

Case description: A 7 months old girl presented with picture of acute kidney injury, associated with persistent miscroscopic hematuria and nephrotic range proteinuria with subtle clinical oedema, foloowing a non specific febrile illness with vomiting and diarrhea. Her initial laboratory investigations showed high urea and creatinine, normal hemoglobin and platelets, normal LDH, low Complement C3, normal soluble membrane attack complex. Kidney biopsy showed picture of MPGN. genetic testing using whole gene sequencing showed heterozygous mutation in exon 9 of the WT1 gene (c.1357T>C p.Cys453Arg). Her clinical course was progressive and despite use of steroids and plasmapheresis, her kidney function never recovered and currently she is on chronic peritoneal dialysis.

Discussion: this association has been described twice previously in the litrature.



Conclusions: WT1 mutation can very rarely associated with MPGN.

P - 167 ACUTE MASSIVE PULMONARY THROMBOEMBOLISM IN A CHILD WITH STEROID-RESISTANT NEPHROTIC SYNDROME

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Introduction: Acute pulmonary embolism (PE) is a rare, but potentially life-threatening complication of nephrotic syndrome which associated with significant mortality in childhood.
Case description: We describe the case of a 2-year-old boy with steroid-resistant nephrotic syndrome (SRNS), complicated by acute massive PE. On admission the boy had severe generalized oedema, blood pressure was 90/50 mmHg. He had proteinuria 3 g/d, hypoalbuminemia 17 g/l, high platelet count $676x10^9$/L, fibrinogen 6 g/l, very high serum D-dimer level >3000 μg/l (NR <300 μg/l) and low antithrombin III level 16% (NR 80-125%), and normal renal function with eGFR 108 mL/min/1.73m^2. He received prednisolone 2 mg/kg/d for 8 weeks without response and kidney biopsywas planned.On the day of performing of kidney biopsy the boy had of unexplained tachycardia to 160 beats/min (95th centile) and *tachypnea to* 50 breaths/min (>99thcentile), his blood oxygen saturation decreased to 93% in room air. His lungs auscultation was normal. His heart sounds were regular, with no added murmurs. The chest radiography was nonspecific. The electrocardiogram showed sinus tachycardia with no any other abnormalities. Cardiac echography demonstrated moderate pulmonary hypertension with the right ventricle dilatation. Computed helical angiographic tomography revealed bilateral proximal massive thrombosis of the pulmonary arteries and acute massive PE was confirmed. Immediate high-dose of unfractionated heparin IV was started with loading dose of 75 IU/kg over 10 min followed by maintenance dose of 20 IU/kg/h by bolus to maintain activated partial thromboplastin time at the range of 60-85 s. The patient proceeded to have emergency open surgical thrombectomy. After surgery long-term anticoagulation with heparin infusion followed by warfarin at a dose of 0.2 mg/kg orally was continued to prevent recurrent of thrombosis. Immunosuppressive therapy of SRNS with Cyclosporine (CsA) was started at a dose of 150 mg/1.73m^2. In one month of CsA therapy the boy achieved of complete remission of SRNS which maintainsfor 6 months. Now he had stable renal function and normal coagulation status maintained by warfarin with his INR at the therapeutic range 2.5-3.0.
Conclusions: We described acute massive PE presented with nonspecific subtle symptoms in the child with SRNS, which needed prompt diagnosis and effective treatment to prevent a fatal outcome.

P - 168 THE CASE REPORT OF IATROGENIC RENAL PHOSPHOLIPIDOSIS

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Introduction: The renal lipidosis are a group of storage disorders that cause generalized or compartmental accumulation of lipid within the kidney. These disorders are classified as primary or secondary. Primary renal lipidosis are rare inherited conditions, such as Fabry's disease. Most secondary renal lipidosis result from the nonspecific metabolic derangements caused by nephrotic syndrome.
Case description: We analyzed the case report with asymptomatic proteinuria.
An 8-year-old boy was referred for persistent asymptomatic proteinuria. As known the first proteinuria (0,33g/l) was diagnosed aged 8 months. Then in the urine constantly observed non-nephrotic proteinuria. Also known that the boy was sick with colds and often received antibiotics. And at the age 2,5 years he was diagnosed with tuberculosis infected about which he received ftivazid. After receiving the proteinuria increased and was about 1 g/day. In the department the physical examination was completely normal. The boys father is ill with chronic glomerulonephritis. Complete laboratory and instrumental examination revealed: urinalysis showed 2,9g/l proteinuria and normal sediment; daily protein excretion was in the nephrotic range (40 mg/m2/h); in the biochemical analysis showed a decrease of total protein (53g/l), albumin(31g/l), increase cholesterol(5,68mmol/l). The renal biopsy was performed to determine the cause of proteinuria. Light and immunofluorescent microscopic examination of the renal biopsy did not reveal any abnormalities, but electron microscopy revealed the electron-dense multilamellar myelin bodies (zebra bodies) within renal tissue. To exclude the Fabry disease we performed α-galactosidase A enzyme level measurements and GLA gene mutation analysis in the patient. He had normal α-galactosidase A levels (64,3 nm / mg / h; range 26,2-96,8 nm / mg / h) and negative GLA mutation analysis.
Conclusions: We have presented the case of a patient with probable iatrogenic phospholipidosis with renal biopsy features morphologically identical to classic Fabry disease.

P - 169 NO EVIDENCE OF RELAPSE IN MCP (CD46) ASSOCIATED ATYPICAL HAEMOLYTIC URAEMIC SYNDROME AT TWO YEARS FOLLOW-UP IN A SIXTEEN-YEAR-OLD BOY INITIALLY TREATED WITH EMPIRICAL PLASMA EXCHANGE. IS TREATMENT WITH ECULIZUMAB ALWAYS WARRANTED?

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Introduction: Atypical Haemolytic Uraemic Syndrome (aHUS) is a heterogeneous disorder associated with complement dysregulation. The overall prognosis is poor, with 25% mortality and 50% progression to end-stage renal disease. A number of mutations in the complement system have been described and prognosis varies according to genotype. *MCP*-mutations are associated with a 70-90% relapse rate, yet the majority of patients remain dialysis independent.
Case description: We report two-year follow-up data on a 16-year-old healthy boy with *MCP*-associated aHUS. Our patient presented with acute kidney injury, thrombocytopaenia and microangiopathic haemolytic anaemia. The diagnosis of aHUS was confirmed according to current UK guidelines and the patient was commenced on corticosteroids, haemodialysis and empirical plasma exchange (PE). PE was performed for 8 days with complete haematologic and renal remission, and corticosteroids were gradually weaned. Complement genotyping demonstrated a heterozygous missense mutation in exon 2 of *MCP* (c.191G>T, p.Cys64Phe). At two years follow-up, there was no evidence of disease activity.
PE is recommended as the first line treatment for aHUS. Evidence to date demonstrates that Eculizumab, a humanised monoclonal antibody terminal complement inhibitor, is superior to PE. Current protocols suggest life-long treatment with Eculizumab Though single *MCP* mutation is associated with a high relapse rate, it carries a good prognosis, and most patients have preserved renal function. PE does not affect outcome in patients with single*MCP*-mutations; consistent with the fact that *MCP* is not a circulating protein.
At two-years follow-up, our patient remained in complete remission without treatment with Eculizumab. There is an increasing body of evidence that the clinical presentation, response to treatment and prognosis are contingent on complement genotype. NICE estimates that Eculizumab costs £340,200 per adult in the first year. Our case supports the consensus that treatment should be individualised according to complement abnormalities, and initial treatment with Eculizumab may not always be warranted.

P - 170 SUCCESSFUL TREATMENT OF ATYPICAL HUS WITH ECULIZUMAB IN EMIRATI CHILD WITH NOVEL DGKE GENE MUTATION

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Introduction: Atypical HUS(a-HUS) is a rare life threatening illness which can result from genetic and autoimmune factors. We are reporting the clinical characteristics and outcomes of a child having a-HUS with a novel gene mutation treated with Eculizumab(Ecu).
Case description: We report the clinical and genetic profile and treatment outcome of a child with a novel DGKE gene mutation on treatment with Ecu. 11 year old Emirati female child was diagnosed with a-HUS at age of 8 months. She had multiple relapsing course(treated with plasma therapy) until Ecu initiation in 2010 . She had recurrence of disease twice post Ecu treatment initiation, the first happened when therapy was interrupted for 6 months and it responded to Ecu resumption. The second recurrence took place when suppression of complement was incomplete as indicated by values of CH50 >10.This was presumably due to Ecu loss in the urine secondary to nephrotic range proteinuria. Subsequently no further recurrences occurred once Ecu dose was increased.
Genetic analysis demonstrated the presence of a novel mutation in the gene coding for DGKE (homozygous for the c.325A>G p.(Lys109Glu) variant in exon 2) . Despite the lack of mutation in genes coding for complement regulating genes, our patient had low complement C3 with some of the recurrences.
Currently she is 2 years post last recurrence, with chronic kidney disease stage 2 ,nephrotic range proteinuria and hypertension on 3 medications.
Conclusions: Novel DGKE gene mutation variant homozygous for the c.325A>G p.(Lys109Glu) variant in exon 2 found in our child has not been reported in literature. Eculizumab has been effective in achieving remission in above patient with this mutation probably suggesting a role for complement activation in pathogenesis of a-HUS in some patients with DGKE mutation.

P - 171 CLINICAL CASE OF THE YEAR: A FETUS WITH LOWER URINARY TRACT OBSTRUCTION

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Introduction: Predicting outcome in fetuses with lower urinary tract obstruction (LUTO) remains a difficult clinical dilemma based on currently available imaging and biochemical parameters. Urinary proteomics hold the promise to improve detection and prognosis at early disease stages of with better accuracy.
Case description: We describe the *in utero* diagnosis of LUTO due to urethral valves in a male fetus of 22 weeks of gestation. Currently available biomarkers were not predictive. The urinary proteomics showed a score highly prognostic for end stage renal disease (ESRD) by the age of 2 years. Because of the severity of renal damage, termination of pregnancy was performed. Severe renal dysplasia was confirmed by a histologic analysis.
Conclusions: Adequate diagnosis, counseling and management of LUTO in fetuses remains difficult clinical dilemma. The prognosis of LUTO in our case remained uncertain based on ultrasound and fetal blood and urine analysis. Fetal urine proteomics analysis predicted a high chance of end-stage renal disease before the age of two years. Post-mortem histologic analysis confirmed severe renal dysplasia with poor prognosis of renal function.

P - 172 EXTREME DISTURBANCES OF ACID-BASE AND ELECTROLYTE HOEMOEOSTASIS IN AN INFANT WITH BARTTER SYNDROME TYPE 4.

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Case description: The patient, born following serial amniotic reductions for polyhydramnios at 32+2 weeks, was noted within days to be polyuric with a marked metabolic alkalosis (venous pH 7.8), hypokalaemia (2.1mmol/L) and renal impairment (urea 20.8mmol/L, creatinine 88-109μmol/L).
The patient experienced persistent serious abnormalities in acid-base (venous pH up to 7.9), potassium (potassium as low as 1.4mmol/L) and volume (hypernatraemic dehydration with sodium up to 173mmol/L) homoeostasis despite treatment with indomethacin and later celecoxib, as well as supplementation with up to 13mmol/kg/day of potassium, 12mmol/kg/day of sodium and volume of 200 ml/kg/day. Complications included repeated episodes of acute kidney injury (creatinine up to 182μmol/L), hypophosphataemic rickets with renal phosphate wasting, intestinal malabsorption, seizures, severe developmental delay and profound hypoventilation with frequent apnoeas. The patient remains uraemic (up to 27mmol/L) with failure to thrive and microcephaly despite adequate feeds. Her eGFR is <30ml/min/1.73m^2. She shows evidence of profound sensorineural deafness. At 8 months of age, medical management with amiloride was trialed in an attempt to stabilize her acid-base and electrolyte balance, albeit at further risk to volume homoeostasis. With this, venous pH improved to 7.5 and plasma potassium to 2.7-3.8mmol/l. In addition her breathing pattern improved, she became more alert and her phosphate wasting resolved. Genetic testing identified a homozygous nonsense mutation in BSND, confirming the clinical diagnosis of Bartter type 4.
Conclusions: The extreme abnormalities of homeostasis experienced in this form of Bartter syndrome are associated with multiple severe complications. Although amiloride treatment worsens the primary problem of salt wasting, this can be managed by appropriate salt supplementation. With treatment, stabilization of venous pH and plasma potassium resulted in a marked improvement of the patient's clinical state.

P - 173 SEVERE PNEUMONIA ASSOCIATED WITH BK VIRUS NEPHROPATHY IN A KIDNEY TRANSPLANTED ADOLESCENT WITH SCHIMKE IMMUNO-OSSEOUS-DYSPLASIA

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Introduction: Schimke immuno-osseous dysplasia (SIOD) is characterized by spondyloepiphyseal dysplasia, immunodeficiency, nephrotic syndrome, and renal failure. We report a case kidney transplanted adolescent with SIOD who developed BKV associated nephropathy (BKVAN) and severe pneumonia.
Case description: An eight-year-old boy with microcephaly and cryptorchidism developed steroid resistant nephrotic syndrome; biopsy revealed focal segmental glomerulosclerosis. He progressed to end stage renal failure and renal transplantation was performed at the age of 15. At first posttransplant year, he had leukopenia with stable serum creatinine level. At the third posttransplant year, he suffered from severe candida esophagitis. Viral serology revealed BKV viruria without viremia. Following reduction in doses of prednisone, tacrolimus and MMF, urine BKV load decreased; 2.5 months later, a sharp increase in serum creatinine occurred. Renal biopsy revealed BKVAN. Prednisone, tacrolimus and MMF were stopped and sirolimus was initiated. Two doses of cidofovir were administered. Though the patient had no spondyloepiphyseal dysplasia, due to recurrent infections, leukopenia and renal involvement, SIOD was suspected.
Analysis of SMARCAL1 revealed a missense mutation on exon 11. Three months later, he developed productive cough, dyspnea and hypoxia. Thorax computerized tomography showed diffuse ground glass appearance on lower lobes of both lungs. Dyspnea and hypoxia deteriorated despite antibacterial and antifungal treatment. Cidofovir injections (2 mg/kg/week) were administered for a probable BKV pneumonia with intravenous immunoglobulin. After 5 doses of sidofovir and intense antibiotic regime, clinical and radiological improvement was achieved.
Conclusions: Recurrent and severe infections following renal transplantation may be suggestive of immune deficiency with mild forms. BKVAN can develop without viremia. BKVAN and associated pneumonia were treated successfully with cidofovir and reduction of immunosuppressive drugs in a kidney transplanted adolescent with SIOD.

P - 174 THE EFFECT OF VAGUS NERVE STIMULATION ON BLOOD PRESSURE - CASE STUDY IN 2 PATIENTS

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Introduction: Sympathetic overactivity is a known risk factor for hypertension. There has been several attempts to treat hypertension by influencig sympathetic part of the autonomous nervous system. However, it is not known, whether there is an impact of parasympathetic stimulation on blood pressure in children and adolescents with pharmacoresistant epilepsy, treated with vagus nerve stimulation (VNS). This method has already been proved to be effective in reducing seizures in patients with pharmacoresistant epilepsy.
Cases description: Two female patients with pharmacoresistant epilepsy, aged 19 and 8 years, were evaluated prospectively. 24-hour ambulatory blood pressure monitoring was done in both of them before and after the surgical implantation of VNS device (205 blood pressure measurements). Both patients were without seizures and used the same drugs during the time of the study, thus eliminating their potential influence on blood pressure. We compared blood pressure in both patients before and after VNS treatment (expressed as average +/- standard deviation) and tested the statistical significance of difference with a students t-test.
Average blood pressure in older patient was 106.1/66.8 mmHg (+/- 14.8/14.7 mmHg) before and 105.0/64.5 mmHg (+/- 10.5/10.6 mmHg) after 2 years of VNS treatment. Average blood pressure in the younger patient was 97.1/58.1 mmHg (+/- 9.8/9.9 mmHg) before and 101.0/60.8 mmHg (+/-8.5/10.3 mmHg) after 4 months of VNS. The difference was statistically non-significant in both patients.
Conclusions: The vagus nerve stimulation, althouh theoretically a promising idea, did not result in a significant reduction of blood pressure in our 2 patients. The limitation is a small number of patients in this pilot study and the presence of normal blood pressure at baseline. Perhaps the influence of parasympathetic stimulation might be significant in patients with elevated blood pressure. We aim to continue the study in VNS epilepsy patients to better understand the possible underlying pathophysiological mechanisms.

P - 175 ECULIZUMAB IN THE TREATMENT OF DENSE DEPOSIT DISEASE

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Introduction: Dense deposit disease (DDD) is associated with nephrotic or nephritic syndromes, progresses with hypertension and frequent kidney failures. Defects in alternative complement pathway cause to DDD. Eculizumab is the C5 monoclonal antibody that may be effective for the treatment of DDD by blocking the end products in the complement pathways. We present two patients with DDD and eculizumab usage in their treatment.
Cases description:
Case 1: A 12-year-old boy with nephritic syndrome, a renal biopsy was performed because of the aggravation of proteinuria and treatment resistant hypertension. He had seizures related PRES. Laboratory tests revealed also increased creatinine level, microangiopathic hemolytic anemia, thrombocytopenia and low C3 level. Biopsy result was suitable with active DDD. C3NeF was positive. Despite treatment with methylprednisolon, cyclophosphamide and plasma exchange, hematuria and proteinuria continued. Eculizumab treatment was initiated. Treatment with eculizumab achieved complete control of renal symptoms and hypertension. The patient has been receiving eculizumab every month during follow-up. Genetic screening is still on process.
Case 2: An 11-year-old boy with nephrotic syndrome developed resistant hypertension and seizures. He was diagnosed as lupus nephritis and he was treated with methylprednisolon, cyclophosphamide, intravenous immunoglobulin, plasmapheresis and rituximab before admission to our center. Laboratory tests at admission revealed microangiopathic hemolytic anemia thrombocytopenia, renal failure and low C3 and C4 level. Biopsy was performed because of the crescent formation. C3NeF was positive. Plasma exchange and eculizumab treatment was initiated. Despite this treatment serum creatinine was elevated and renal function worsened. During follow-up, routine dialysis was started. Genetic screening is still on process.
Conclusions:
Eculizumab can be an effective treatment in DDD. Although it cannot be always improve renal function. Different genetic and clinical factors can affect the prognosis of the disease. However more studies should be done in order to understand the efficacy of eculizumab in children with DDD.

P - 176 PROPHYLACTIC ECULIZUMAB THERAPY FOR ATYPICAL HEMOLYTIC UREMIC SYNDROME IN A PEDIATRIC RENAL TRANSPLANT PATIENT

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Introduction:
Atypical hemolytic uremic syndrome (aHUS) is observed with microangiopathic hemolytic anemia, thrombocytopenia and acute renal failure.

The results of the kidney transplantation are not satisfactory due to recurrence risk of aHUS and graft loss. The use of prophylactic eculizumab before and after transplantation can change this outcome. We present a transplanted child, who has renal failure due to aHUS and the usage of prophylactic eculizumab before and after the transplantation.
Case description: A boy, diagnosed with aHUS at the age of 2.5 years, developed chronic renal failure in spite of the plasma infusion and exchange. He was taken into peritoneal dialysis programme. A renal transplant from the father was performed on the patient at the age of 4 years. CFH, CFI, C3 levels were normal before transplantation both for recipient and donor. Genetic mutation analysis is still under process. Five sessions of daily plasma exchange were performed before transplantation. Prophylactic eculizumab was used one day before the transplantation, and he was provided with eculizumab within the first day after the transplantation, and once in a week during the 4-week period. After 4th dose, eculizumab was continued every 2 weeks. During follow-up creatinine, hemoglobin, platelet and LDH levels were monitored at normal levels. There was no evidence of recurrence in follow-up period.
Conclusions:
Eculizumab is an effective and safe therapy for preventing disease recurrence and maintaining graft functions in patients with aHUS. Large studies are needed for identification of optimal treatment duration and definite treatment protocol.

P - 177 RELAPSING NEPHROTIC SYNDROME AS A CONSEQUENCE OF [IMMUNE-DEPOSIT-NEGATIVE] NON-IGA MESANGIOPROLIFERATIVE GLOMERULONEPHRITIS" IN A 4 YEAR OLD AFRICAN GIRL.

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Introduction:
We report a 4-year-old African girl presenting with steroid dependent nephrotic syndrome in whom renal biopsy shows the rare entity of "non-IgA mesangioproliferative glomerulonephritis".
Case description:
Her renal history starts in 2014 when she was admitted to a PICU service with hypertension, and fluid overload. Lab tests: severe hypoalbuminemia (8 g/L), proteinuria (4+), hematuria (3+) and renal failure (eGFR:91.5 ml/min/1.73 m² Schwartz Paediatric GFR). Chest X-ray revealed pneumonia and post-infectious glomerulonephritis was suspected. Renal biopsy showed mainly mesangioproliferative changes with some degree of endocapillary proliferation. IF: negative for IgA, IgM, C3 and C1Q. IgG weakly positive. EM: no deposits. Treatment: diuretics, human albumin and steroids (60 mg/m² QD for 6 weeks, 40 mg/m² alternate day for 4 weeks, followed by steroid taper) and went into complete remission. During steroid taper she developed a relapse of severe nephrotic syndrome (protU 52 g/g creat) with ascites; ultrasound: inhomogenous liver and bilateral nephromegaly. Lab values: normal/negative for CRP, C3 (2/3 samples, 1/3:decrease), C4, IgA, presence of M protein, CIC, ANF, ANCA, a-PLAP2-R, cryoglobulins, HCV, HIV, Hep.A, Mycoplasma (PCR) and mycobacterium tuberculosis (PCR). Alfa-1-antitrypsine low (69 mg/dl-genetic testing running). C3d mildly elevated. (Second) renal biopsy was performed which again showed prominent mesangioproliferative glomerulonephritis with some degrees of focal endocapillary proliferation. IF: negative except for trace IgM. She was again treated with high dose steroids + cyclosporin, which resulted in complete remission.
Conclusions:
We propose our patient suffers from steroid resistant nephrotic syndrome attributable to the uncommon entity "*immune-deposit negative non-IgA Mesangioproliferative glomerulonephritis*" (MesProl-GN), a mesangioproliferative GN distinct from IgA nephropathy, C1Q nephropathy and IgM nephropathy. This disease seems to be prevalent mainly in developing countries. >90% of patients present with nephrotic syndrome:60% steroid responsive, 20% steroid dependent, the remaining 20% steroid resistant. Steroid dependent cases generally respond well to Tacrolimus.

P - 178 HETEROZYGOUS ACTN4 GENE NOVEL MUTATION PRESENTED AS INFANTILE NEPHROTIC SYNDROME: CASE REPORT AND REVIEW OF THE LITERATURE

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Introduction:
Infantile onset nephrotic syndrome is one of the challenging cases for us as pediatric nephrologists. It has a wide array of differential diagnosis. In most of instances it is resistant to steroid therapy. In areas where consanguineous marriage is prevalent the hereditary causes should be considered. ACTN4 gene mutation is one of the causes underlying familial focal and segmental glomerulosclerosis (FSGS) and it is usually autosomal dominant. Overall ACTN4 mutations seem to account for 4% of familial FSGS.
Case description:
Our patient is a 20month old Saudi male who presented with a picture of nephrotic syndrome at the age of 6 month. He was referred to our center by the age of 9 months. A full panel of workup was done including renal biopsy and full genetic study. Lab investigations were consistent with nephrotic syndrome. Renal biopsy of the patient revealed FSGS. His gene panel revealed a heterozygous c.2680G>A (p.Gly894Ser) variant in the ACTN4 gene.
Conclusions:
Review of literatures revealed few reported cases of FSGS with ACTN4 gene mutation. The usual presentation described in the literatures is in the teenage years or later. So, we report this case as the first reported one with FSGS secondary to ACTN4 gene mutation that clinically presented before the first birthday. In addition, the detected ACTN4 gene mutation in our case is a novel one that might explains the early onset of clinical presentation.

P - 179 A CASE OF POST-TRANSPLANT THROMBOTIC MICROANGIOPATHY SUCCESSFULLY TREATED WITH ECULIZUMAB

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Introduction: De novo thrombotic microangiopathy (TMA) is a rare post-transplant complication which may lead to graft loss. It may be due to various reasons, mainly calcineurin inhibitor use or antibody mediated rejection.In this report we present a case of TMA manifested in

early post-transplant period, which was successfully treated with eculizumab.

Case description: A 17 year-old boy who had been on peritoneal dialysis for 5 years received a kidney transplant from a 64 year-old HLA 3 mismatch deceased donor; cold ischemia time was 13 hours. He received induction therapy with prednisolone and anti-thymocyte globulin. He had no urine output on the first day; renal artery was intact on Doppler ultrasonography. Acute tubular necrosis was primarily suspected as the donor was marginal. At the end of the first week, as graft function did not improved, a renal biopsy was performed which was consistent with TMA.Hemoglobin, thrombocyte and lactate dehydrogenase values were within reference ranges; panel reactive antibody (PRA) class I was 10% and class II 33% positive. Tacrolimus was switched to everolimus; also, as antibody mediated rejection could not be ruled out, plasmapheresis therapy was initiated. On the post-transplant 29th day, after 10 sessions of plasmapheresis, when serum creatinine was 3.23 mg/dl, a therapy with eculizumab was introduced.

After the third dose of eculizumab, serum creatinine declined to 1.68 mg/dl. On the post-transplant 5th month, he was receiving eculizumab every 14 days in addition to everolimus, mycophenolate mofetil and prednisolone, and his urine output was 2500 ml/day with a serum creatinine of 1.58 mg/dl and estimated glomerular filtration rate of 45.5 ml/min/1.73 m2

Conclusions: The therapy options of post-transplant TMA is limited. Eculizumab may be an alternative regimen in TMA, which could potentially cause graft loss if not treated appropriately.

P - 180 PARVOVIRUS ASSOCIATED ANAEMIA IN A RENAL TRANSPLANT ADOLESCENT

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Introduction: Anaemia is a important problem in renal transplant recipient and has several etiologies. Human parvovirus B19 may lead to persistent viraemia, erythropoietin resistant pure erythroid aplasia and also may trigger acute rejection that cause chronic renal graft dysfunction in renal transplant recipient. In this case we present parvovirus related anaemia in an adolescent renal transplant receiver who responded to intravenous immunoglobulin (IVIG) treatment.

Case description: 17 years old boy was on a chronic haemodialysis program last three years that received a decased donor kidney transplant. immunosuppressive treatment with prednisolone, tacrolimus and mycophenolate mofetil was then initated. Anemia occur in the first month. Serologic examinations regarding viral infections revealed CMV, EBV and BKV (-) results. Anaemia-related assessments revealed aplastic crisis. Parvovirus B19 PCR was very high. Immunosuppressive drug doses were held constant for the following five days of 400 mg/kg IVIG treatment.

HPV B19 does not have a specific antiviral drug, hence reduction of immunosuppressive treatment and/or IVIG may be helpful. In this case we present parvovirus related anaemia in an adolescent renal transplant receiver who responded to intravenous immunoglobulin (IVIG) treatment.

Conclusions: When anaemia with reticulocytopenia develops in renal transplant recipient, a possible parvoviral infection must be considered. The treatment of patients depend on the clinical setting, and additional IVIG treatment in patients with allograft dysfunctioning can lead to positive results.

P - 181 POSTERIOR URETHRAL VALVES IN ASSOCIATION WITH OESOPHAGEAL ATRESIA

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Introduction: Urinary tract anomalies are the second most common defects associated with oesophageal atresia after cardiac defects. Describing these anomalies may elucidate developmental pathways.

Case description: A male infant born at 33 weeks gestation to healthy unrelated young parents had an antenatal diagnosis of hydroureteronephrosis and thickened bladder wall but with normal amniotic fluid volume. He was catheterised at birth. Oesophageal atresia with tracheo-oesophageal fistula was diagnosed after failure to pass a nasogastric tube. The fistula was closed on day 1 but attempts at end-to-end anastomosis of the oesophagus resulted in severe bradycardia requiring cardiac massage so anastomosis was performed a few days later. Creatinine dropped from 200umol/l to 83umol/l by week 3. At this time posterior urethral valves were ablated at cystoscopy. He had a small atrial septal defect which closed spontaneously but no vertebral, anorectal or limb anomalies. Medical treatment for chronic kidney disease was optimised. He developed Enterococcal meningitis aged 4 weeks with negative blood and urine cultures. He also required repair of an inguinal hernia and circumcision.

DMSA scan at 4 months of age showed left 96% function and a left loop ureterostomy was performed because of increasing left hydroureteronephrosis on ultrasound. By 5 months he was not thriving and had recurrent urinary tract infections. Intervening bowel loops necessitated laparoscopic-assisted PEG insertion during which multiple hernias of Morgagni were noted and repaired. Feeding was optimised and he thrived with no further UTIs. At 16 months he sustained two near-miss choking episodes secondary to oesophageal dysmotility and he required oesophageal dilatation on one occasion. He had cochlear implants inserted because of sensorineural hearing loss. His creatinine remained stable at 60-70umol/l during this time.

Conclusions: We present a male infant with oesophageal atresia, tracheo-oesophageal fistula, multiple hernias of Morgagni and, uncommonly, posterior urethral valves with stable renal function at 18 months.

P - 182 DETERMINING THE ETIOLOGY OF PEDIATRIC HYPERTENSION; A HARD NUT TO CRACK

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Introduction: It is imperative to differentiate between primary and secondary hypertension in the pediatric age group before settling the diagnosis. A proper long term treatment plan would be difficult without such differentiation. Finding the cause of secondary hypertension can be a challenging task. It usually requires meticulous clinical evaluation with possibly extensive medical imaging and laboratory investigations.

Case description: Hereby we present a twelve year old female with Fanconi anemia who underwent hematopoietic stem cell transplantation twice. Post 2nd transplant, she received cyclosporine as Graft versus Host Disease (GvHD) prophylaxis. Unfortunately, she developed complications like hypertension and electrolyte imbalance (hypokalemia, hypophosphatemia and hypocalcemia). Subsequently, cyclosporine was stopped and Mycophenolate mofetil (MMF) (75 mg/kg/day) was used as an alternative. However, hypertension persisted turning into unresponsive disease despite multi-drug antihypertensive regimen. Such morbidity was thoroughly investigated to look for the underlying etiology.

Cardiac causes of hypertension like coaractation of the aorta was excluded through echocardiography. Moreover, both types of renal hypertension (parenchymal and vascular) were ruled out via renal ultrasound, DMSA scan, kidney function tests and CT angiography of the renal vessels respectively. Endocrine causes of hypertension were screened by checking

urinary levels of valinylmandelic acid and homovanilic acid (VMA&HVA) along with serum cortisol levels and renin-aldosterone profile. Finally, endocrine workup revealed hyperaldosteronism with normal renin. A complete review of her medications chart and their side effect, revealed that the MMF could beth cause of hyperaldosteronism. MMF has been rarely linked to such an adverse event. Accordingly, MMF dose was reduced and the aldosterone level normalized rendering the hypertension easily tamed.

Conclusions: MMF-induced hyperaldosteronism has been scarcely reported in the literature, and to our knowledge never in pediatric age group. This case emphasizes the role of medications in causing morbidities such as hypertension.

P - 183 PROTEUS SYNDROME – NEPHROLOGICAL AND ONCOLOGICAL CHALLENGE

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Case description: Girl with congenital feet hypertrophy with hexadactyly presented at the age of 22 months with haematuria. Wilms tumor in the right kidney was found. The patient unterwent oncological treatment including right side nephrectomy and chemotherapy. After 6 months right ovary multicystic tumor had to be removed. At the age of 4 years nephroblastoma of the left kidney was diagnosed. Nephron sparing surgery of the remaining kidney was possible and chemotherapy was prolonged over 15 months.

4 years later the angioma in left hip region and small pelvis was diagnosed. The lower part of the body showes progressing hypertrophy. Vulnerable skin lesions of nevus and angioceratoma type developed in axillar and iliacal regions and needed sclerotisation.

The patient stays under supervision of nephrologist because of persistent massive haematuria and small nephron mass. GFR measured with Iohexol test at age 13 showed diminished kidney function (77 ml/min/sBSA). Microalbuminuria 50 mg/d was the indication for nephroprotection with ACEI. The reason of hematuria stays unclear (pelvis angioma infiltrating ureters?).

Conclusions: Proteus syndrome is a very rare disease with progressive body deformations and vessels malformations cased by genetic mosaicysm with activating mutation of AKT1 kinase gene. The main complications are thrombosis and pulmonar embolism. At the age of 18 years the patient should be sent to adult center with multidisciplinary profile, which seems to be another challenge.

P - 184 BILATERAL FUNGUS BALLS PRESENTING WITH ACUTE RENAL FAILURE IN A PRETERM INFANT

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Introduction: Fungus balls in the renal pelvis is a rare cause of acute kidney failure among newborns and infants.

Case description: A 5-month old male presented with respiratory problems and decreased urine output. Past medical history revelaed that he was diagnosed as acute pyelonephritis and treated with several broad-spectrum antibiotics when he presented with fever and vomiting 45 days ago. He was born as 26 weeks with a weight of 680 grams and stayed at NICU for 75 days; he had been on mechanical ventilation for 45 days. There was no consanguineous between his parents. On admission, he had hypertension (100/60 mmHg), tachycardia (152 bpm), tachypnea (72/min). His height was 43cm (<3p) and weight 2700gr (<3p). He had generalized edema and signs of pulmonary edema. Abdomen was distended and both kidneys were easily palpable. Hemoglobin was 9.0 g/dl, leukocyte 21.700/mm3, platelet 203.000/mm3, C-reactive protein 21.7 mg/dl, procalcitonine 32 ng/ml, BUN 55 mg/dl, serum creatinine 3.8 mg/dl with an estimated glomeruler filtration rate (eGFR) of 6.8 ml/min/m2. Urine analysis revealed positive leukocyte esterase and nitrite test; urine microscopy showed 12 leukocyte per area and fungus cells in yeast morphology. Both blood and urine cultures were positive for Candida albicans. An ultrasonography showed enlarged kidneys (right 77 mm, left 70 mm) with bilateral grade 3 hydronephrosis accompanied by multiple milimetric cysts consistent with bilateral fungus balls in both renal pelvises completely obstructing.

Bilateral nephrostomy catheters were inserted and a therapy with both systemic and localized (via nephrostomy) liposomal amphotericin B was started. His renal functions recovered rapidly. Left and right fungus balls diasappeared on US at the 12th day and 8th week of therapy, after when treatment was stopped and he was discharged.

Conclusions: Children who are born premature and treated in NICU with broad spectrum antibiotics should be evaluated for UTIs caused by fungus.

P - 185 THE COURSE OF ATYPICAL HEMOLYTIC UREMIC SYNDROME IN PATIENT WITH CFI MUTATION

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Introduction: Atypical hemolytic uremic syndrome (aHUS) is a multisystem pathology with high-risk of death. The long-term prognosis, treatment efficacy and outcome oftransplantation may be indicated by the results of genetic screening.

Case description: 3-year-old girl got sick with a fever, cough, anuria (09-07-08). Coombs-negative anemia (Hb 54 g/l, schistocytosis), thrombocytopenia (80 thousand/mcl), hyperasotemia (Ur 19 mmol/l, Cr 230 mcmol/l), respiratory insufficiency, fluid-electrolyte imbalance, arterial hypertension was diagnosed on 11-07-08. Duration of anuria was 18 days. Hemodialysis (№ 30), infusion of fresh frozen plasma (FFP) was conducted. Diuresis recovered gradually, Hb 104 g/L, PLT 180 thousand/mcl, proteinuria 1.65 g/l, reduction of azotemia (Ur 16,6 mmol/l, Cr 120 mcmol/l). After 2 months stupor, convulsions, dyspnea, anasarca was developed, Cr 500 mcmol/l, LDH 750 U/L, Hb 93 g/L, PLT 226 thousand/mcl.

Renal biopsy revealed chronic thrombotic microangiopathy(05-11-08). FFP №12 and one plasmaexchange was used. ESRD with started of dialysis developed after 1year. Relapse of aHUS after 3 years started with abdominal pain, exsicosis, BP 145/95 mmHg, the blood amylase 3687 units/l, Hb 88 g/L, PLT 90thousand/mcl, C3 43 mg/dl, LDH 780 U/l, Ur 27.4 mmol/l, Cr 667,2 mcmol/L, ADAMTS-13 49.5%. Pancreatonecrosis was diagnosed as aHUS complication. Mutation of CFI (exzon 2) c.191C<T (p.Pro64Leu) was revealed. Ekulizumab was started in December, 2012. 22-08-14 aHUS relapsed with haemorrhagic rash, BP 170/100 mmHg., Hb 85 g/L, PLT 86 thousand/mcl) after discontinuation of Eculizumab therapy. Monoclonal antibody therapy resumed. 12-03-15 kidney transplantation was performed without discontinuation of Eculizumab.

Conclusions: aHUS is a multisystem disease with outcome in ESRD and extrarenal complications in the form of pancreaticnecrosis, cerebrovascular disorders, arterial hypertension. Eculizumab therapy made it possible to avoid combined liver-kidney transplantation. The patient belongs to the group of medium-risk of recurrence after renal transplantation and needs further treatment of Eculizumab.

P - 186 CRYPTOCCOCAL MENINGITIS IN THE PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND CD4+ LYMPHOCYTE DEFICIENCY

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Introduction: Opportunistic infections are not frequently seen in systemic lupus erythematosus (SLE), but they could be fatal in the majority of cases. Immunosuppressive therapy is the strongest risk factor but there are other factors predisposing to infection in SLE patients and some of them are related to the disease itself.
Case description: We present a patient with the previously known SLE, whose renal disease reactivation was complicated by a series of potentially fatal infections.
Seventeen years old male patient was diagnosed with SLE at the age of 13. Initial renal involvement was classified as diffuse global proliferative lupus nephritis. Euro -Lupus protocol was performed and the complete remission achieved.
At the beginning of the second relapse renal biopsy had been repeated and diffuse global proliferative and sclerosing lupus nephritis was confirmed.
The third Euro - Lupus had just started, when Salmonella sepsis occurred and the therapy resulted in complete recovery. At the time for 6th cyclophosphamide, headache and double vision appeared. Cranial CT revealed hydrocephalus. CSF analysis showed pleocytosis, mild proteinorachia and severe hypoglycorachia. At the CSF sediment smear Cryptococcus neoformans (CN) had been found and confirmed by CSF culture. Dual antifungal therapy during 4 weeks was performed. Two weeks later inercurrent Pneumococcal sepsis was resolved by standard therapy. After CSF culture and sediment smear had become negative for CN, the patient was discharged with fluconazole and 15 mg of prednisone.
Three weeks later he was readmitted with the relapse of cryptoccal meningitis. This time, beside standard therapy, flucytosine had been used. Clinical recovery was complete, CSF culture sterile and direct smear normal. Flow cytometry, repeated twice, revealed low number of CD4+ lymphocytes. Selective IgA deficiency was also found.
After a year, our patient is in the remission of SLE, on 10 mg of prednisone and fluconazole prophylaxis.
Conclusions: Underlying systemic disease, longstanding strong immunosuppressive therapy and congenital deficiency, could cause low CD4+ lymphocytes level and consequently, our patient's susceptibility to opportunistic infections.

P - 187 AN UNUSUAL PRESENTATION OF CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME IN AN ADOLESCENT

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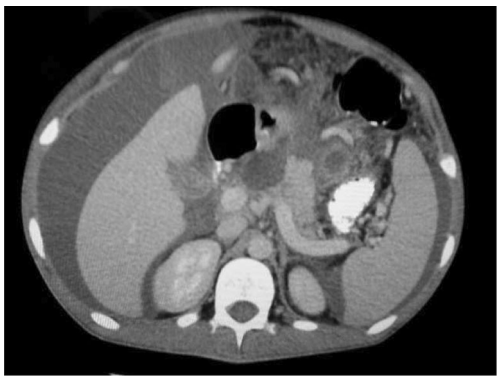
Introduction: Antiphospholipid syndrome (APS) is characterised by recurrent thromboses in the presence of circulating antiphospholipid antibodies. Catastrophic antiphospholipid syndrome (CAPS) is a rare and accelerated variant of APS affecting mainly microvasculature. CAPS may evolve primary or secondary to autoimmune diseases particularly during the course of systemic lupus erythematosus (SLE).
Case description: Here we present a 17 year old male admitting with headache. Medical history was unremarcable except a convulsive episode passed prior to day before admission. Physical examination revealed a blood pressure of 160/90 mmHg with normal systemic findings. Laboratory investigations revealed, hypokalemia, metabolic alcalosis thrombocytopenia with positive direct coombs test and nephrotic range proteinuria in urinary examination. In urinary ultrasonography (US) middle and lower pole of left kidney was found atrophied. Doppler US of renal artery revealed total occlusion in the left main renal artery due to thromboses. Antinuclear antibodies (ANA) and anti double stranded dna (ds-DNA) was positive by immunoflorescent assay. Direct coombs test, antiphospholipid antibody (APL), anti cardiolipin antibody (ACL) and lupus anticoagulant tests were positive in high titers. Brain MRI scan showed multiple subcortical lesions located on the cerebellar and cerabral hemispheres, especially on the parietal and frontal cortex, interpreted as secondary process which indicates an inflamatory demyelinating lesion. On 19th day of clinical follow up, patient was diagnosed as acute necrotising pancreatitis while evaluating for abdominal pain (figure-1). Renal biopsy, performed from normal kidney showed findings compatible with class-2 lupus nephritis. The patient was accepted as probable CAPS secondary to SLE with central nervous system, renal and gastrointestinal system involvement developed in a short period of time. The patient was treated succesfully with warfarin, steroid, cyclophosphamide, plasma exchange and IVIG.



Conclusions: Although mortality due to CAPS is still high, with prompt diagnosis and early multimodal therapeutic interventions , it is not a rule to be fatal.

P - 188 CHRONIC INAPPROPRIATE ANTIDIURESIS IN CHILDHOOD. EXPERIENCE WITH TOLVAPTAN

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Introduction: The syndrome of inappropriate antidiuresis (SIAD) is one of the most common causes of hyponatremia: it's a disorder of sodium and water balance, characterized by urinary dilution impairment and hypotonic hyponatremia, in the absence of renal disease or any non-osmotic stimulus, able to induce antidiuretic hormone (ADH) release. SIAD can be manifestation of a wide range of diseases, including cancer, head trauma, hydrocephalus and epilepsy. Usually transient and self-limited, is easily controlled in the short term with fluid's restriction and sodium supplementation. More difficult is the management of the chronic SIAD, especially in children. We report our experience with tolvaptan, an orally active vasopressin V_2-receptor antagonist that promotes aquaresis.
Case description: The efficacy of tolvaptan was evaluated in a 4 years old child with chronic hyponatremia after surgery for suprasellar arachnoid cyst. Patient was assigned to oral tolvaptan at a dose of 3.75 mg daily (0.46 mg/Kg/die). Serum sodium concentrations achieved to 127-131 mEq/L and the drug was well tolerated, without any side effects.

Therefore, the dose of tolvaptan was increased to 7.5 mg daily, based on serum sodium concentrations and kidney function.
Aquaretic drugs induce an increase in urinary volume and urinary free water, associated with a decreased urinary osmolarity with a consequent increase in plasma sodium. This belong to a family of vasopressin receptor antagonist, V_2 in particular, that regulate tubular water reabsorption. Tolvaptan has increased serum sodium concentration, allowing liberalization of the water's introit and suspension of oral supplementation of NaCl.
Conclusions: In our little patient with euvolemic hyponatremia, tolvaptan was effective in increasing and maintaining serum sodium concentrations, with values greater than 130 mEq/L, without side effects and allowing the child a free fluid intake and diet.

P - 189 ATYPICAL HEMOLYTIC UREMIC SYNDROME IN CHILD: A CASE REPORT.

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Introduction: Atypical hemolytic uremic syndrome (aHUS) is a rare disease related to genetic mutations in the alternative complement pathway. Diagnosis of aHUS relies on 1) No associated disease 2) No criteria for Shigatoxin-HUS 3) No criteria for thrombotic thrombocytopenic purpura. New approach in therapy of aHUS is the application of humanized monoclonal antibody against complement component C5 - eculizumab.
Case description: a 4-year-old girl presented to the emergency department of our hospital with complaints of atony, icteritiousness, repeated vomiting. The childs condition is assessed as severe due to the uremia, hemorrhagic syndrome, anemia. Objective status: sopor, facial swelling, skin pallor, ochrodermia, petechial hemorrhage, ecchymosis on her hands, blood pressure 130/80 mm Hg, hepatosplenomegaly, oliguria during the day. Laboratory: hemoglobin 79 g/L, platelets 50,000, schistocyte 2%, reticulocytosis, increased indirect bilirubin, lactate dehydrogenase 1365,4 E/L, reduction of complement component C3 to 56 mg/dl, azotemia, glomerular filtration rate 53 ml/min, metabolic acidosis, proteinuria, ADAMTS-13 level was 79%. Exhibited diagnosed aHUS. Disease progression led to the development of stage V of chronic kidney disease. Hemodialysis was started for treatment 3 times a week. The child received dialysis for 4 months. Given the lack of response to therapy, eculizumab was prescribed by scheme. Within the first week of takeneculizumab, a significant improvement of all clinical and laboratory parameters was observed. After 7 months of therapy, hemodialysis was cancelled. Currently, all laboratory parameters within the normal range. The child continues receiving eculizumab. Eculizumab did not cause side effects.
Conclusions: the described case report demonstrates the importance of knowledge criterion of aHUS and positive dynamics on the background of eculizumab therapy, which should be received by patient through out life.

P - 190 IMPROVEMENT IN RENAL FUNCTION AFTER ISOLATED PRE-EMPTIVE LIVER TRANSPLANTATION IN A 15-MONTH-OLD CHILD WITH PRIMARY HYPEROXALURIA TYPE 1

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Introduction: Primary hyperoxaluria type 1 (PH1, MIM #259900) is a rare autosomal recessive inborn error of glyoxylate metabolism, caused by mutations in the *AGXT* gene (MIM#604285), leading to the overproduction of endogenous oxalate and progressing to end-stage renal disease (ESRD) during childhood or adolescence in majority of patients.
Case description: We report our experience of improvement in renal function and reduction of urinary oxalate excretion after isolated preemptive liver transplantation (PLT) in a child with PH1.
A 3-month-old girl, first child of healthy unrelated parents, presented with urinary tract infection and ultrasound signs of medullary nephrocalcinosis. There was no familial history. On admission her weight was 6.1 kg (25^{th} centile) and height 62 cm (25^{th} centile). She had increased 24-h urinary oxalate to creatinine ratio (Ox/Cr) 0.91 mmol/mmol (reference range (RR) <0.37), bilateral medullary nephrocalcinosis stage 3, and serum creatinine level 39 μmol/L with eGFR 63.3 mL/min/1.73m^2. Direct selective sequencing of the *AGXT* gene showed a heterozygous compound missens c.508G>A (p.Gly170Arg; rs121908529) and frame-shift c.33dupC (p.Lys12Glnfs; rs398122322) mutations and PH1 was confirmed. Supportive therapy to prevent renal failure using oral pyridoxine was administered with progressively increased doses from 5 to 20 mg/kg/d. High fluid intake was started with tube feeding of 3 L/1.73m^2/d for stone prevention, citrates supplements were used to inhibit urinarycrystallization. After 3 months of high doses of pyridoxine therapy her urinary oxalate excretion was not decreased (Ox/Cr 0.88 mmol/mmol; RR <0.26) and non-sensitivity to pyridoxine was suggested. By the age of 13 months the girl had stable decreased eGFR 41.5 mL/min/1.73m^2, hyperkalemia 5.74 mmol/L, increased 24-h urinary Ox/Cr to 0.65 mmol/mmol (RR <0.26). Her 35-year-old father decided to be a donor for an PLT. At the age of 15 months isolated orthotopic PLT of left lateral sector was performed to avoid the complications of systemic oxalosis before further eGFR declining. The immunosuppressive protocol included methylprednisolone (4 mg/d), mycophenolic acid (360 mg/d), and tacrolimus (3 mg/d). Her renal function was improved with eGFR to 93.9 and 116.4 mL/min/1.73m^{2}at 6 and 12 months after PLT, respectively. The 24-h urinary Ox/Cr was decreased to 0.37 mmol/mmol and 0.13 mmol/mmol (RR <0.14) at 6 and 12 months after PLT, respectively. Ultrasound revealedimprovement of medullary nephrocalcinosis from previously homogenous to heterogeneous appearance. 16-months after PLT her liver graft is functioning well.
Conclusions: We presented the case of improvement in renal function and reduction of urinary oxalate excretion after successful isolated living related PLT in a child with infantile form of PH1. With early diagnosis of PH1, isolated PLT may prevent progression to ESRD and the need for kidney transplantation.

P - 191 RENAL MASS IN A TWO YEARS OLD GIRL: XANTHOGRANULOMATOUS PYELONEPHRITIS

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Introduction: Xanthogranulomatous pyelonephritis is a severe, atypical form of chronic renal parenchymal infection often mimicking neoplastic renal disorder. It is rare in the pediatric age group.
Case description: A 2-year-old girl was admitted for anorexia, abdominal pain, fatigue, weight loss. Abdominal sonography was charectirezid by atropic left kidney having a 2 cm mass lesion with hypoechogenic solid and cystic area while static renal scintigraphywith 99m Tc-DMSA

demonstrated no function in the affected kidney. Magnetic resonance imaging disclosed atropic left kidney with a mass located in the middle, near the pelvicalcyeal system. Multiple pathologic lypmh nodes were seen near the mass and paraaortic region.
Explorative surgical exsicion of non functional kidney for histological examination showed extensive mixed chronic cellular infiltrate and mostly foamy histiocytes. She is doing well and started to gain weight at 4-month of follow up.
Conclusions: Here, we present a 2-year-old girl with xanthogranulomatous pyelonephritis to emphasis in the differential diagnosis of renal mass.Being suspicious fot XP is mandatory the correct preoperative diagnosis and appropriate management. The true preoperative diagnosis may be diffucult in children but it seems to be possible by the help of dynamic contrastenhanced MRI.

P - 192 INFLAMMATORY PSEUDOTUMOR OF THE URINARY BLADDER

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Introduction: An inflammatory pseudotumor of the urinary bladder is a rare benign lesion with a good prognosis in children. However one of the differential diagnoses is embryonic rhabdomyosarcoma.
Case description: We report a case of an inflammatory pseudotumor of the urinary bladder in a 4 year-old female who presented with a history of fever, painful urination, suprapubic pain and intermittent gross hematuria. An intravesicular mass (3x 2,8 x 2,5 cm) was noted on renal-bladder ultrasound, and magnetic resonance. A rhabdomyosarcoma was suspected after clinical, radiological, and surgical work-up. Histological examination of the transurethral biopsy demonstrated inflammatory pseudotumour of the bladder that was confirmed by a review examination. Patient has been kept in close surveillance; she is symptom free and without any evidence of recurrence after 1 year of follow-up.
Inflammatory pseudotumor of the bladder is a benign proliferative lesion of the submucosal stroma that cannot be distinguished from malignant tumors of the bladder either endoscopically or radiographically.

P - 193 TYPICAL OR ATYPICAL HEMOLYTIC UREMIC SYNDROME, AND THE USE OF ECULIZUMAB – TWO ILLUSTRATIVE CASES

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Introduction: Typical hemolytic uremic syndrome (HUS) in children is caused by verotoxins producing enteropathogens, mostly Escherichia Coli 0157:H7 in our country. Atypical HUS designs HUS not due to Escherichia Coli and whose causes include, streptococcus pneumoniae, methyl malonic aciduria, deficiency of von Willebrand proteinase ADAMST 13, and genetic disorder of the complement.
Treatment of HUS relies on supportive measures while treatment of aHUS includes plasmapheresis and specific treatment. Recently, the monoclonal antibody eculizumab has been proposed for the treatment of aHUS and many clinicians now believe that eculizumab should be the new first-line standard of care.
Cases description First case is a 9-months old girl with vomiting symptoms followed by seizures. Initial workup showed HUS. The evolution was characterized by progressive renal failure and cardiogenic choc. In the absence of obvious gastroenteritis symptoms and taking her young age and the severity of the cardiac involvement into consideration, congenital aHUS was suspected and eculizumab was initiated. The next day, the patient was placed under cardio-respiratory assistance but her cardiac and neurologic state continued to worsen and she died. Full workup showed no evidence of aHUS but E. Coli type O121 was found on stool analysis.
Second case is a 5-years old boy with vomiting symptoms, loss of consciousness and seizures. Workup showed renal failure and hemolysis. Plasmapheresis was first initiated. Renal biopsy showed thrombotic microangiopathies. Atypical HUS was suspected and eculizumab was administered as well as hydroxycobalamine because of elevated homocysteinemia. The child recovered. Later results confirmed the diagnosis of methyl malonic aciduria with homocysteinemia.
Conclusions: Discussion and conclusions Diagnosis of typical HUS versus aHUS remains tricky. Workup continues to take many days leaving the clinicians with a choice between several therapeutic. With the emergence of eculizumab, it becomes crucial to develop faster diagnostic tools and to adapt HUS treatment protocols.

P - 194 ANTI-FACTOR H AUTOANTIBODY–ASSOCIATED HEMOLYTIC UREMIC SYNDROME - FIRST CASE IN ROMANIA TREATED WITH ECULIZUMAB

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Introduction: Anti-Factor H Autoantibody with deficiency of complement factor H-related (CFHR) proteins represents a unique subgroup of complement-mediated atypical HUS (aHUS).
Case description: An 11 years old, girl, admitted to our Pediatric Nephrology Department one day after the onset of symptoms. She was anuric. Initial blood work showed decreased Haemoglobin, decreased Platelets, increased Lacticodehydrogenase, increased Ureea and Creatinine, increased liver and pancreatic enzymes, decreased Haptoglobine, decreased C3 and normal C4.
Blood and serum were sent for extensive complement and genetic testing to Semmelweis University, Budapest. The results showed the presence of Anti-Factor H Auto antibodies and the determination of copy numbers for Complement Factor H related Genes 1 and 3 (*CFHR1*, *CFHR3*) revealed zero copies in the patient (deletion), and heterozygous deletion in both parents.
During first month of hospitalization, the patient presented neurological complications with seizures, pulmonary and gastro-intestinal bleedings. She received plasma therapy, hemodialysis, Dexamethasone for a short period of time, and, 30 days after onset, Eculizumab infusions were started. After 11 months of treatment the patient has normal renal function and no neurological sequelae. The complement follow-up was done regularly, and at each determination the Anti-FH Auto antibodies were present with decreased factor H levels, decreased C3, decreased Factor B and decreased ADAMTS13, showing that there is ongoing complement activation but effectively stopped at C5 with Eculizumab. Mychoplenolate Mophetil as single immunosuppressant therapy was introduced.
Conclusions: Eculizumab as symptomatic therapy is very effective in DEAP-HUS to stop the disease progression but does not prevent the anti-FH antibody formation. The need of immunosupression is mandatory.
In patients with multi organ involvement and with severe course of disease, stopping Eculizumab should be done with great caution.
AKNOWLEDGEMENT: The treatment of this patient would not have been possible without the unconditioned help of Alexion Pharmaceuticals, of Prof. Dr. Zoltan Prohaszka for complement testing and follw-up, and of Dr. Johannes Hofer for the advice regarding immunosupression.

P - 195 PIERSON SYNDROME: CHALLENGES OF RENAL REPLACEMENT THERAPY AND TRANSPLANT IN A RARE CAUSE OF CONGENITAL NEPHROTIC SYNDROME

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Introduction: Renal replacement therapy in children less than 2 years presents many challenges, with renal failure frequently accompanied by multiple co-morbidities. We present a case of a male infant born rapidly at 36+6 weeks weighing 2.72kg. He was initially treated for sepsis due to respiratory distress and received 7 days of IV antibiotics. Renal and liver function was not checked during this time. He was readmitted at 5 weeks of age in extremis with oedema, hypoalbuminuria, proteinuria, microcoria and renal impairment. We will discuss the presentation, complications and consequently the management to renal replacement therapy and transplant work up of this complex case.
Case description: On transfer to our tertiary centre he was ventilated, severely fluid overloaded with significant metabolic acidosis and cardiovascular compromise requiring inotropic support. He remained oliguric despite management with albumin and frusemide and required CVVH. Renal management was complicated by massive proteinuria resulting in several episodes of life threatening sepsis. Venous clots associated with line placement despite anticoagulation forced PD catheter placement and strict fluid medical management. Medical nephrectomy was undertaken using ACE inhibitors and indomethacin to stabilise protein losses and fluid management. Pupils did not dilate and he was significantly myopic, not displaying fixing and following.
Genetic testing revealed homozygous R246w mutation in the LAMB2 gene which causes a lack of B2 Laminin both in the basement membrane and iris; a known association with Pierson's Syndrome. His parents were both heterozygous for this mutation. A combination of CVVH, HD and PD was required with all modalities due to sepsis, thrombosis and technical line problems. IVIG was given regularly due to very low immunoglobulins and several episodes of overwhelming sepsis. Medical nephrectomy stabilised fluid management however significantly compromised nutrition which had to be frequently altered. Visual correction for extreme myopia was required to optimise ocular development.
Conclusions: Renal replacement in infants continues to pose significant challenges however our case was complicated by severity of disease and proteinuria with overwhelming infection and clot formation. This resulted in multiple modalities of dialysis and challenging fluid and electrolyte management when dialysis was not possible due to access. At 3.5 years the child continues on PD as an outpatient and work up for transplantation is ongoing.

P - 196 PERIRENAL URINOMA AND A LOSS OF KIDNEY FUNCTION AS A COMPLICATION OF POSTERIOR URETHRAL VALVE

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Introduction: Perirenal urinoma (PU) represents an extravasation of urine inside the renal fascia. It is an uncommon diagnosis in children, usually associated with an obstruction to lower or upper urinary tract. Incidence of PU in patients with posterior urethral valves is estimated to be 3 to 10%, with increasing incidence probably due to availability of ultrasonography.
Case description: A male newborn was diagnosed prenatally with bilateral hydronephroses and oligohydramnios.
Serum creatinine level was increased, the patient was prone to metabolic acidosis, hyperkalemia and hyponatremia. In the second week of life an ultrasound examination detected a massive PU on the right. The diagnosis was confirmed by a CT scan. Dynamic radionuclide scan of the kidney with Tc^{99m}mercaptotriglycylglycine (MAG-3) revealed a non-functioning right kidney. Based on these findings and worsening clinical condition, a percutaneous drainage of PU was performed. Sequent ultrasound examinations showed a complete regression of PU. Voiding cystourethrogram showed high grade bilateral refluxes. A definitive resolution of infravesical obstruction was achieved by electroresection of the posterior urethral valve. A proximal urine derivation was performed on the left, in order to preserve the function of the sole functioning kidney. Dynamic radionuclide scan of the kidney at the age of 6 months showed no functional renal parenchyma on the right, eGFR was normal.
Conclusions: A patient with a posterior urethral valve developed a PU and loss of function of the affected kidney. Since there was no data on the separate function of kidneys previous to development of PU, we can only assume that a loss of function was caused by compression and prolonged compromise of renal blood supply, in conjunction with infection and congenital dysplasia of the kidney.

P - 197 SEVERE DIABETIC KETOACYDOSIS, HYPERTRIGLYCERIDEMIA, AND PANCREATITIS IN A 5 YEARS OLD CHILD TREATED WITH PLASMA EXCHANGE

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Introduction: A mild increase in serum lipid concentrations is a common feature of diabetic ketoacidosis (DKA). Severe hyperlipidaemia with milky plasma is rare. It may occur at presentation of diabetes 1, exposing the patient to the risk of acute pancreatitis (AP).
Case description: We report a pediatric patient with a new-onset insulin-dependent diabetes mellitus (IDDM) who initially presented in severe diabetic ketoacidosis (DKA) with extreme hyperlipidemia, milky plasma, and acute pancreatitis AP, treated with a two courses of Plasma Exchange. 5 years old girl was admitted to the Intensive Care Unit with severe diabetic ketoacidosis, severe hypertriglyceridemia and hypercholesterolemia (pH 6.84, HCO3 <3 mmol/L, glucose 22 mmol/L, triglycerides 241 mmol/L, cholesterol 40.1 mmol/L) deteriorated consciousness and acute pancreatitis (serum amylase 630 IU/L, urine amylase 2042 IU/L, s lipase 1005 IU/L). Abdominal CT revealed necortizing acute pancreatitis.
On the following measures of treatment with parenteral rehydration, insulin, total pareteral nutrition,diet, 2 course of Plasma Exchange (PE) there was a stabilization of the clinical status and normalization of laboratory findings.
Conclusions: In the begining, it was not clear whether the primary disease was hyperlipidaemia complicated by acute pancreatitis producing the metabolic upset or diabetes mellitus presenting as severe hyperlipidaemia. The best way to rapid decrease hyperchylomicronaemia was PE. Genetic defects which could have caused hypertriglyceridemia was excluded.

P - 198 A RARE CASE: LIDDLE SYNDROME WITH NEPHROCALCINOSIS

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Introduction: Lidddle Syndrome is a rare autosomal dominant form of monogenic hypertension. Because of the distal tubulus epithelial sodium channel (ENaC) defects, hyperfunction of channel occurs. It leads to decreased sodium excretion and increased potassium excretion. Although there are hyperaldosteronism findings such as hypertension, metabolic alkalosis, hypokalemia, hypercalciuria; renin and aldosterone levels found to be low in this syndrome. Nephrocalcinosis was found in only a few cases.
Case description: A ten year old boy was diagnosed as Liddle syndrome according to the findings of hypertension, hypopotasemic metabolic alcalosis, low serum aldosterone, low urine sodium levels and increased serum potassium levels. Nephrocalsinosis was detected on ultrasonography. If clinically hyperaldosteronism findings present; Cushing syndrome, renal arterial stenosis, endocrine pathologies such as congenital adrenal hyperplasia and pheochromocytoma should be excluded.
Conclusions: Our patient was diagnosed as Liddle syndrome after the exclusion of other pathologies. Nephrocalcinosis being as a rare finding in this rare syndrome is worth to be published.

P - 199 XANTHOGRANULOMATOUS PYELONEPHRITIS: A PEDIATRIC CASE REPORT

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Introduction: We report a case of a 3 year old boy with an atypical presentation of chronic pyelonephritis.
Case description: A 3 year old boy, with history of urinary tract infections and nephrocalcinosis from 6 months of life, is valued for two weeks of asthenia and malaise. Inicial laboratories exhibited a hemoglobin of 5.6g/dl, leuckocytosis: 19900mm3, neutrophilia (65%), creatinine 0.5mg/dl, and an urocultive positive for Proteus mirabilis >100000 CFU; renal ultrasound reports image compatible with tumor mass and stones in the right kidney, whereby magnetic resonance scan of the abdomen was performed. This scan evidenced a Xanthogranulomatous Pyelonephritis. It was decided to complete 21 days of intravenous antibiotic treatment and subsequently perform a right laparoscopic nephrectomy. Tumoral lesion was discarded by the immunohistochemistry (CEA, CD10, CD38, CD30, CD20, CD68, Kappa, Lambda), and the macroscopic and histological findings confirmed the diagnosis of Xanthogranulomatous Pyelonephritis (Figure 1). After the surgical procedure the clinical evolution was satisfactory and the patient was discharged.
Conclusions: Xanthogranulomatous pyelonephritis, uncommon in pediatric age, is an atypical and severe presentation of the pyelonephritis characterized by destructive and granulomatous inflammation in the renal parenchyma. Its etiology is not completely understood. It is believed that the disease results from a defect of macrophages to process the bacteria, plus the presence of kidney stones. Diagnosis is made by renal ultrasound, tomography and MRI, nevertheless its confirmation is made by histology. After antibiotic administration for local control of infection, treatment of choice is surgical (nephrectomy). Early diagnosis and treatment of the affected kidney unit decreases the high morbidity and mortality of the disease, and improve prognosis

P - 200 ACTINOMYCOSIS IN A CHILD WITH SYSTEMIC LUPUS ERYTHEMATOSUS.

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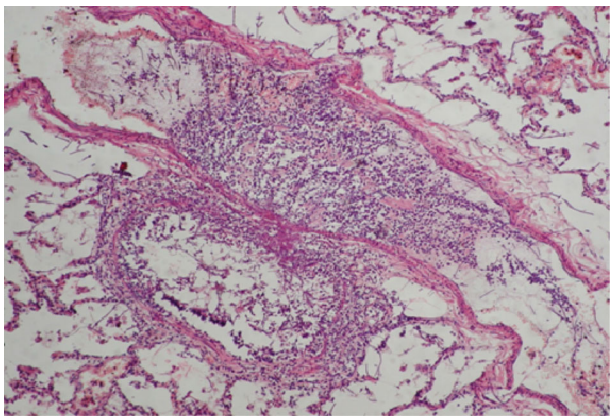
Introduction: In our hospital we observed a case of systemic lupus erythematosus complicated by the development of pulmonary actinomycosis in a child of 17 years old.
Case description: The child has been sick from the age of 13 when SLE started. Hospitalization in our clinic is associated with the development of sore throat, fever, throat ache, a decrease in urine output. On examination we observed typical skin butterfly eruption on the face. She had anuria. During the examination the native DNA antibody and LE-cells. In smears of mucus from the throat and nasal fungi of the genus Candida were found. On the third day a syndrome of multiple organ failure developed which was fatal.
After the section done diagnosis was clarified. Basic: SLE (lupus nephritis with specific interstitial syndrome periarterial bulbous sclerosis spleen damage microvascular as kapilyarit, arteriolit, venulit). Complications: Pulmonary actinomycosis with the defeat of the walls of the bronchi and peribronchial extension to the pulmonary parenchyma. Chronic renal failure, acute renal failure, nephrosclerosis. Disseminated intravascular coagulation.



A sample of lung tissue. Bronchial wall and surrounding veins are densely infiltrated by leukocytes karyorrhexis phenomena; there is filaments actinomycete mycelium the gaps in branching; the integrity of the structures in place infiltrative growth of the fungus is damaged.
Conclusions: Their identification is possible with transbronchial biopsy. Pathogenis no spore-forming rods that are beginning to grow from the 5th - 7 th day. A specific feature of this case was the emergence and rapid progression of actinomycosis, which was not diagnosed for a short child′s stay in the hospital.

P - 201 ORAL PENICILLIN ASSOCIATED ACUTE KIDNEY INJURY IN AN INFANT WITH ACUTE PYELONEPHRITIS

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Introduction: Oral penicillin V, a beta-lactam antibiotic used to treat certain bacterial infections, is widely prescribed in children. Beta-lactam administration may be associated both with allergic and non-allergic reactions. In addition, acute kidney injury (AKI) has been repeatedly reported mainly in adult patients. AKI is determined by tubular injury resulting in the development of acute tubulointerstitial nephritis (ATIN). We report a case of an infant with AKI due penicillin-associated ATIN and concomitant acute pyelonephritis.

Case description: An 18-month-old girl was admitted to our hospital with oliguric AKI. Both her birth and family history were unremarkable. She was commenced on oral penicillin V treatment for acute tonsillitis with fever 6 days before admission. Generalised macular rash with eyelid oedema appeared 2 days after starting antibiotics. Penicillin was further administered despite the suspicious allergic reaction.
Upon admission, she was afebrile, normotensive and oliguric with generalised oedema. Her chest was clear to auscultation, and abdomen was mildly distended without signs of peritoneal irritation. Her laboratory results showed elevated renal parameters (urea 12.4 mmol/l, creatinine 263 μmol/l) and metabolic acidosis (bicarbonate 12.2 mmol/l), mild leukocytosis in the blood count and hypogamaglobulinemia with normal C3, C4 and negative autoantibodies. Urinalysis revealed 2+ protein, 3+ blood, 4+ leukocytes. Renal ultrasound showed bilateral kidney enlargement with mild parenchymal lesion. Antibiotic treatment with cefuroxime and symptomatic management was started. The patient required a short period of peritoneal dialysis. Additionally, significant bacteriuria of Enterococcus faecalis was found, confirming the presence of concomitant acute pyelonephritis (AP). Kidney biopsy was performed at the same time and was consistent with the diagnosis of drug-induced ATIN with concomitant AP. Plasma creatinine and proteinuria normalised by 35 days and 40 days, respectively.
Conclusions: To our current knowledge, we are the first to present a case of ATIN caused by oral Penicillin V administration in a child.

P - 202 THE CASE OF ACTINOMYCOSIS IN A CHILD WITH SYSTEMIC LUPUS ERYTHEMATOSUS.

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Introduction: In our hospital we observed a case of systemic lupus erythematosus (SLE) complicated by the development of pulmonary actinomycosis in a child of 17 years old.
Case description: The child has been sick from the age of 13 when SLE started. Hospitalization in our clinic is associated with the development of sore throat, arthralgia, fever, throat ache, a decrease in urine output. During the examination the native DNA antibody and LE-cells. In smears of mucus from the throat and nasal fungi of the genus Candida were found. The child's condition was extremely severe. Child received nessesary treatment. On the third day of the childs stay in the hospital a syndrome of multiple organ failure developed which was fatal.
After the section: SLE. Complications: Pulmonary actinomycosis with the defeat of the walls of the bronchi and peribronchial extension to the pulmonary parenchyma, acute renal failure. A sample of lung tissue. Bronchial wall and surrounding veins are densely infiltrated by leukocytes karyorrhexis phenomena; there is filaments actinomycete mycelium the gaps in branching; the integrity of the structures in place infiltrative growth of the fungus is damaged.
Conclusions: Actinomycetes are not allocated with phlegm. Their identification is possible with transbronchial biopsy. Pathogenis no spore-forming rods that are beginning to grow from the 5th day. A specific feature of this case was the emergence and rapid progression of actinomycosis, which was not diagnosed for a short child′s stay in the hospital.

P - 203 PEDIATRIC UROLITHIASIS: 10 YEARS' EXPERIENCE

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Introduction: The aim of this study is to investigate the clinical findings, etiologic causes and outcomes of pediatric urolithiasis from an endemic region of Turkey.
Material and methods: Medical records of pediatric patients referred between 2005 and 2014 to our unit (a tertiary nephrology department) with the diagnosis of pediatric urolithiasis were reviewed. Age, gender, family history, presenting symptoms, imaging procedure for diagnosis, metabolic evaluation and outcome results were recorded. SPSS 16 were used for statistical analysis.
Results: 350 patients <18 years with the diagnosis of pediatric urolithiasis were the subject of study. Diagnostic modality was USG in 331 patients (94.6%), CT in 2 patients (0.6%), direct grapy in 7 patients (2%) and stone passage in 13 patients (3.7%). M/F ratio was 1.5/2. Family history of urolithiasis was present in 172 (49.1%) and consanguinity between the parents was present in 55 (15.7%) patients. Presenting symptoms were: flank pain (n= 83; 23.7%), urinary tract infection (n= 39; 11.1%), history of stone passage (n= 13; 3.7%), irritability (n=32; 9.1%), vomiting (n= 20; 5.7%) and incidental (n= 102; 29.1%). Stones were located in renal parenchyma for 319, in bladder for 2, in ureter for 17, in both renal and ureter for 12 patients. Stone size were ≤3 mm in 91(26%) patients, >3 and<10 mm in 176(50.3%) patients, ≥10 mm in 31(8.9%) patients and nephrocalcinosis in the remaining 48(13.7%) patients. Metabolic abnormalities were found in 165 patients (hypercalciuria 27.4 %(n=96), hypocitraturia 9.1%(n=32), hyperoxaluria 5.7%(n=20), cystinuria 2%(n=7),and hyperuricosuria 2.9%(n=10). Seventy three patients required ESWL or a urologic intervention. Seventy patients are stone free. The remaining patients are in follow up with residual stones and are under medical treatment.
Conclusions: Pediatric urolithiasis is a very heterogeneous group of disease with difficult diagnostic and therapeutic processes. Outcome is not favorable and strict follow up is required.

P - 204 CAN URINARY BIOMARKERS SUCCEED DIAGNOSTIC VALUE OF RENAL SCINTIGRAPHY IN PATIENTS WITH URETEROPELVIC JUNCTION DISRUPTION?

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Introduction: The aim of this study is to evaluate the efficacy of urinary biomarkers as an easy to use, cost-effective and noninvasive alternative to renal scan for assessment of obstruction in patients with unilateral ureteropelvic junction disruption.
Material and methods: The study included 39 patients diagnosed with unilateral ureteropelvic junction disruption. Patients were divided into 2 groups according to diuretic half-time in renal scan. There were 15 cases with obstruction, and 24 patients had non-obstructive dilatation. Cystatin C, β2-microglobulin, KIM-1, MCP-1, osteopontin and NGAL markers were analysed in urine samples. Hence the current data regarding the clinical usage of these markers is insufficient, ROC curves were formed to estimate cut-off values and detect marker's ability to distinguish obstruction. Two cut-off points were defined by ROC for Cystatin C, β2 microglobulin and MCP-1. Sensivity, specificity, positive and negative predictive values were obtained for each curve cut-off point.

Results: Sensivity values to detect obstruction were 80% for Cystatin C, 80% for β2 microglobulin, 86,7% for MCP-1 and 80% for osteopontin. MCP-1 has obtained 73,3% sensivity, 62,5% specificity and β2 microglobulin has obtained 60% sensivity, 83,3% specificity in their second cut-off point. Detailed sensivity, specificity and predictive values of biomarkers are summarized in table (Table-1).
Conclusions: Cystatin C, β2-microglobulin and MCP-1 have high sensivity to assess obstruction. However, Cystatin-C and osteopontin have yielded lower specificities in the cut-off point with high sensitivity. Although it would be early to render a decision without the support of further clinical investigation, we believe MCP-1 and β2-microglobulin may have their application as non-invasive clinical tests in the future.

P - 205 PREDICTIVE RISK FACTORS FOR RENAL SCARRING AFTER THE FIST URINARY TRACT INFECTION

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Introduction: Children with vesicoureteral reflux (VUR) are likely to develop renal scarring after the febrile urinary infection (UTI). Renal scarring is often associated with the risk of later hypertension and chronic kidney disease. Renal scarring may also occur in the absence of VUR. However, study results on the risk of renal scar formation , other than VUR, in children after the first febrile urinary tract infection remains controversial.
Material and methods: Children presented with first febrile UTI were enrolled into study. Acute UTI was diagnosed by urine culture >100,000 colonies of a single pathogen. All children had renal sonography at the diagnosis onset. Voiding cystoureterogram was performed in all children <2 years of age and in all children over 2 years of age with documented hydronephrosis on ultrasound. The presence of renal scar was assessed in all children with technetium-99m labeled dimercaptosuccinic acid (DMSA) scan after 6 months.
Results: A total of 100 children, 82 girls and 18 boys, aged 2 month to 15 (5.14+ 3.96) were enrolled in this study. Forty-two patients were younger than 3 years. Hydronephrosis was found in 24%. VUR in 54%, and renal scars in 44 children. Children with grade III to IV had greater incidence of VUR. Scars were more common in boys (27%) and in children <3 years (78% vs. 37%, p<0.01). Of 44 children with renal scarring 39 (88%) had VUR. Approximately 55% of patients had a temperature above 38° C. Renal scars were more common with urinary tract infections from an organism other than Escherichia coli (p<0.01). There were no relations between renal scarring and degree of fever or white cell counts.
Conclusions: Boys 3 years or younger, organisms other than E-Coli, and gross VUR were risk factors for the presence of renal scars in children after acute pyelonephritis. Keywords: Renal scar, Vesicoureteral reflux, Urinary tract infection, Children

P - 206 PROGNOSTIC VALUE OF AMBULATORY BLOOD PRESSURE MONITORING FOR LEFT VENTRICULAR HYPERTROPHY' DEVELOPMENT IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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Introduction: Left ventricular hypertrophy (LVH) is independently associated with cardiovascular outcome both in the general population and in adults with chronic kidney disease (CKD). Several studies have shown a high correlation of blood level and abnormal patterns of ambulatory blood pressure monitoring (ABPM) with abnormal left ventricular mass and function, cerebrovascular and cardiovascular events and mortality in adult patients. The prognostic value of ABPM for cardiovascular damages in children remains unknown.
The aim of study was to determine the prognostic significance of ABPM for development of LVH in children with CKD.
Material and methods: Casual blood pressure, 24-h ABPM, echocardiogram, biochemical profiles were obtained in 210 children (M=13 years; M:F=0,89:1; eGFR=86±18 ml/min/1,73m^2) with CKD including obstructive uropathy, kidney dysplasia, cystic kidney diseases, Alport syndrome and glomerulonephritis. 157 children (74,7%) received hypotensive therapy. Left ventricular mass established by Deverex methods and indexed to height ^{2,7} (LVMI) was compared with age-specific percentile curves (P.R.Khoury, al., 2009).
Results: Blood hypertension was revealed in 28 pts (13,3%) by casual blood pressure measurement (CBPM) and in 142 (67,6%) by ABPM. LVH had 33 pts (15,7%). There were weak correlation of LVMI with day systolic (r=0,33, p=0,04), diastolic (r=0,25, p>0,05) and night systolic (r=0,31, p=0,05), diastolic (r=0,31, r=0,05) blood pressure load, pulse blood pressure (r=0,3, r=0,05). Children with blood hypertension had higher risk of LVH respect the patients with normal blood pressure by CBPM: OR=3,35 (95%CI 1,77;6,32). To exclude the effects of antihypertensive medicines on ABPM patterns the data of 53 pts (M=11,5 years, M:F=0,76:1; eGFR=83±16 ml/min/1,73m^2) without hypotensive therapy were analyzed. The children with blood hypertension by CBPM had OR=4,3 (95%CI 1,01;18,2) of LVH compared to patients with normal blood pressure. LVMI correlated with day systolic (r=0,43, p=0,04), diastolic (r=0,31, p=0,05) and night systolic (r=0,4, p=0,04), diastolic (r=0, 25, r>0,05) blood pressure load, pulse blood pressure (r=0,35, r=0,05).
Conclusions: The study confirmed the relationship of LVMI and blood pressure level in children with CRD. It was no demonstrated the additional predictive value of ABPM for LVH' development in our patients. Holding a single ABPM with possible overdiagnosis of blood hypertension as a consequence (67,6% of patients) and lack of data on the duration of hypertension could influence on our study's results.

P - 207 THE RENAL FINDINGS AND RENAL FUNCTIONS IN PATIENTS WITH NEUROFIBROMATOSIS TYPE 1

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Introduction: The aim of this study was to evaluate renovascular and genitourinary findings, and estimate glomerular and tubular kidney functions of patients with neurofibromatosis type 1 (NF1).
Material and methods: We evaluated renovascular and genitourinary findings and kidney function tests (glomerular and tubular tests) of the patients with NF1 followed in pediatric neurology department in our hospital and healthy children (control group) who have same age and gender.
Results: Forty-six children with NF-1 (20 girls and 26 boys) and 33 healthy children (15 girls, 18 boys) were evaluated. The mean age were 10.1 ± 4.6 years (age 3-18 years) and 10.12 ± 4.26 years, respectively.Mean systolic and diastolic blood pressure of NF1 group was significantly higher compared with control group.Blood pressure was above 95 percentile in 10.9 % and above 99 percentile in 2.1% of NF1 group. Renal artery stenosis was found a patient with NF1. Mean eGFR value of the NF1 group were calculated to be significantly lower than control. Six patients with NF1 had GFR values below of 90 ml/min. There was no significant difference in proteinuria compared with control. Tubular phosphor reabsorption values of NF1 group were calculated significantly lower and uric acid excretion higher than control.
Conclusions: To our knowledge, this is the first study investigating the structural and functional assessment of kidney in children with NF1. In our study, possibility of hypertension, urinary tract anomalies and impairment of renal function tests in NF1 patients have been concluded to be high compared to the healthy group.

P - 208 RENAL BRIGHT ECHOES: CALCULI OR SONOGRAPHIC MIMICS OF CALCULI

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Introduction: Ultrasonography (USG) is a noninvasive way of diagnosing urinary system calculi. However, for small renal calculi, recognition and diagnostic accuracy are less reliable during infancy. The aim of this study is to investigate infants with renal echogenicity to explore misdiagnosis and serious causes of renal calculi.
Material and methods: Medical records of infants referred to our unit with the diagnosis of infantile urolithiasis between 2005 and 2014 were reviewed. Our policy was to re-perform urinary system USG with a linear probe to exclude sonographic artifacts or normal common structures that may have been mimicking renal calculi. After accurate diagnosis with USG, these infants were evaluated for metabolic abnormalities. SPSS 16 was used for statistical analysis.
Results: 176 patients <1 year with the diagnosis of infantile urolithiasis were evaluated. Repeated USG revealed normal urinary systems without any calculi or echogenicities in 38 patients. Any other examination was not performed on these patients. In the remaining 138 patients, diagnoses of urinary system calcification became definite with calcification sizes of ≤3mm in 54 (39.1%) patients, >3 and <10 mm in 59 (42.8%) patients, ≥10mm in 3 (2.2%) patients, nephrocalcinosis was detected in the remaining 22 (15.9%) patients. All the calcifications were localized in renal parenchyma with more than three echogenic foci; only two were localized in the ureter. Metabolic abnormalities were found in 66 patients (high vitamin D level 2.9 %(n=4), hypercalciuria 28 %(n=39), hyperoxaluria 2.9 % (n=4), hypocitraturia 8.8 % (n=12), cystinuria 2.2% (n=3), hyperuricosuria 2.9% (n=4). 34 patients are stone free, 102 patients are in follow up with residual renal calcifications.
Conclusions: Infantile renal echogenicity can be a misdiagnosis because of ultrasonographic artifacts and brightness of normal renal structures. However, renal calcifications could be a serious indicator of metabolic abnormalities. A careful USG evaluation is needed to avoid unnecessary metabolic investigations.

P - 209 NEUTROPHIL TO LYMPHOCYTE RATIO AND MEAN PLATELET VOLUME ARE NOT ADEQUATE PARAMETERS TO PREDICT GASTROINTESTINAL OR RENAL INVOLVEMENT IN HENOCH-SCHÖNLEIN PURPURA

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Introduction: Henoch-Schönlein Purpura (HSP), newly termed as IgA vasculitis is the most common systemic vasculitis of childhood. Previously, neutrophil to lymphocyte ratio (NLR) and mean platelet volume (MPV) were evaluated in patients with HSP and a relationship with gastrointestinal (GI) bleeding has been reported. The aim of this study was to evaluate NLR and MPV values and their predictive role for GI and renal involvement in HSP patients.
Material and methods: We reviewed the medical files of 217 patients with HSP. Complete blood counts were performed during admission to the center. According to the presence of renal or GI involvement NLR and MPV values were evaluated. Variables were expressed as medians and 25th and 75th percentile. Differences between the groups according to NLR and MPV values were evaluated by Mann-Whitney U test. Receiver operating characteristic (ROC) curves were used to find out a cutoff value for predicting renal or GI involvement in HSP.
Results: Ninety five patients (44%) had GI and 22 patients (10%) had renal involvement. NLR and MPV values according to the GI and renal involvement are summarized in the table. Statistically significant levels of high NLR and MPV were recorded in patients with GI involvement and high NLR was recorded in patients with renal involvement. The area under the ROC curve (AUC_{ROC}) analysis showed that NLR could be a moderately strong predictor of GI (AUC_{ROC}=0.718, 95% CI=0.64-0.78, p=0.000) or renal (AUC_{ROC}=0.719, 95% CI=0.62-0.81, p=0.001) involvement in HSP. A cutoff NLR value was found as 3.17 for GI involvement and as 4.13 for renal involvement with a very low sensitivity (59%, 55% respectively).

Table 1: Neutrophil to lymphocyte ratio and mean platelet volume values (median, 25th and 75th percentile) according to the presence of gastrointestinal (GI) and renal involvement

	Patients without GI involvement	Patients with GI involvement	*p* value	Patients without renal involvement	Patients with renal involvement	*p* value
Neutrophil tolymphocyte ratio	2.07 (1.26-3.06)	3.62 (2.09-5.56)	**0.000**	2.39 (1.39-3.83)	4.25 (2.72-5.60)	**0.001**
Meanplateletvolume(fl)	6.70 (6.16-7.41)	7.05 (6.39-7.82)	**0.023**	6.8 (6.28-7.50)	7.0 (6.46-8.31)	0.2

Conclusions: It is concluded that NLR and MPV are not adequate parameters to predict GI or renal involvement in HSP. The clinical findings and clinician's attention are more precious as always.

P - 210 TIMING FOR ULTRASONOGRAPHIC EVALUATION OF URINARY TRACT IN INFANTS AFTER HYDRATION

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Introduction: The aim of the study was to determine the optimum time for ultrasonographic evaluation of urinary tract in infants after hydration.
Material and methods: Twenty seven infants (17 male) with hydronephrosis were evaluated with consecutive ultrasound (US) examinations before and after hydration. First ultrasound were performed after 2 hours thirst. Then patients were breastfed during 10 minutes (min) or 150-200ml formula were given. Following US examinations were performed 15, 30, 60, 90 min after hydration. Feeding was repeated in the same way after the US performing 60th minute. Kidney size, parenchymal width, antero-posterior pelvic diameter (APPD), renal calyceal dilation, distal ureteral diameter (DUD), urine volume in bladder were evaluated in each US examination and voiding time was recorded.
Results: APPD in 15th, 30th and 60th min were comparable to each other and significantly higher than in thirstiness ($p<0.05$). APPD in 90th min

was significantly wider than the others ($p<0.05$). The measurements of kidney size and parenchymal width were not different in any US examination. DUD in thirst was significantly lower than 90th min measurement ($p=0.045$) but not different than the others. DUD in 15thmin was significantly lower than the measurements in 30th, 60th, 90th min($p<0.05$) because urine volume in bladder in 15th min was significantly lower the measurements in 30th, 60th min ($p<0.05$).

Conclusions: APPD is affected by hydration in infants. Kidney size and parenchymal width do not change after hydration. DUD is related to urine volume in bladder rather than hydration. Thirty minutes after the average hydration seems to be the optimal time for US examination of urinary tract in infants.

P - 211 ORAL ZINC SULFATE AS ADJUVANT TREATMENT IN CHILDREN WITH NEPHROLITHIASIS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL

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Introduction: we decided to assess the effectiveness of oral zinc sulfate as adjuvant treatment in children with nephrolithiasis.

Material and methods: This research was a randomized, double-blind, placebo-controlled clinical trial. 102, 1 month to 11 years old children with a first nephrolithiasis were recruited. Patients were randomly divided into two equal groups. Intervention group received conservative measures for stones and 1 mg/kg/day (maximum to 20 mg/day) oral zinc sulfate syrup, for 3 months. Control group in addition to conservative measures, received placebo, for 3 months. Patients were followed for 9 months, in 5 steps (at the end of 1, 2, 3, 6 and 9 months after the treatment) for the size and number of stones in kidneys by ultrasonography.

Results: Only, at the end of the first month, the average number (intervention: 1.15 ± 3.78, control: 1.3 ± 2.84) ($p=0.001$) and size (cm) (intervention: 0.51 ± 1.76, control: 0.62 ± 1.39) ($p=0.001$) of stones was significantly lower in the intervention group, and in the other follow-up points, there was no significant therapeutic efficacy in oral zinc adjuvant treatment compared to conservative treatment alone. Also, during the 9-month follow-up, the number and size of stones in both groups decreased significantly (both: $p<0.0001$) in a way that the decrease in the intervention group showed no difference with the control group.

Conclusions: Adjuvant treatment with zinc is not more effective than consecutive treatment in children with nephrolithiasis.

P - 212 EARLY DIABETIC NEPHROPATHY AND ENDOTHELIAL DYSFUNCTION IN CHILDREN WITH TYPE 1 DIABETES MELLITUS

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Introduction: The microvascular complications of type 1 diabetes are known to increase with duration of the disease. The extent of vascular disease in Type 1 DM may reflect duration of the disease and severity of chronic metabolic derangements. The aim of this study was to analyze the relation between the duration of diabetes and the microvascular complication markers such as microalbuminuria, vascular endothelial growth factor, angiopoietin-2, arterial stiffness and ABPM.

Material and methods: Forty children with Type 1 DM and 40 healthy children were included in the study. 20 children 5 to 9 years following the onset of diabetes were included in DM-1 group, and 20 children ≥10 years following the onset of diabetes were included in DM-2 group. All the children had 24 h urine microalbumine excretion, HbA1c level, renal function tests, lipid profile, Ang-2 and VEGF levels. All children also underwent 24 h blood pressure monitoring. Arterial stiffness was assessed with PWA and PWV using Vicorder device and carotis intima thickness was measured with Acuson device.

Results: 24 h urine microalbumine excretion was higher in DM-1 and DM2 groups compared to controls ($p=0,037$, $p=0,006$ respectively). No significant difference was found in HbA1c levels between DM-1 and DM-2 groups. Systolic, diastolic and mean blood pressure of daytime, night time and 24 h z scores were found significantly higher in DM-1 and DM-2 groups compared to controls ($p<0.001$). Systolic and diastolic blood pressure loads (>%30) were significantly higher in DM-1 and DM-2 groups compared to controls. Mean cIMT was not higher in DM-1 and DM-2 group compared to controls. There was no significant difference between the groups regarding carotid distenbility, elasticity RAW and SDS, stifness RAW and SDS. Pulse wave velocity level was higher in DM-2 group compared to control ($p=0.02$). VEGF levels were found higher in DM-1 and DM-2 groups compared to controls ($p<0.001$). Ang-2 levels were higher in DM-2 group compared to controls ($p<0.001$). No significant difference was found in Ang-2 levels between DM-1 and control groups ($p<0.5$). There was a significant difference in Ang-2 levels between DM-1 and DM-2 groups ($p=0,017$). Significant positive correlation was found between Ang-2 and 24 h urinary microalbumine excretion.

Conclusions: Incipient microvascular complication and endothelial damage were demonstrated in children with DM. Strict glycemic control are recommended for reducing the microvascular complication in diabetic children.

P - 213 PODOCYTE PPAR-GAMMA ACTIVATION WILL PREVENT PROGRESSION IN DIABETIC KIDNEY DISEASE

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Introduction PPAR-gamma is a prominent member of a family of nuclear transcription factors (the PPARs) that has a role in a diverse number of cellular functions. Agonists of PPAR-gamma have been used as insulin sensitising drugs for the treatment of type 2 diabetes until recently. Data from clinical trials suggests a renoprotective role for these agents. At a cellular level, PPAR-gamma agonists are podocyte protective. The mechanisms for this are unclear.

Podocyte insulin signalling is integrally linked with survival. We hypothesise that PPAR-gamma is podocyte protective in part because of an effect on insulin signalling.

We aim to demonstrate that the PPAR-gamma agonists will reduce progression of kidney disease in models of diabetic nephropathy.

Material and methods: Using well established immortalised mouse and human podocyte cell lines, protein expression regulated by rosiglitazone has been determined through SILAC based proteomics. Our in vivo work is centred on a transgenic mouse model in which PPAR-gamma is selectively knocked down in the

podocyte. We will observe the progression of nephropathy in these animals after inducing the development of diabetes.
Results: We have previously shown that PPAR-gamma is expressed at a protein level in immortalised human podocytes and that these cells respond to treatment with rosiglitazone by enhancing basal and insulin stimulated glucose uptake through the translocation of GLUT 1. We have also shown that rosiglitazone enhances insulin signalling (through MAPK) in podocytes rendered insulin resistant. We can demonstrate, at mRNA level, that stimulation of immortalised mouse podocytes with rosiglitazone produces an increase in a number of PPAR-gamma responsive genes (IRS-2, UCP-1, LPL).
Conclusions: Through proteomics experiments and study of the podocyte specific PPAR-gamma null transgenic mouse, we will gain new insights into the mechanisms through which PPAR-gamma acts within the podocyte. Therapeutics aimed at specific components of the pathways may provide an exciting new option for the future treatment of diabetic nephropathy

P - 214 GLYCATION AND CARBAMYLATION IN DIABETES AND CHRONIC KIDNEY DISEASE

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Introduction: Chronic kidney disease (CKD) and diabetes are diseases prone to molecular aging acceleration through carbamylation and glycation. These two nonenzymatic post-translational modifications are characterized by the addition of oses (for glycation) or isocyanic acid, coming from urea decomposition (for carbamylation), on the same binding sites of proteins and thus can compete. Our aim was to evaluate their competitive effect *in vitro* and *in vivo* conditions reproducing diabetes and CKD.
Material and methods: *In vitro*, albumin was incubated with glucose, urea or cyanate in different conditions. *In vivo* CKD was induced/or not in diabetic (*db*/*db*) or non-diabetic (*db*/+) mice by sub total nephrectomy, or cyanate was administrated for 6 weeks to non diabetic (*db*/+) and diabetic (*db*/*db*) mice to amplify carbamylation. Carbamylation (homocitrulline (Hcit), carbamylated hemoglobin (cHb)), and glycation (carboxyméthyllysine (CML), fructosamines) markers were measured by LC-MS/MS or colorimetric assay, glycated hemoglobin (HbA_{1c}) was measured by immunologic assay.
Results: After 3 weeks of albumin incubation a reciprocal inhibition of 30% ($p< 0.05$) between glycation and carbamylation was evidenced. After 5 weeks of CKD, plasma Hcit concentrations were similar in diabetic and in non-diabetic mice, whereas fructosamines and HbA_{1c} were significantly decreased in diabetic-CKD mice compared to diabetic-non CKD ones ($p < 0.05$). After 6 weeks administration of cyanate, fructosamines and HbA1c were also significantly decreased (-10% and -35% respectively) in diabetic-cyanate mice compared to diabetic-water group ($p<0.05$).
Conclusions: In conclusion, our results show that glycation and carbamylation compete for common binding sites and can both inhibit the other reaction *in vitro* depending on the accessibility and the number of free binding sites. However, they suggest that, *in vivo*, carbamylation gets the upper hand. Thus, classical markers of diabetes metabolic control should be interpreted with caution in diabetic patients with CKD.

P - 215 ALL-TRANS RETINOIC ACID PREVENTS OXIDATIVE STRESS-INDUCED LOSS OF RENAL TIGHT JUNCTION PROTEINS IN TYPE-1 DIABETIC MODEL

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Introduction: Type I diabetes is more frequent in children than Type II. As in the case of the adult feature, Type I diabetes leads to renal damage in the long term. We previously reported that streptozotocin(STZ)-induced diabetes decreased the expression of renal tight junction (TJ) proteins: claudin-5 in glomerulus, and claudin-2 and occludin in proximal tubules through an oxidative stress dependent way (Molina-Jijon et al., Free Radical Biology and Medicine, 2014). Now we investigated whether all-trans retinoic acid (atRA), a compound that plays a relevant role in kidney in uterus development (Lelievre-Pegorier et al., Kidney Int. 1998) and that possesses antioxidant properties, prevents loss of TJ proteins in STZ-treated rats.
Material and methods: atRA was administered daily by gavage (1 mg/kg) from days 3-21 after STZ administration. Changes in TJ proteins were assessed by confocal microscopy and by Western blotting. Functional renal tests were performed.
Results: atRA attenuated loss of body weight, proteinuria and increased natriuresis but it did not prevent hyperglucemia. Other metabolic alterations, such as: increased kidney injury molecule (KIM-1), oxidative stress, protein kinase C (PKC beta 2), NADPH oxidase subunits ($p47^{phox}$ and $gp91^{phox}$) expressions and endothelial nitric oxide synthase (eNOS) uncoupling, and decrease nitric oxide synthesis, Nuclear factor-erythroid-2-related factor 2 (Nrf2) and heme oxygenase-1 (HO-1) expressions were also attenuated by atRA. Decreased expressions of occludin, claudins-2 and -5 induced by diabetes were ameliorated by atRA. We also found that diabetes induced tyrosine nitration (3-NT), SUMOylation and phosphorylation in serine residues of claudin-2 and atRA prevented these changes.
Conclusions: atRA exerted nephroprotective effects by attenuating oxidative stress and preventing loss of renal TJ proteins, during early stages of diabetic nephropathy

P - 216 THE RENOPROTECTIVE EFFECT OF SODIUM-GLUCOSE COTRANSPORTER2 (SGLT2) INHIBITOR DAPAGLIFLOZIN IN TYPE 1 DIABETES

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Introduction: SGLT2 inhibitors are approved only in type 2 diabetes and their use is limited in renal impairment. Here we investigated the effect of

Dapagliflozin (DAPA) in the prevention of type 1 diabetes (DM1) induced nephropathy (DN).
Material and methods: DM1 was induced in male Wistar rats with streptozotocin (65 mg/bwkg, *ip.*). Animals were treated *po.* with DAPA either in monotherapy (D+DAPA, 1 mg/bwkg/day, six weeks), or in combination with LOS (D+DAPA+LOS, LOS: 20 mg/bwkg/day, three weeks). Healthy (C) and vehicle- treated diabetic (D) animals were used as well (n=6-8/group). Metabolic and renal parameters were determined and histological evaluation of the kidneys was performed.
Results: Blood pressure was not influenced by the treatments. In diabetic animals DAPA monotherapy and also the combination with LOS reduced weight loss and water consumption, decreased serum glucose (D: 37±2.7; D+DAPA: 17.7±5.6; D+DAPA+LOS: 18±6.1; mmol/L), fructosamine, lipid, creatinine and urea levels, and improved GFR (D: 0.6±0.04; D+DAPA: 1.09±0.08; D+DAPA+LOS: 0.9±0.12 mL/min/100g), FeNa and reduced the albuminuria. There was no difference between the mono- and combined therapy. DAPA decreased the DM induced mesangial matrix expansion and tubulo-interstitial fibrosis. The combined treatment was even more efficient.
Conclusions: DAPA improved the metabolic and renal parameters and decreased the histological lesions of the diabetic kidneys suggesting the possibility of clinical application in the prevention of DM1 associated nephropathy.
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P - 217 NOCTURNAL HEMODIALYSIS IMPROVES MORBIDITY AND QUALITY OF LIFE IN COMPARISON TO PERITONEAL DIALYSIS IN ADOLESCENT PATIENTS

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Introduction: Renal transplantation is the method of choice for end stage renal disease in childhood and adolescence. Without preemptive transplantation, average waiting time for kidney transplantation exceeds several years. This period has to be bridged with dialysis, either hemodialysis (HD) or peritoneal dialysis (PD). Both methods are classified as equally efficient. In this study, we analyzed whether an intermittent, nocturnal hemodialysis program (NHD) should be favored over an intermittent, automated PD program in adolescent patients.
Material and methods: 13 patients from our NHD program were compared with 13 PD patients matched for gender, age and weight. We analyzed Kt/V, arterial blood pressure, phosphate and albumin serum levels. Hospitalization days, dietary restrictions, phosphate binders and antihypertensive drugs were investigated before starting dialysis and after 6 months after being enrolled in each program.
Results: Kt/V on NHD was significantly higher than Kt/V on PD ($p<0.001$). Mean arterial blood pressure after 6 months on NHD was significantly lower in comparison to initiation of dialysis despite reduction of antihypertensive medication ($p<0.001$). On PD, arterial blood pressure and antihypertensive treatment remained unchanged. Serum phosphate levels fell significantly on NHD ($p<0.001$); on PD, phosphate levels remained. After 6 months on NHD, none of the patients had any dietary or fluid restrictions. In the PD group, almost every patient had restrictions. Serum albumin levels improved under NHD ($p<0.02$), whereas albumin levels under PD did not improve. As a marker for quality of life, hospitalization days were significantly less for NHD patients than for PD patients ($p<0.001$).
Conclusions: Initiation of NHD improves morbidity and quality of life significantly in comparison to PD. In older children and adolescents, NHD should be the dialysis method of choice, if it is individually and logistically possible.

P - 218 CENTRAL VASCULAR ACCESS FOR ACUTE HAEMODYALISIS: POWER PICC DUAL LUMEN 5 FR CATHETER OFF-LABEL USED

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Introduction: Central Venous Catheters (CVC) represent, worldwide , the primary hemodialysis access in children with ARF. The ideal CVC delivers an adequate flow, it has a long use-life and a low complications rate. CVC in neonates and small infants are uneasy and unstable: survival is inversely correlated to the patients weight. Smaller patients need smaller catheters.
Material and methods: The unavailability of ad hoc-sized devices reduces the options of choice regarding the catheters to be implanted in newborns and infants. The recent availability of Power PICC Dual Lumen 5 Fr polyurethane high flow catheters, led the authors to investigate new possibilities concerning catheters suitable for neonate and small infant haemodialysis. In fluid dynamics the Poiseuilles law establishes a correlation between the flow rate of a fluid flowing through a long pipe and the pressure drops. It directly correlates the pressure gradient through the pipe with the flow rate, the pipe length and the fluid viscosity and it correlates inversely with the 4^{th} power of the pipe radius
Results: In this work the authors report on the experience made with Power PICC Dual Lumen catheters (5 Fr diameter, 60 cm length and 10 ml / min flow rate). The vascular device was cut and reduced to 7.5 cm length in agreement with the Poiseuille´s law. The patient: a six months old male, body weight 5,900 g. At the birth, left renal agenesis and right pyelectasy without reflux, at 5 months of age: oligo-anuria P.A. 110 / 75 mm Hg U.S. scan: increase of pyelectasy hyperkalemia and metabolic acidosis. The experimental device was implanted in the infant via percutaneous, US guided, with axial approach to the right internal jugular vein.
Conclusions: A series of five haemodialysis were successfully carried out by connecting to Prismaflex System eXeed II®: Blood flow: QB 60 ml / min, Dialysate Flow QD:2000 ml / h Filter polysulfone 0,2 m2, until both diuresis and renal function improved following successful pielostomy.

P - 219 PLEURAL-PERITONEAL OR PERICARDIO-PERITONEAL LEAK IN CHILDREN ON CHRONIC PERITONEAL DIALYSIS – A SURVEY FROM THE EUROPEAN PAEDIATRIC DIALYSIS WORKING GROUP

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Introduction: Pleural or pericardial effusions secondary to pleuroperitoneal (PPF) and pericardio-peritoneal fistula (PcPF) are a rare but serious complication of peritoneal dialysis (PD). The incidence of PPF and PcPF in children on PD remains unknown and there are no guidelines on the subsequent renal replacement therapy for these children.
Material and methods: We conducted a 10-year survey across all centres in the European Paediatric Dialysis Working Group to review the incidence, diagnostic techniques, therapeutic options and outcome of children on chronic PD with PPF and/or PcPF.
Results: Of 1506 children on PD there were 10 cases (8 of PPF, 1 each of PcPF and PPF + PcPF); prevalence of 0.66 % or 3.9 cases per 1000 patient-years on PD. Median age at presentation was 1.5 (IQR 0.4 – 2.4) years (90% were < 3 years) with a median time on PD of 4.3 (1.3 – 19.8) months. Eight children had abdominal herniae and 7 underwent abdominal surgery in the preceding 4 weeks. Symptoms at presentation were respiratory distress (90%), reduced UF (40%) and tachycardia (30%). Diagnosis was made on x-ray in all, with ultrasound confirmation in 7. All children had an ECHO, pericardial effusion was present in 2. In 3 children the management was conservative, whereas in 7 thoracentesis was performed (with pleurodesis in 3). In all children PD had to be stopped at some point to achieve complete resolution of the effusion, and could be restarted successfully in only two. At final follow-up 4.4 (1.6–6.5) years later, 8 children had a functioning renal transplant, 1 child remained on HD and one died.
Conclusions: PPF and PcPF are rare in children on chronic PD, but are associated with significant morbidity, requiring a change of dialysis modality in all. Risk factors for PPF include age <3 years, herniae and recent abdominal surgery.

P - 220 EXPERIENCE OF A DEDICATED VASCULAR ACCESS CLINIC FOR CHILDREN ON HAEMODIALYSIS

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Introduction: The importance of arteriovenous fistula (AVF) formation for vascular access in children on haemodialysis is underestimated. Great Ormond Street Hospital, London runs a dedicated vascular access clinic by a transplant surgeon, paediatric nephrologist and ultrasound angiologist for assessment and surveillance of AVFs in children on haemodialysis. We report the results of new AVFs formed.
Material and methods: This is a prospective study of children seen in the Vascular Access Clinic at Great Ormond Street Hospital, London since June 2013. The children are assessed by clinical examination and ultrasound mapping of upper limb arteries and veins bilaterally before proceeding to surgery. Postoperatively, the children are reviewed at 6 weeks to assess fistula maturation by ultrasound and clinical exam. Patients with an existing AVF's entered into a surveillance program of 6-monthly volume flow assessment by ultrasound examination off dialysis.
Results: Sixteen fistulas were made (8 brachiocephalic, 6 basilic vein transpositions, 2 radiocephalic) median age 9.5 (2.9 – 17.3) years, weight 24.4 (14.0-67.0)kg. Pre-AVF ultrasound mapping of vein and artery showed a median diameter of 3.0 mm in both. Maturation scans at of 6-weeks after fistula formation showed median flow through the fistula of 1013 ml/min. Two cases required angioplasty to achieve maturation. Fistulas were considered suitable for needling after a median of 8.6 (5.14 – 61.86) weeks when the flow rates 1079 ml/min (600.0-1787.0). All AVFs were used successfully for dialysis. At follow-up (median 25 weeks after fistula formation) the blood flow through the fistula was 972 ml/min.
Conclusions: Successful AVF formation is possible even in very small children with a dedicated clinic. Clinical examination and ultrasound assessment is key to forming functional fistulae.

P - 221 EFFECTS OF HEMODIAFILTRATION IN AN INTERMITTENT NOCTURNAL DIALYSIS PROGRAM

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Introduction: In pediatric patients on conventional hemodialysis, morbidity is high and quality of life is poor. For improving morbidity and quality of life intensified hemodialysis programs have been developed. It has been demonstrated that these programs significantly improve uremia associated parameters. To analyze whether such a program can be further optimized, we performed a prospective observational study adding hemodiafiltration within a pediatric intermittent, nocturnal hemodialysis program.
Material and methods: 7 adolescent patients were investigated (median age 15.2 [12.7-16.3]). Patients were enrolled from conventional hemodialysis (HD) into the intermittent nocturnal hemodialysis (NHD) program. After 3 months on NHD, patients were switched to intermittent nocturnal online hemodiafiltration (NHDF) for three months and then back to NHD. We analyzed Kt/V, arterial blood pressure, phosphate, iPTH and calcium serum levels. Dietary restrictions, phosphate binders and antihypertensive drugs were investigated.
Results: Kt/V was significantly higher on NHD and NHDF in comparison to conventional HD ($p<0.001$). In the NHDF setting, Kt/V was even higher than in the NHD setting ($p<0.01$). Phosphate and iPTH were reduced after switching from conventional HD to NHD and NHDF ($p<0.001$). There was no difference between NHD and NHDF. Serum calcium levels remained unchanged in all settings. On conventional HD, all patients needed phosphate binders, whereas none of the patient on NHD and NHDF needed any phosphate binder. Mean arterial blood pressure was significantly reduced on NHD and remained in the same range on NHDF despite reducing antihypertensive medication ($p<0.001$). All dietary and fluid restrictions could be lifted on NHD and NHDF.

Conclusions: Nocturnal intermittent dialysis dramatically improves uremia-associated parameters in children. At least in our study, hemodiafiltration was able to further increase dialysis efficacy. However, the major benefit arises from the intensified dialysis. Longer prospective studies are needed to investigate, whether NHDF improves CKD-associated comorbidities.

P - 222 SURFACE ACTIVE PHOSPHOLIPID SYNTHESIS AND REGULATION IN HUMAN PERITONEAL MESOTHELIAL CELLS

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Introduction:
Human peritoneal mesothelial cells (HPMC) secrete surface active phospholipids (SAPL) presumably protecting the peritoneum from frictions, erosions and adhesions. Addition of SAPL to peritoneal dialysis (PD) fluid in humans increased ultrafiltration and reduced peritoneal transport rates. Regulation of peritoneal SAPL homeostasis, however, is unknown.
Material and methods:
Omental HPMC were isolated from four non-uremic patients. Young (passage 2-3) and senescent HPMC (>Hayflick-limit, senescence-associated-ß-galaktosidase positive) were analyzed for the expression of key genes of the Kennedy pathway (rt-PCR) and synthesis and secretion of 12 SAPL (24h, ESI-mass-spectrometry).
Results:
HPMC SAPL composition differs from pneumocytes, only 9% of all SAPL are Di-Palmitoyl-Phosphatidyl-Choline (DPPC) as compared to 60% in pneumocytes. Glucose (0.1-4.25%) dose dependently reduced the SAPL content of HPMC and SAPL secretion by up to 80 and 50%, calcium (1.0-2.5mmol/l) by 75 and 50%, respectively. The glucose degradation product 3,4DGE (0.1-100μM) and pH (5.5-8.1) had no systematic effect on gene expression and SAPL turnover. Low and high GDP fluids (1.5-2.3% glucose) reduced HPMC SAPL content and secretion by half. Icodextrin reduced total SAPL secretion by 60%, only DPPC secretion increased (6-fold). Dexamethason exposure for 24h increased total SAPL and DPPC secretion to 2 and 1.5-fold compared to control and reduced cellular SAPL content by half. Senescent HPMC expression levels of cholinkinase-alpha, phosphatidylcholin-transferase and of the rate limiting phosphocholincytidyl-tranferase were 1.5-, 2-, and 6 fold higher than in young cells, SAPL content 4-fold and secretion rate 80% higher (1.63 nmol/ml/100000HPMC/24h). PKA activator forskolin increased gene expression up to 2.3-fold and SAPL-secretion 4-fold.
Conclusions:
HPMC SAPL composition substantially differs from pneumocytes. SAPL synthesis and secretion are suppressed by glucose, calcium, low and high GDP PD fluids and icodextrin. The latter has been suggested for prevention of postoperative adhesions. Senescence as induced by chronic PD upregulates SAPL secretion and may protect the peritoneal membrane from PD associated sequelae.

P - 223 DIALYSIS MODALITY UPTAKE AND OUTCOMES IN AUSTRALIAN ADOLESCENTS AND YOUNG ADULTS

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Introduction:
Adolescent and Young Adult patients (AYA) represent a small proportion of patients with end-stage renal failure. The challenges of dialysis differ markedly in AYA compared to adults and younger children, yet little has been published on this group. This study was undertaken to describe characteristics of AYA aged 13-20 years between 2000 and 2010 receiving dialysis in Australia, and examine associations between demographic characteristics, dialysis modality, complications and outcomes
Material and methods:
Young Australians aged 13-20 years who commenced dialysis between 1/1/2000 and 31/12/2010 according to the Australian and New Zealand Dialysis and Transplant Registry were investigated.
Results:
230 AYA commenced dialysis during the study period, aged median 17.2 (IQR 15.8-18.6) years. 50.9% of patients were male. Haemodialysis (HD) was the initial modality in 161 patients (70%). Demographic characteristics were similar between dialysis groups. HD was preferred in all states apart from Queensland, where Peritoneal Dialysis (PD) and HD were used with equally (p=0.0006).
There was no difference in growth parameters or waiting time to transplantation according to dialysis modality. AYA managed by an adult centre waited significantly longer for and had a significantly greater number of changes in dialysis modality prior to transplantation, compared to those managed in paediatric centres. HD patients had lower mean haemoglobin levels within the first year (106.3+/-18.1 g/L vs 113.4+/-20.6, p=0.013).
Significantly fewer HD patients attended school full time than PD patients in the first year of dialysis (p=0.0001) and 1-2 years from starting dialysis (p=0.006). Remoteness of residential area did not influence school attendance.
Conclusions:
HD is used more often as the initial modality in Australian AYA. Dialysis choice does not appear to be influenced by patient characteristics, remoteness of residential area, dialysis outcomes, or impact on school attendance. Future research is required to examine the reasons that HD is preferred over PD in this patient group.

P - 224 PRACTICAL INDICATIONS OF DIALYSIS IN CHILDREN WITH CKD STAGE 5 – A RETROSPECTIVE QUESTIONNAIRE BASED STUDY

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Introduction:
We investigated the indications for commencing chronic dialysis in children with end stage kidney disease (ESKD) at our unit over a recent 5-year period.
Material and methods:
Of 86 children who commenced RRT (renal replacement therapy) we included 44 who electively commenced on chronic dialysis. 25 childrenpresented early, were analysed as two sub-cohorts, those with slowly falling eGFR(n=14) as Grp-1 and with CKD stage 4/5 from infancy(n=11) as Grp-2. For this group a questionnaire with known indications (clinical and biochemical) for commencing dialysis and choice of dialysis modality was taken by key members of our multidisciplinary team(MDT). Case-notes were reviewed for the 19 children presenting late (<3months to commence dialysis following presentation).
We excluded children who were followed at other units(n=25), failing transplants(n=2) and pre-emptive transplantations(n=15).
Results:
In the late presenting group the common indications were low-eGFR(64%), fluid-overload(47%), increasing urea(37%) and hypertension(37%).
The response-rate of questionnaire was 75% with common indications for commencing dialysis were low-eGFR(76%), faltering growth(44%), hyperkalemia(34%). Unsustainable high frequency of hospital

visits(52%), non-adherence to medical advice(28%) and additional social concerns(52%) were identified as nonmedical reasons. Three common responses in Gpr-1 were low-eGFR(86%), hyperkalemia(28%) and uremia(21%) while in Grp-2 low-eGFR(64%), hyperkalemia(73%) and growth-restriction(71%).
Complex social and family issues were identified in 57% and 45% of children in Grp-1 and Grp-2 respectively. Social reasons were contributory towards choosing modality in Grp-1(n=8) compared to Grp-2(n=1)(p=0.013). Inclination to choose haemodialysis in Grp-1 was also found (p=0.0129).
Conclusions:
This survey identifies that the indications of chronic dialysis in children are different from common adult indications. Although these depend on the aetiology and age of onset, common determinants are low-eGFR, hyperkalemia and impaired growth but hypertension and fluid overload are less prevalent. Family related factors play an important role in choosing the modality of dialysis. Due to limitations of this study we suggest a larger prospective study preferably a pan-European multi-centre study.

P - 225 HOW PROMISING IS THE CARPEDIEM DIALYSIS MACHINE TO TREAT NEONATAL AND PAEDIATRIC PATIENTS WITH ACUTE RENAL FAILURE?

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Introduction:
Among neonatal and paediatric patients admitted on ICU, 8-20% develop acute kidney injury (AKI). With current haemodialysis machines, non-accurate weight loss and large extracorporeal blood volumes imply important risks. Recently, CARPEDIEM (Bellco, Italy) has become available for Slow Continuous Ultrafiltration (SCUF) or Continuous Veno Venous Hemofiltration (CVVH) in paediatric patients of minimum 2.5kg.
Material and methods:
Three roller pumps guarantee precise flows for blood (2-50mL/min) and infusion/ultrafiltration (0-500mL/h). Fluid balance is controlled by scales. Three kits are available: HCD0075/015/025 with polysulfone dialyser of 0.075/0.15/0.25m², 27/33/41mL priming volume, and maximum ultrafiltration 2.5/4/5mL/min.
Results:
We treated 2 patients: male (M) (14weeks, 5.2kg, MOF and CMV) and female (F) (30months, 13kg, AKI). A jugular 6.5Fr double lumen catheter was inserted, and the HCD025 kit was used once (M) and twice (F). The kit was primed with 25mL 60% packed cells and 25mL 4%SOPP (M) and with NaCl and 10mL 20%HA (F) to avoid haemodynamic complications (M) and coagulation (F). A bolus of heparin was given at start [150IU (M) and 300IU (F)] and during the session [75IU/h (M) and 200IU/h (F)]. Predilution CVVH (substitution 4-4.3mL/min) was performed with blood flow 20-30mL/min (M) and 30-45mL/min (F), and ultrafiltration 500mL/24h. Continuous CVVH however needed to be stopped already after 10h due to haemodynamic instability (M) and after 9h and 8h due to, respectively, technical problems related to ultrafiltration and anticoagulation problems while using heparin (F). Both patients survived but the male needed CVVHD during 8 more days. During operation we ran into different technical bottle necks: i.e. lactate (no bicarbonate) dialysate bags, limited ultrafiltration, no heating system, no haemodialysis and no citrate anticoagulation possible.
Conclusions:
CARPEDIEM seems a promising machine to treat paediatric and neonatal patients with AKI when (limited) ultrafiltration and low efficiency dialysis is needed, but modifications are necessary to fulfill more neonatal dialysis needs.

P - 226 VENTRICULO-PERITONEAL SHUNTS IN CHILDREN ON HEMODIALYSIS: A SURVEY OF THE EUROPEAN PEDIATRIC DIALYSIS WORKING GROUP (EPDWG)

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Introduction:
Dialysis in children with concomitant ventriculo-peritoneal shunts (VPS) is rare. Registry data suggests that peritoneal dialysis (PD) is safe in children with VPS, but little is known on hemodialysis (HD) in children with VPS.
Material and methods:
We performed a 10-year survey to determine the prevalence, risk factors and outcome for children with VPS on HD in 15 dialysis units participating in the European Pediatric Dialysis Working Group.
Results:
Eleven cases of HD with a VPS were reported in 15 pediatric units over the last 10 years (prevalence 1.33%; 321.8 patient months). HD or haemodiafiltration (HDF; n = 2) was the sole dialysis modality: no patient received peritoneal dialysis (PD) at any point and no patient switched to PD as a result of symptoms. One shunt was ventriculo-atrial. Median HD vintage was 2.4 years (inter-quartile range 1.70- 3.0). Median age at start of dialysis was 9.6 years (6-15.0). Vascular access consisted of central venous line (CVL) in 6 and arterio-venous fistula in 5 children. There were no reports of shunt infection or meningitis despite 3 CVL infections in 2 patients. Symptoms of hemodynamic instability were reported in 6 children (56%) at least once per week: hypotension or hypertension occurred in 36% (n=4) and nausea, vomiting and headaches in 18% (n=2), with less frequent hemodynamic instability in 4 others. Seizures on dialysis occurred less than once a month in 2 children (20%). One centre used prophylactic mannitol each session; and one commenced mannitol following advent of symptoms. On final follow-up at 4.0 years median (interquartile range 0.38-7.63), three patients remain on HD and eight have a functioning transplant.
Conclusions:
HD in children with a VPS is rare and is associated with frequent symptoms of hemodynamic instability, but no episodes of VPS infection or meningitis even in those with CVL sepsis.

P - 227 LIMITATION OF FUNCTIONAL MOTOR SKILLS AMONG CHILDREN WITH END STAGE RENAL DISEASE ON DIALYSIS IN MALAYSIA.

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Introduction:
Limitation of functional motor skills among children with end stage renal disease (ESRD) is not an uncommon clinical encounter. The magnitude of this problem has never been investigated in our country. Objectives: To evaluate the prevalence of functional motor limitation among children with ESRD and to correlate bone health parameters with overall motor function level.
Material and methods:
Data retrieved from the National Renal Registry for year 2014 for children less than 18 year old. Motor function assessed and categorized using the Gross Motor Function Classification System (GMFCS). Statistical analysis was performed using SPSS 20.0.
Results:
Four hospitals with paediatric nephrologist participated in the study. A total of 95 patients included; 21 underwent chronic hemodialysis while 74 were on peritoneal dialysis. Mean age was 12.7±3.5 year old. Median duration on dialysis 2.9(1.5,4.9) years. All patients were on oral calcium carbonate, 10% were prescribed with additional Lanthanum carbonate, 92% of patients had oral calcitriol and 1 patient was given high dose oral cholecalciferol. None were given intravenous calcitriol. Mean serum calcium was 2.1±0.4mmol/L and phosphate 1.7±0.4 mmol/L. Median for alkaline phosphatase was 249(160,418) U/L and intact parathyroid hormone (iPTH) 228.0(80.0,549.5) pg/ml. 69.5% were categorized with GFMCS Level I (no limitation), 26.3% of the children with GFMCS Level II (some limitation), 1% with GFMCS Level III (needing assistive mobility device), 2.1% with GFMCS Level IV (needing assistive mobility with adult assistance) and 1.1% with GFMCS Level V (no means of independent mobility). Mean pain score was 0.64±1.0. Four children sustained fractures (4.2%). Intact PTH level correlated with their GFMCS level. Pearson Correlation was 0.37 ($p<0.05$). No correlation demonstrated in between alkaline phosphatase and GFMCS level.
Conclusions:
Prevalence of children on dialysis with functional motor limitation was 30.5% (GFMCS level II and above). Those affected were found to have higher iPTH level.

P - 228 SURVIVAL OUTCOME OF CHILDREN UNDER 2 YEARS REQUIRING RENAL REPLACEMENT THERAPY DUE TO END-STAGE RENAL FAILURE: 1973-2014

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Introduction:
Treatment of end stage renal failure in children less than 2 years of age is increasingly prevalent. Outcome data is often based on small patient cohorts with logistic challenges following transition to adult services. We present a retrospective longitudinal cohort of infants receiving RRT for ESRF over the last 41 years in Scotland and describe their long term outcome.
Material and methods:
Patients were included if they had commenced RRT between 2nd July 1973 and 20th May 2014 and were less than 2 years of age. In this cohort the first child was dialysed in 1982. Patients who recovered renal function following RRT for acute renal failure were excluded from the study.
Results:
30 patients (23 male) had a median time of follow up of 9.6 years. 288.3 patient years were analysed. 14 patients were deceased, with a mean age at death of 54.4 months. Median age at commencing RRT was 210 days of age. 4 patients had HD, 11 had PD and 15 patients had both therapies. Median number of days from RRT to first transplant was 878.5 days with no pre-emptive transplants. 18 patients received a renal transplant, 3 patients required re-transplantation. Median age at transplant was 3.83 years. 6 patients developed malignancy.
Conclusions:
The outcome of end stage renal failure in children less than 2 years of age remains poor. Despite technological advances in RRT, we have not seen a significant change in overall mortality in this population over this time. This possibly reflects increasing inclusion of infants who previously would not have been considered for RRT.

P - 229 EVALUATION OF NUTRITIONAL BLOODS IN PAEDIATRIC DIALYSIS PATIENTS

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Introduction:
Little is known about micronutrient/supplementation needs in children receiving long-term dialysis. Patients at our unit receive pyridoxine and Dialyvit® daily with 3 monthly monitoring of blood concentrations including selenium, manganese, copper, zinc, folate and vitamins A, D, B12 and E. The objective of this survey was to evaluate the proportion achieving normal ranges over a recent 2-year period.
Material and methods:
Retrospective review, including all children on chronic dialysis, for nutritional blood results time-averaged over the initial 6-month period of dialysis.
Results:
20 children (5 PD, 15 HD)with mean±SD age 9.4±6.6 years (10 boys). There were 10 white British/English, 3 Asian, 1 Black and 1 white Turkish ethnicity. Serum folate and vitamin E concentrations were in range in 55% and 25% only with others being above normal range. All children had Vitamin A and B12 concentrations above normal range. Vitamin D levels were sufficient in 53% with the rest in the deficient/insufficient ranges.
For the minerals/trace elements, 47% (n 8/17), 62% (n 8/13), 73% (n 11/15) and 81% (n 13/16) achieved normal ranges for zinc, manganese, copper and seleniumrespectively. Deficiencies were seen for zinc (n 9/17), copper (n 4/15) and selenium (n 1/16) whilst 12.5% (n 2/16) and 38% (n 5/13) had selenium and manganese levels above normal ranges. Despite standard pyridoxine supplementation there was no vitamin B6 monitoring.
Conclusions:
Closer monitoring of nutritional bloods are required which should include vitamin B6 monitoring. Standard pyridoxine supplementation should to be reviewed once a clearer understanding of the current vitamin B6 blood levels in our population is known.

P - 230 EFFECTS OF COMBINATION OF HIGH DOSE ORAL FOLATE AND VITAMIN B12 IN LOWERING THE PLASMA LEVELS OF HEMOCYSTEINE IN DIALYSIS PATIENTS

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Introduction:
Hyperhomocysteinemia is a well defined risk factor for cardiovascular diseases. This study was conducted to evaluate response to high dose oral folate (10 mg/daily) and sublingual high dose (1mg/daily) vitamin B12 in dialysis cases with hyperhomocysteinemia
Material and methods:
32 dialysis cases including 11 CAPD (31.4%) and 21 hemodialysis (66%) subjects and one patient (3%) who was on both modalities at the same

time were enrolled. They included 15 girls (46.9%) and 17 boys (53.1%). Majority of our patients received low doses of folate and vitamin B12 supplements.Chi square and T tests were used for data analysis. Mean plasma homocysteine levels before and after intervention compared by paired sample test and P value< 0.05 considered as a significant difference . First(week 0)all case were screened for hyperhomocysteinemia and serum folate and vitamin B12 levels were measured .Then those with hyperhomocysteinemia (plasma homocystein levels ≥15 μmol/L) received oral folate 10 mg and sublingual vitamin B12,1 mg /daily for 12 weeks. In the end of treatment(week 12) serum folate and vitamin B12 concentration and plasma levels of homocysteine were measured again

Results:

Of 32 cases 18 subjects (56.2%) had hyperhomocysteinemia.Serum folate and vitamin B12 levels were normal or high in all case. Plasma homocysteine levels dropped in all cases except one (6.25%) subject, but just in half of patients it reached normal range(<15 μmol/L). A significant decrease in homocysteine levels was found by comparing the plasma levels before and after the treatment (P=0.0001).

Conclusions: Hyperhomocysteinemia and functional vitamin B12 deficiency are common in dialysis Patients. Oral folate 10 mg/ daily in combination with sublingual vitamin B12 mg/day for 3 months is effective treatment for hyperhomocysteinemia. Keywords: End stage renal failure, Homocysteine, Folate, vitamin B12

P - 231 EIGHT YEARS EXPERIENCE WITH IN-CENTER NOCTURNAL HEMODIALYSIS

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Introduction:

Important comorbidities related to conventional hemodialysis, shortage of donorkidneys and decrease of quality of life , increases the need for alternative hemodialysis treatment in children.

Material and methods:

We retrospectively analysed the files of six children treated with intermittent nocturnal hemodialysis (3*8 hours) in University Hospital Ghent between 2006 and 2014. Data were collected every 3 months and were correlated with findings in literature.

Results:

We observed a significant decrease of the use of antihypertensive medication. The level of phosphate and the CaXP product showed a tendency to decrease together with the need for lower doses of phosphate binders.

In contrast with literature we could not detect a significant difference for Hb,parathormone(PTH) recombinant hyman erythropoëtine(RHuEPO) and ironsuppletion. Generally appetite was markedly better, but all the children complained of disruption of sleep.

Conclusions:

We conclude that intermittent nocturnal hemodialysis is a valuable alternative treatment for children > 8 years with ESRD. We observed better clearance of some known uremic toxines and a decrease of amount of medications. One important side-effect is disturbance of sleeppattern which might influence cognitive functions.

P - 232 CONTINUOUS AMBULATORY PERITONEAL DIALYSIS IN CHILDREN – EEXPERIENCE FROM EASTERN INDIA

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Introduction:

Indian data on chronic pediatric perfitoneal dialysis is limited.

Material and methods:

25 children (≤18 years) with end stage renal disease have been initiated on continuous ambulatory peritoneal dialysis at our center over the last 32 months.

Results:

Median age at last follow-up of was 10.3 (range 5.1 -17.4) years (74% male). 36% (n=9) needed urgent dialysis, whereas the rest were known to be suffering from chronic kidney disease for median 4.1 (range 0.4 to 10.8) years. Median age at onset of CAPD was 9.2 (range 3-16.5) years and median duration of CAPD was 15 (range 6- 48) months. Only 6 (24%) were local city residents and for the rest median distance from nearest pediatric dialysis centre was 102 (range 17 to 689) kilometre. Post initiation, four (16 %) children required catheter reposition because of poor fluid drain, but of these, only one needed catheter change. Usual CAPD prescription was 3 to 4 exchanges of 4 to 6 hours duration with dwell volume of 1L/ m2 of body surface area. Twelve (48 %) children developed peritonitis as per standard definition [5]. Overall, peritonitis rate was 0.85/year of peritoneal dialysis use. E. coli was the commonest organism (82%). None had exit-site infection. Only a single episode of fungal peritonitis was reported. Culture negative peritonitis was seen in 5 (20 %) cases. Duration of CAPD significantly correlated with peritonitis (P=0.006). Significant improvements were seen in various laboratory parameters except serum albumin and creatinine. One child was lost to follow up at 1 month. Of the rest, 9 (36%) underwent successful transplantation while on CAPD, 5 (22%) were switched to hemodialysis for recurrent peritonitis (2 subsequently underwent transplantation), 4 (16%) died on CAPD and 5 (20%) are still on CAPD for median duration of 9 (range 3 -14) months. Of the 4 deaths, three were associated with peritonitis and all of them had compliance issues due to financial constraints.

Conclusions:

Pediatric CAPD is a viable option in India as 43% of children finally progressed to transplantation

P - 233 SAFETY AND EFFICACY OF ONLINE-HEMODIAFILTRATION IN PEDIATRIC POPULATION

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Introduction:

Objective: To describe safety, tolerability and efficacy of online-hemodiafiltration (OL-HDF) in children on chronic hemodialysis.

Material and methods:

Single-centre, observational, retrospective study, including pediatric patients on chronic (>3 months) hemodialysis who have been on OL-HDF >1 month. We analyzed adequacy and purification parameters, hemodynamic stability and tolerability and clinical features.

Results:

We included 7 patients, all with subcutaneous central catheter. Primary disease: 1 structural, 1 glomerular, 4 hereditary, 1 graft loss. 2 patients had hypertension and 3 had left ventricular hypertrophy. Median age at start of dialysis 8.5 years (range 2.4-14). Median time on OL-HDF: 5.2 months (1.5-12). A Fresenius 5008® machine was used in 3 patients, in the other 4 we used a Fresenius 4008® machine. Average replacement volume was 11 L/m^2/session.

A higher clearance of β_2-microglobuline was observed with OL-HDF (reduction ratio per session 79.4% vs 66.7%, p=0.018), with the same urea reduction ratio (79.1%) and Kt/V (1.66 vs 1.65). The technique was

well tolerated, and there were fewer episodes of hypotension among patients on OL-HDF (0.21 episodes/patient/week vs 0.58; p=0.028). In one of the hypertensive patients we were allowed to discontinue hypotensive drugs.
Height z-score at follow-up: -1.2, with growth rate +2.8. 3 patients received growth hormone. There were no differences between OL-HDF and hemodialysis regarding dose of iron supplement, erythropoietin or phosphate binders, serum levels of albumin nor parathormone. At follow-up (21 months; 7-84), 4 patients had received a kidney transpantation and 3 remained on dialysis.
Conclusions:
OL-HDF is a safe, well-tolerated and effective technique for pediatric population. It guarantees hemodynamic stability and better medium-size molecules depuration. Due to the short time on OL-HDF of our patients, potential benefits of this depuration (growth, cardiovascular morbidity) cannot be evaluated.

P - 234 ENCAPSULATE PERITONEAL DIALYSIS AFTER SHORT-TERM CONTINUOUS AMBULATORY PERITONEAL DIALYSIS.

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Introduction:
Encapsulated Peritoneal sclerosis is a devastating complication of long term CAPD with high glucose containing solution. High awareness to detect the earliest stage of EPS might help to improve survival. We present three children on short term CAPD who developed EPS.
Material and methods:
Diagnosis of EPS was based on 1- clinical criteria of outflow failure, abdominal pain, bloody effluent, abdominal mass , wasting, 2- thickening of peritoneum in abdominal CT sacn with and without contrast or racoon eye. 3- In the case of perioneum specimen, pathological findings in favor of EPS.
Results:
Among thirty children on CAPD with dextrose containing dialysate with acidic PH , three childen presented with outflow failure, abdominal pain and tenderness, bloody effluent, abdominal mass. The demographic and clinical presntaiton of children are shown in table below.

	CASE1	CASE2	CASE3
Age(yrs)	6.5	14	11
Underlying disease	CAKUT	CAKUT	cystinosis
Duration of dialysis (months)	10	10	12
History of transplantaion	No	No	Yes
Episodes of overload	No	Yes	Yes
Episodes of Peritonitis	No	No	No
Dialysis fluid	Low glucose	Low and high glucose	High glucose solution
PET	High-high average	High, High average	NA
Presentation	Culturenegative peritonitis Abdominal painFever Outflow failure	Abdominal mass Bloody effluentFever Diarrhea	Fever Abdominal mass Abdominal pain
Abdominal CT scan	Focal thickening	Abdominal mass	Peritoneal thickening
Pathology	In favor of EPS	NA	NA
Medication	PrednisolonMycophenolate Tamoxifen	PrednisolonAzathioprin Switch to hemodialysis	Switch to hemodialysis
Surgery	Adhesiolysis Catheter replacement	Un operable	appendectomy
Outcome	Still on CAPD	Death	Still on hemodialysis

Conclusions:
Children on acidic glucose containing solution might be at risk of EPS even in short term dialysis. Howvere, genetic tendency can not be rulled out.

P - 235 INTENSIVE THERAPEUTIC PLASMA EXCHANGE IN CHILDREN WITH ACUTE AUTOIMMUNE NEUROLOGICAL DISORDERS

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Introduction:
There is a growing evidence for autoimmunity in acute central nervous system (CNS) disorders.
Material and methods:
Here we present a series of 8 children aged 2-12 years with transverse myelitis, Bickerstaff's brainstem encephalitis, neuromyelitis optica and acute paraneoplastic or unspecified encephalitis in whom therapeutic plasma exchange (TPE) was used as a second-line or rescue treatment. An intensified protocol including five consecutive TPE sessions followed by clinical evaluation and tapering of TPE was applied.
Results:
A total of 104 TPE sessions using Spectra Optia® device were performed. During a single session 80-110ml/kg of plasma was exchanged using a combination of a 4% albumin solution and fresh frozen plasma. Six episodes of TPE-related adverse events were documented. Fibrinogen concentrations decreased after the first TPE session and remained stable afterwards. One patient died in the course of the acute illness. Of the remaining seven patients three children achieved a complete resolution of symptoms. Two children are paraplegic after a follow-up of 3 to 17 months.
Conclusions:
We conclude that intensified daily TPE is feasible even in small children. Even though in our series the role of TPE can only be inferred, we find the clinical outcome encouraging in a setting where TPE was used as a rescue therapy.

P - 236 SINGLE PASS ALBUMIN DIALYSIS (SPAD) AND PLASMAPHERESIS FOR COPPER TOXICITY IN ACUTE WILSON'S DISEASE

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Introduction:
Wilson's disease is a disorder of copper metabolism that results in accumulation of copper in tissues. In acute Wilson's disease, patients present with fulminant liver failure, encephalopathy and haemolytic anaemia due to copper release from necrotic hepatocytes. Several extracorporeal techniques have been used to clear the copper and to safely bridge to liver transplantation.
Material and methods:
We report our experience with two patients in whom we used a combination of plasmapheresis and single pass albumin dialysis (SPAD) or SPAD alone.

Results:
A 13 year old boy (patient 1) and a 19 year old girl (patient 2) presented with fulminant hepatic failure, haemolytic anaemia and acute kidney injury.
Patient 1 was treated with SPAD on days 2-6 with addition of daily plasmapheresis days 3-6. Serum copper decreased from 48.7 μmol/L to 25.8 μmol/L (47% decrease) after the first session of plasmapheresis, and from 35.5 μmol/L to 21.5 μmol/L (39.4% decrease) after the second session. Mean decrease of copper was 43.2% and serum copper level was 16.2 μmol/L after 4 sessions of plasmapheresis. He underwent successful liver transplantation on day 6.
Patient 2 commenced SPAD day 3 and 4. Serum copper decreased from 22.3 μmol/L to 15.9 μmol/L (28.7% decrease) after the first treatment. She underwent successful liver transplantation on day 4 post-presentation.
Conclusions:
Our data suggests that SPAD with or without plasmapheresis, is effective in reducing serum copper levels as a bridge to liver transplantation in Wilson's disease. Plasmapheresis may be more effective but is associated with rebound increase in copper levels between sessions.

P - 237 ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN UNDERGOING PERITONEAL DIALYSIS

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Introduction:
The aim of this study was to investigate ADHD in children with end-stage renal disease (ESRD) undergoing continuous ambulatory peritoneal dialysis (CAPD) and to compare the results with those of healthy children.
Material and methods:
This case-control study was conducted for six months (December 22, 2013 to June 21, 2014) on five to 16-year-old children, visiting the Pediatric Dialysis Unit of Amirkabir Hospital, Arak, Iran, and Taleghani Hospital, Kermanshah, Iran. A total of 100 children with ESRD who had undergone CAPD for at least six months and 100 healthy children were included in this study as case and control groups, respectively. ADHD was diagnosed by Conners Parent Rating Scale-48 (CPRS-48) and DSM-IV-TR criteria, and was confirmed through consultation by psychologist.
Results:
The ADHD inattentive type was observed in 16 cases (16%) with CAPD and five controls (5%) ($P = 0.01$). Moreover, ADHD hyperactive-impulsive type was observed in 27 cases (27%) with CAPD and seven controls (9%) ($P = 0.002$). Despite these significant differences, no children was diagnosed with ADHD combined type among all subjects.
Conclusions:
Inattentive type and hyperactive-impulsive type of ADHD are more prevalent in children with ESRD undergoing CAPD. Therefore screening methods for ADHD is necessary in these patients.

P - 238 LDL APHERESIS IN CHILDREN WITH HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA: A CASE SERIES

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Introduction:
Homozygous familial hypercholesterolemia (HoFH) is a rare genetic disorder, clinically characterized by markedly elevated low-density lipoprotein (LDL-C) levels, exten-sive xanthomas, and premature and progressive atherosclerotic cardiovascular disease. Extracorporeal removal of LDL-C through LDL-apheresis is an effective way to lower circulating LDL-C levels. Currently, several LDL-apheresis methods are available. The aim of this study was to evaluate the effect of LDL-apheresis, utilizing the DSA (dextran sulphate adsorption) technology, on LDL-C levels, xanthomas and carotid intima-media thickness (c-IMT) in pediatric patients with HoFH.
Material and methods:
In this case series, we selected three pediatric HoFH patients for whom maximal statin therapy failed to reduce their LDL-C levels sufficiently. In these patients, weekly LDL-apheresis was started using Kaneka liposorber 15 with dextran sulphate cellulose columns to selectively remove LDL-C from the plasma. Levels of LDL-C were measured prior to and after each procedure. C-IMT measurements were performed by one experienced sonographer before the start of apheresis and approximately 1.5 year after performing apheresis. Additionally, medical photographs were made before and one year after apheresis.
Results:
Three HoFH patients aged 6 (girl), 10 (boy) and 11 (girl) years were included. Their LDL-C levels before (and after) maximum statin therapy were 20.8 (13.3),16.9 (9.3), and 15.5 (11.2)mmol/L, respectively. All patients had extensive cutaneous xanthomas (knee, elbow).
Mean plasmapherese dosage was 50 cc plasma/ kg during sessions of 60-85 minutes. The mean acute reductions in LDL-C after a single LDL-apheresis session were 77%, 74% and 69%, respectively. The mean LDL-C levels during a stable period of on average 9 LDL-apheresis sessions were 4.1, 4.7 and 4.0 mmol/dL, respectively. Furthermore, a significant regression of cutaneous xanthomas was observed in all patients (Figure 1). In one patient, c-IMT decreased substantially (0.420 mm to 0.391 mm); c-IMT results for the other two patients will shortly be available. LDL-apheresis was well tolerated; only mild side effects in 1 patient during the first 5 shifts (dizziness, shivering, mild nausea) were reported.
Conclusions:
Our findings suggest that LDL-apheresis (DSA) in children with homozygous FH is a safe and effective method to lower LDL-C levels, decrease c-IMT and to significantly reduce xanthoma size.

P - 239 LAPAROSCOPIC FIXATION OF A MALFUNCTIONING TENCKHOFF CATHETER USING THE PIRS METHOD - PRESENTATION OF TWO CASES.

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Introduction:
Malfunction of a peritoneal catheter is the most common complications of peritoneal dialysis in children.The paper presents a novel laparoscopic method - PIRS (percutaneous internal ring suturing) - with the catheter being fixed to the anterior abdominal wall in two cases of malfunctioning peritoneal catheters.
Material and methods:
The Patient 1 (15 yrs old) presented with an untypical displacement of the catheter tip (paraspinally cephalad - oriented) which was failed to be visualized by ultrasound and was detected on plain X-ray.Following the initial classic surgical revision, only a short-term improvement was achieved then the new method was used. In the second patient (5-month old male infant) dialyzate outflow was stopped, but no catheter tip displacement was observed. Intraoperatively, the catheter was found to be embedded in a peritoneal pocket, what rendered it normal functioning impossible. The catheter tip required repositioning and placement in the proper location above the right iliac ala.

Results:
The novelty of the technique employed in Patient 1 is the use of a single visual port, which to date has been described solely in adult patients. In Patient 2, it was necessary to insert an additional instrument in order to reposition the catheter tip to an appropriate location. Subsequently, peritoneal dialysis was successfully continued in both children. The presented method of catheter fixation a new own modification of the previously described technique.
Conclusions:
Based on literature reports and own experience it seems worthwhile to popularize laparoscopy as the method of choice in treatment of malfunctioning peritoneal catheters o in children.

P - 240 HOW TO ADAPT PROMETHEUS® THERAPY IN CHILDREN WITH ACUTE LIVER FAILURE?

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Introduction:
Prometheus® (FMC, Germany) serves as bridge to transplantation or recovery in adults with liver failure. When applied in children, the system offers specific challenges due to the large extracorporeal volume (700-750mL). We therefore developed an adapted protocol for the application in children.
Material and methods:
Blood circuit is primed with 2L isotonic saline, while plasma circuit is filled with 2U fresh frozen plasma or 400mL SOPP. Next, for children with body weight BW<25kg, a solution of 60-65% packed cells (PC) is infused in the inlet blood line at 40mL/min. After the priming phase, blood and plasma flow are increased to at least 100mL/min and 200mL/min, respectively, and dialysate flow is set at 300mL/min. Regional citrate anticoagulation is done with a calcium-free dialysate, while, eventually, heparin is added to the priming solution. Post-treatment, the circuit volume is either not reinfused (BW<25kg) or reinfused using isotonic saline (BW>25kg), with a volume depending on the hydration status and the originally infused volume of PC. Reduction ratio RR (%) of urea, creatinine (Crea), bilirubin (bili), and ammonia (NH3) were calculated from pre and post treatment serum concentrations. Primary and secondary patient outcome was evaluated.
Results:
Eight children (5male), 8.6±5.9years old, BW 32±21kg, with an uncuffed double lumen dialysis catheter [8-14Fr Femoralis (n=6), 9Fr Jugularis (n=2)] were treated according to this protocol. In total, 19 sessions were executed using FX40 (n=13), FX50 (n=3), and FX60 (n=3) dialysers during 6.5±0.9h with blood flow 149±45mL/min and albumin flow 226 ±49mL/min. RRs were 70±15%(urea), 34±14% (Crea), 44±16% (bili), and 36±10% (NH3). Primary survival rate was 100%. Four patients were transplanted of which 1 died within 30 days after discharge from ICU, one died 9 months after treatment due to primary disease, and the remaining three fully recovered.
Conclusions:
In conclusion, this adapted Prometheus® protocol is promising for the treatment of children with liver failure.

P - 241 EXTRACORPOREAL TREATMENT IN CHILDHOOD INTOXICATIONS; 16 YEARS OF EXPERIENCE

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Introduction:
Main treatment approach in intoxication cases is rapid clerance of intoxicating material from body and supportive treatment. We aimed to evaluate patients who we followed for intoxication and treated with extracorporeal treatment in last 16 years.
Material and methods:
A total of 1154 cases followed by Uludag University Faculty of Medicine, Department of Pediatric Nephrology and 25 of these cases treated with utilization of extracorporeal treatment methods between January 1998-December 2013 were retrospectively evaluated in terms of epidemiologic and clinical features.
Results:
Age of patients varied between 1 month and 18 years with a mean of 8,4±5,8 years. 654 (%56,6) and 500 (%43,4) of cases were girl and boy; respectively. Cases of intoxication were most frequently aged between 11-18 years (%42, 6). There was a total of 25 cases treated with extracorporeal methods. Among them, 17 (%68), 6 (%24), 1 (%4) and 1 (%4) cases were treated with extracorporeal treatment methods due to medications, mushroom intoxication, organophospate, and ethyl alcohol intoxication. 11 (%64,7) of cases treated with extracorporeal methods due to drug intoxication were intoxicated with amytriptyline. For the first time in literature, one case of amytriptyline intoxication was treated with selective plasma exchange and case was dramatically recovered. Only one case (during treated with HP due to organophospate intoxication) of extracorporeal treatment died.
Conclusions:
It was concluded that HP treatment in Amitriptyline intoxication is an effective and life-saving treatment method.

P - 242 PERITONEAL DIALYSIS FOR TREATMENT OF CHILDREN WITH END STAGE RENAL DISEASE IN BULGARIA – 20 YEARS EXPERIENCE

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Introduction:
Peritoneal dialysis (PD) is the preferred form of chronic dialytic therapy in children. There is only one pediatric dialysis unit in Bulgaria. PD was started in 1993 as continuous ambulatory PD (CAPD) and automated PD (APD) was introduced in 2003.
Material and methods:
This retrospective study includes all 72 children with end stage renal disease (ESRD), treated by PD in Pediatric Dialysis Unit, Sofia between 1993 and 2012. Girls are 40 (56%) and boys 32 (44%). The mean age is 10,29±4,46 years. The youngest patient is 3 months old and the oldest 17 years. CAKUT is leading cause of ESRD (46%), followed by FSGS (15%). In all patients straight Tenchhoff catheter was placed surgically. CAPD was used in 61 children (85%) and APD in 11 (15%).
Results:
In 9 children (13%) PD is the first dialytic modality, in 52 (72%) PD is the main therapy after short hemodialysis (HD) and 11 (15%) moved from HD to PD because of vascular access failure. A total of 2013 months PD were registered, mean 27,96±25,5, ranging from 1 to 109. From 72 patients, 29 (37%) were switched to HD, 19 (24%) transplanted, 13 (17%) reaching 18 years of age transferred to adult dialysis units, 12 (15%) died, 3 (4%) recovered partially renal function and 2 (3%) continued on dialysis. Patients survival is 88% at 3 years and 83% at 5 years. Cardiovascular complications resulted in 8 deaths (67%), peritonitis in 2 (17%), pulmonary involvement in systemic vasculitis in 1 (8%) and catheterization of subclavian vein in 1 (8%). Comorbidities and social factors increase significantly mortality risk. Modality survival is 69% at 3 years and 63% at 5 years. Peritonitis was the reason for switch to HD in 20 (69%) cases.

Conclusions:
PD is a good option for treatment of children with ESRD. Results, achieved in Bulgaria are comparable with data from European and North American registries. Cardiovascular causes are most frequently responsible for patients mortality and infectious complications for modality failure.

P - 243 IMPACT OF RECOMBINANT HUMAN ERYTHROPOIETIN TREATMENT ON LEFT VENTRICULAR MASS AND CARDIAC FUNCTION IN PATIENTS WITH END STAGE RENAL DISEASE ON HAEMODIALYSIS

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Introduction:
The aim of this work was to demonstrate the effect of rHu EPO therapy on LVH and LV systolic function in patients with end stage kidney disease.
Material and methods:
Thirty two patients were enrolled in this study, 14 females and 18 males. Their age ranged from 5 to 17 years along with 15 age and sex matched healthy subjects as controls. The inclusion criteria were; the presence of renal anemia , adequate serum iron status with serum ferritin level of 100 ng/ml or more and a transferrin saturation of >20%, normotension or controlled hypertension and no history of valid heart disease or other systemic illness. We analyzed the laboratory and echocardiographic data before starting EPO treatment and after treatment in period of follow up ranged between 4 and 9 months with a mean of 5.8+/-1.5 months.
Results:
Hb level increased from 8.5+/-1.87 to 9.3+/-1.7 gm/dl, Hct level increased from 25.78+/-6.59% to 28.88+/-5.5%, LVMI showd reduction from 108.8+/-41.97 to 97.13+/-43.9 g/m^2 , SV decreased from 59.58+/-21.17 to 53.9+/-18.49 ml and finally CO decreased from 5.74+/-2.2 to 5+/1.5 L/minute.
No significant change was detected regarding the HR, EDV, &ESV. LV systolic function was normal at the start of the work and remained so in the follow up examination.
Conclusions:
We concluded that in patients with ESRD on chronic hemodialysis, LVH regression can be obtained after partial correction of anemia with rHu EPO which can be also associated with reduction of the high CO encountered in these cases. Weather this regression would improve outcome in haemodialysis patients remain to be established.

P - 244 CHRONIC PERITONEAL DIALYSIS: TWENTY-ONE YEAR EXPERIENCE IN A SINGLE CENTRE IN TURKEY

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Introduction:
Continuous ambulatory peritoneal dialysis (CAPD) has been utilized in the treatment of children with chronic kidney disease in children since 1993 in our centre. In this study we evaluated the outcome of CAPD over a period of twenty years at our institution.
Material and methods:
We retrospectively evaluated the medical charts of our patients from the hospital records between 1993 and 2014. Data was collected for clinical and demographical features, etiology of chronic kidney disease, laboratory parameters, duration of peritoneal dialysis, cause of termination of CAPD, rate and risk factors of peritonitis and survival analysis.
Results:
179 patients, 105 females and 74 males had been followed during 20 years . Mean age at dialysis initiation was 130.14±54.8 months (7-240). The mean duration of follow up was 15 months (0.5 -232); and it was 7 months (0.5-60 months) for patients under the age of the two years and 15 months (0.73 and 232) for children above two years of age. Only 12 (6.7 %) of these patients were on automated peritoneal dialysis (APD). Thirty of the patients (21.8 %) were switched to haemodialysis, 46 (25.7 %) were transplanted, 7 (3.9 %) were transferred to adult system and 35 (19.6 %) to other centers. Renal functions returned to normal in 3 (1.7 %) patients. A total of 11 peritonitis episodes occurred. Fifty five patients (30.7 %) died during follow up.
Conclusions:
There was a significant difference in the follow up time for children under the age of two years. Gender did not influence the follow up time. We also observed that peritonit rates increased significantly with the longer duration of follow-up. Etiology did not effect the survival. The age of the patient and the rate of the peritonitis were the most important factors on the patient survival.

P - 245 HEMODIALYSIS IN ALBANIAN CHILDREN

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Introduction:
Renal replacement therapy is required for patients who have acute or chronic renal dysfunction, which results in serious uremic toxicity or derangement of electrolytes and acid base balance. In children, standard dialysis modalities are temporary measures to maintain fluid, nutrition and electrolyte balance. The ultimate goal of treatment in end stage renal disease is renal transplantation
Material and methods:
All patients who received hemodialysis between September 2010 and September 2014 were enrolled in the study.
Results:
27 children have received hemodialysis treatment over 4 years; 14 females and 13 males, aged from 6 months to17 years old. 14 cases had acute kidney injury, 11 of them are completely recovered. Of 13 children with chronic kidney disease, 4 of them underwent live-related renal transplantation, 4 children are left to continue their treatment at other centers, abroad, 2 children are now in conservative treatment, the others continue the dialysis treatment in our center. 3 children died (2 acute cases, 1 chronic case) 9 children came from Kosovo.
Conclusions:
Our center was the only center of reference for cases from Albania, but also from Kosovo.

P - 246 SERUM FOLATE AND VITAMIN B12 LEVELS IN HEMODIALYSIS PATIENTS: IS THERE ANY CORRELATION WITH PLASMA HEMOCYSTEINE LEVELS?

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Introduction:
This study was conducted to determine serum folate and vitamin B12 status in hemodialysis patients and find any correlation between plasma homocysteine and serum levels of these vitamins ?All patients were supplemented by folate 2.5-5 mg/day and 15 cases were received oral Vitamin B12 3-6 μg day. Serum folate levels <1.5 ng/ml and > 17 defined as low (deficiency) and high respectively. For vitamin B12 levels < 120

pg/ml, 120-160 pg/ml, 160-970 pg/ml and >970 pg/ml were defined as deficient, borderline, normal and high levels respectively. Plasma hemocysteine levels>15 μmol/L were defined as hyperhemocysteinemia. Correlation between the vitamins' levels and plasma Hemocysteine levels were checked by Pearson correlation test and P-values <0.05 and r>0.7 were defined as a good (significant) correlation.

Material and methods:

19 hemodialysis subjects enrolled the study

Results:

13 patients (68.4%) had hyperhemocysteinemia. No cases had folate or vitamin B 12 deficiency .There was no significant differences in mean Serum folate and vitamin B12 levels between those with normal and high plasma hemocysteine levels (P= 0.278 and 0.607 respectively)

Conclusions:

The supplementary folate and vitamin B 12 dosages that we used result in high serum levels in majority of patients .In addition hyperhemocysteinemia may be accompanied by normal and even high serum levels of these vitamins. We concluded that there is no correlation between normal and high serum levels of these vitamins and plasma Homocysteine levels.

Key words: Hemodialysis, hyperhemocysteinemia, Folate, Vitamin B12

P - 247 THERAPEUTIC PLASMA EXCHANGE IN PEDIATRIC SLE, A CASE SERIES.

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Introduction:

Paediatric literature is scanty on utility of TPE in SLE.

Material and methods:

We hereby present three cases; Thrombotic Thrombocytopenic purpura (TTP), diffuse alveolar haemorrhage (DAH) and crescentic glomerulonephritis which were treated with TPE as an adjunctive therapy.

Results:

TPE was carried out in haemodialysis units using membrane filtration technique. Demonstrable benefit of TPE was seen in all three cases.

Conclusions:

In refractory pSLE, TPE may be a useful tool and should be considered.

P - 248 AN ANALYSIS OF PATIENTS STARTING RRT IN PAEDIATRIC CENTRES AT AGE <16 YEARS, BETWEEN 1995 AND 2013. A UK RENAL REGISTRY REPORT ON BEHALF OF THE BAPN

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Introduction:

To describe trends in incidence, age and primary renal diagnosis (PRD) at start of renal replacement therapy (RRT) in the UK for all patients aged <16 years.

Material and methods:

Retrospective analysis of patients aged <16 years from all 13 paediatric nephrology centres commencing RRT between 1995 and 2013 from UK Renal Registry (UKRR) data.

Results:

2027 children commenced RRT between 1995 and 2013, with average annual RRT incidence between 103 and 129 patients per year.

Peak age groups at commencing RRT were 12 - <16 years (33%) and 8 - <12 years (21.9%). A trend towards earlier onset of RRT over time was observed, however this did not reach statistical significance (p=0.2).

The most frequent PRDs overall were renal dysplasia (27.2%) and glomerular disease (20.5%). We observed a highly statistically significant change in the distribution of PRDs by time period over the study duration ($p < 0.0001$). Table 1 depicts an extract of salient changes in PRD from 1995-1999 and 2010-2013.

Table 1: Incidence of PRD by time period for the diagnoses with maximum change over study duration.

	Incidence (%)	
PRD	**1995-1999**	**2010-2013**
Renal Dysplasia	24.95	31.43
Glomerular Disease	21.65	13.57
Reflux Nephropathy	8.87	3.1
Drug Nephrotoxicity	4.86	0

The decline in glomerular disease and nephrotoxicity may be attributable to improved treatment and preventative medicine. The decrease in reflux nephropathy and increase in renal dysplasia possibly reflects changes in common diagnostic criteria and improved diagnostics.

Conclusions:

Although the incidence of established renal failure (ERF) in childhood is predominantly stable, there are discernable changes in the underlying causes with structural renal disease dominating as glomerular disease, reflux and nephrotoxicity become less frequent and a trend to younger age at start of RRT. Further research would be valuable to explain the changes seen and in planning services for children with ERF.

P - 249 MUTATION IN COMPLEMENT SYSTEM GENES OF HEMOLYTIC UREMIC SYNDROME, GENOTYPE-PHENOTYPE CORRELATION AND TREATMENT

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Introduction:

Primary aHUS (idiopathic or familial) related to parafunction of complement system's alternative pathway.Our study is aimed that research mutation of complement system genes on sporadic aHUS patients and determine effect of genotype-phenotype relation on treatment and prognosis.

Material and methods:

This study was performed on 14 patients with nonimmune hemolytic anemia, trombocytopenia and HUS. Female/male rate was 4/10, the average of ages were 7,45 ± 0,8. No one had history of diarrhea and everyone had oliguria, high creatin and high GFR, STECH was negative on stool, schistocytes and reticulocytosis were on pheripheral smear, direct coombs was negative, LDH was high, haptoglobulin was low, C3and C4 were normal, ADAMTS13 activation was normal and therefor primary sporadic aHUS was diagnosed.Molecular genetic analysis of complement factor H (CHF), complement factor I (CFI), complement factor B (CFB), membrane cofactor protein (MCP/CD46) and C3 gene were performed every patients.Level of MCP and CFH antibody was analysed by ELISA.

Results:

In our study the patients with normal levels of C3, CFH, MCP and MAC were found to have 7 mutations in complement system genes.Different DNA variants were determined in CFH gene in 12 patients. 4 out of these variants were considered as mutation as related to the disease. We determined His402Tyr and Val62Ile synonymous mutations in 8 and 2 patients, respectively. There was no transposition of nucleotide in 2 patients. It was found Arg150Arg in 10 patients, Pro168Pro synonymous mutation in 1 patient and ArgTrp mutation in 3 patients in CFB gene. Ser268Ser synonymous mutation was detected in CFI gene in 6 patients. MCP-CD46 gene showed no transposition of nucleotide

Conclusions:
In our study although the patients diagnosed with aHUS had normal levels of serum C3, CFH, MCP, MAC, they were found to have mutations in CFH and CFB genes. Located in complement system. Although the patients with aHUS were normal for serological levels of C3, CFH, MCP, MAC, genetic evaluation is necessary.

P - 250 ALTERNATIVE PATHWAY COMPLEMENT ACTIVATION IN C3 GLOMERULOPATHY

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Introduction:
Glomerular pathologies characterized by isolated deposition of C3 are nowadays called C3 glomerulopathies (C3G) and include dense deposit disease and C3 glomerulonephritis. It is thought that C3G can be caused by systemic dysregulation of the alternative complement pathway, however, the exact mechanism of complement pathology in C3G patients is poorly understood. To get more insight in complement regulation in C3G, we performed a thorough analysis of alternative pathway activation in nine patients in acute phase of C3G.
Material and methods:
In nine biopsy-proven C3G patients, background levels of complement activation markers C3b/c and C3bBbP (alternative pathway), and TCC (terminal pathway) were measured in EDTA plasma using ELISA and compared to the results of 19 healthy controls. Moreover, the patients were screened for DNA aberrations in alternative complement pathway genes *CFH*, *CFI*, *C3*, *CFB* and *MCP*. Presence of anti-FH autoantibodies was analyzed by ELISA.
Results:
Patients with acute phase C3G showed elevated plasma levels of C3b/c ($P<0.05$), C3bBbP ($P<0.001$) and TCC ($P<0.05$), indicating alternative complement pathway activation in C3G.
Conclusions:
We demonstrated significantly elevated complement activation biomarkers in acute phase C3G. These data indicate that alternative complement pathway activation is involved in the pathogenesis of C3 glomerulopathy and can be detected in blood samples. The assays to detect complement activation biomarkers may be important to monitor complement activation in C3G patients receiving complement inhibition therapy.

P - 251 THE COMPLEMENT SYSTEM IS ALTERED ON SEROLOGICAL AND GENETIC LEVEL IN BOTH INFECTION-INDUCED AND COMPLEMENT-MEDIATED HUS

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Introduction:
The role of the complement system in the atypical form of HUS (aHUS) has been investigated tremndously in recent years. It is known that HUS-associated bacteria, like shiga-toxin producing *Escherichia coli* (STEC) and *Streptococcus pneumoniae* (SP), can evade the complement system by binding complement regulators. We hypothesized that a dysregulation of the complement system has an important role in the pathogenesis of infection-induced HUS as well.
Material and methods:
Newly diagnosed children with STEC-HUS, SP-HUS, or aHUS were enrolled in this study. Serological profiles (C3, FH, FI, AP activity, C3d, C3bBbP, C3b/c, TCC, aFH, aO157-H7 LPS) and genetic profiles (*CFH*, *CFI*, *CD46*, *CFB*, *C3*) of the alternative complement pathway were prospectively determined in the acute and convalescent phase of disease. Serological profiles were compared to 90 age-matched controls.
Results:
Thirty-eight patients were included in the study (26x STEC-HUS, 11x aHUS, 1x SP-HUS). In 40,5% of the patients, including 28% of the STEC-HUS patients and the only SP-HUS patient, we identified a genetic and/or acquired complement abnormality. In the acute phase, the levels of the alternative pathway activation markers C3d, the C3d/C3 ratio, C3bBbP, and C3b/c were increased in all patients groups, whcih normalized to control levels in remission. The activation markers were significantly higher in aHUS patients than in STEC-HUS patients.
Conclusions:
In both infection-induced HUS and aHUS patients the complement system is activated in the fluid phase in the acute phase of disease, but nog in remission. The C3d/C3 ratio displayed the best discrepancy between acute and convalescent phase and betwee STEC-HUS and aHUS, and might therefore be used as a biomarker in diagnosis and disease monitoring. The presence of genetic and/or acquired complement aberations in STEC-HUS and SP-HUS patients indicates that genetic screening might be important in these patients as well.

P – 252 HEMOLYTIC-UREMIC SYNDROME AND RENAL LONG-TERM SEQUELAE - AN OBSERVATION OF 262 PATIENTS

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Introduction:
Renal impairment can persist in children with HUS. Here, we present long-term follow-up data of 262 patients.
Material and methods:
In this retrospective study, we analysed clinical and laboratory data of 262 children with HUS. Renal sequelae we defined as the existence of at least one of the following parameters: proteinuria ≥300 mg/l or ≥1+ (dipstick), mean arterial pressure > 90 percentile, need for antihypertensive medication, and GFR <90ml/min/1,73m². Patients were divided into two groups (1:1976 to 1995 and 2: 1996 to 2014).
Results:
We identified 262 children with the diagnosis of HUS (Gr. 1: n=185, Gr. 2: n=77). 245 survived the acute phase. 179 patients were seen for a 1-year follow-up visit. Here, 82 (45,8%) presented with renal sequelae (Gr. 1: 61/126 (48,4%), Gr. 2: 21/53 (39,6%)). At the 2-year follow-up visit, 68 of 140 children (48,6%) displayed renal sequelae (Gr. 1: 52/99 (52,5%), Gr. 2: 16/41 (39%)) and at the 5-year follow-up visit, 39 of 70 (55,7%) (Gr. 1: 30/52 (57,7%), Gr. 2: 9/18 (50%)). At the 1-year follow-up visit, we found a significant correlation between antihypertensive therapy in the acute phase and persistence of renal sequelae (Gr. 1: p=0,024, Gr. 2: p=0,003). The same could be shown for anuria >7 days (Gr. 1: p<0,0001, Gr. 2:p<0,05). Dialysis in the acute phase was only in group 2 a significant risk-factor (p=0,003). No significant correlations were found for age and gender.
Conclusions:
Renal residual damage persisted in >40% of the patients but there was no data in >50% of all cases – underlining the importance of a consequent long-term

follow-up. Analysis for risk-factors for renal sequelae was inconsistant (1- to 5-year-follow-up), with the strongest correlation for antihypertensive therapy (i.e. hypertension) during the acute phase as well as anuria >7 days.

P - 253 FAILURE OF IMMUNOSUPRESSION TO ALLOW INTERRUPTION OF ECULIZUMAB IN ANTI-FACTOR H ANTIBODY ASSOCIATED ATYPICAL HEMOLYTIC UREMIC SYNDROME

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Introduction:
Atypical hemolytic uremic syndrome (aHUS) due to circulating anti-Complement Factor H (CFH) autoantibodies concerns 10-20% of children with aHUS. Early initial therapy with plasma exchange in addition to immunoppressive treatment is recommended by the available literature. Antibody testing might be a valuable tool for monitoring treatment response though the acceptable blood level is rather arbitary. Whereas the efficacy of eculizumab in the acute phase of severe cases has been recently reported, its role in the maintenance therapy is not yet established.
Material and methods:
We report a case of a 8 year-old boy of Nigerian origin who presented aHUS involving acute kidney failure, cerebral ans cardiac thrombotic microangiopathy. Plasma exchange did not improve the clinical symptoms but treatment with eculizumab permitted a favorable clinical outcome. As he had positive anti-CFH autoantibodies (1800 AU/ml {positive threshold:1000 AU/ml}, an immunosuppressive treatment with mycophenolate mofetil was initiated in order to achieve withdrawal of eculizumab pulses. The rate of anti-CFH autoantibodies remaining high 6 months later (1086 AU/ml), a cure of rituximab was added and permitted a reduction of anti-CFH autoantibodies (850 AU/ml, 2 months later).
Results:
Nevertheless, the disease recurred, as hemolysis and abrupt increase of CH50 were identified, when treatment with eculizumab was delayed for 4 days. Remission occured immediately after eculizumab treatment was restaured. Immunosuppressive therapy did not allow prevention of recurrence despite reduction of antibody level.
Conclusions:
We report the beneficial role of eculizumab not only in the acute phase but also in the maintenance therapy of CFH autoantibody-positive aHUS.

P - 254 LONG-TERM OUTCOME AND PROGNOSTIC INDICATORS IN HEMOLYTIC-UREMIC SYNDROME

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Introduction:
The aim of this study is to describe the long-term renal outcome of children diagnosed with diarrhea-associated-hemolytic uremic syndrome (D-HUS) and atypical-HUS (aHUS) and to identify clinical and laboratory predictors of poor prognosis.
Material and methods:
We retrospectively reviewed the medical records of 95 children (53 males) suffering from HUS followed in our hospital from 1975 to 2013. Secondary thrombotic microangiopathies excluded.
Results:
Mean age at diagnosis was 2.8 ±2.3 years. 79 patients had D-HUS and 16 had aHUS (8 with mutations in their complement genes).

After a mean period of follow-up of 8.2 ±5.7 years, 27 patients (28.4%) showed any sign of chronic kidney disease (CKD): decreased glomerular filtration rate (GFR) in 18/95 patients, proteinuria in 26/95 and hypertension in 7/95. Eight children (5 with atypical HUS) evolved to end-stage renal disease (ESRD) at a median time of 6 years. All of them were successfully transplanted without recurrences.Two patients died on follow-up.
Clinical and laboratory data at the onset and follow-up analysed for prognostic significance are summarized in table1.
Patients with aHUS have a greater risk of ESRD (31.2%vs3.8%;p<0,001) and higher prevalence of hypertension (25%vs3.8%;p=0.003).

Data at diagnosis	**Non CKD**	**CKD**	**p**
Hemoglobin (g/dL)	8.1 ±2.2	9.5 ±2.5	0.009
Polymorphonuclear leukocyte count (cell/mm^3)	9853 ±5915	13180 ±6575	0.033
Length of oliguria (days)	7.6 ±5,7	16.9 ±15	0.002
Admission (days)	19.8 ±12.2	34 ±20.7	<0.001
Need for dialysis	62%	85.2%	0.027
Hypertension	42.6%	74%	0.006
Proteinuria at discharge	49.2%	96.1%	<0.001
Data on follow-up			**p**
GFR<90 mL/min/1,73m^2	1.7%	46%	<0.001
Proteinuria	6.1%	84.6%	<0,001
Hypertension	1.5%	15.3%	0,009
Ultrasound abnormalities	4.4%	77.7%	<0,001

Conclusions:
In our series 28 % of children whith HUS developed any degree of CKD in the long-term follow-up. Duration of oliguria/anuria, an elevated polymorphonuclear leukocyte count, presence of hypertension and proteinuria at diagnosis; and ultrasound abnormalities, hypertension or proteinuria on follow-up were predictors of poor renal outcome. Progression to ESRD was more common in children with aHUS.

P - 255 CLINICAL DEBUT OF HEMOLYTIC-UREMIC SYNDROME IN CHILDREN

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Introduction:
Objectives: To describe acute signs and symptoms in children with Hemolytic-Uremic Syndrome (HUS) and to assess clinical differences between diarrhea-associated-HUS (D-HUS) and atypical-HUS (aHUS).
Material and methods:
Single centre, descriptive, retrospective study. Period 1975-2013. Included patients with clinical diagnosis of HUS, with or without diarrhea, familial and recurrent cases, or known abnormalities in complement regulation. Secondary thrombothic microangiopathies excluded.
Results:
95 patients (53 males). Age at diagnosis 2.8 years (±2.3). 83% had diarrea, shiga-toxin *E.coli* was isolated in only 10% of stool cultures. Hemoglobin at diagnosis 8.5 g/dL (±2.4), 93% of patients requiring transfusion. 60% (57 patients) develop oliguria (2/3 anuria). 65 patients receive dialysis (89% peritoneal dialysis) for a median time of 10 days (range 1-65). 49 patients (52%) had hypertension during hospitalization,

although only 20% remain at discharge. 27 patients had neurologic complications and 28 gastrointestinal involvement.
At the end of acute phase, 64% had normal glomerular filtration rate, 61% persistent proteinuria and 43% microscopic hematuria. Diagnosis of D-HUS in 79 patients, aHUS in 16 (8.5%), 8 with complement regulation abnormalities (3 anti-factor H antibodies, 3 mutations in MCP, 1 in factor B and 1 DGKE). Patients with aHUS presented less often with diarrhea (6.3%vs98.7%;p<0.001) and had more respiratory symptoms (50%vs6.3%;p<0.001). Oliguric phase was longer (18.3 days vs 9.7;p=0.022) as time to platelet count recovery (11 days vs 7.6;p=0.023) and length of hospital stay (31.8 days vs 22.4;p=0.037). They were more often hypertensive at discharge (43.7%vs15.4%;p=0.01).
Conclusions:
HUS causes an often oliguric acute kidney failure, that usually requires transient dialysis. Extrarenal involvement is common. 8.5% of patients in our series have aHUS, characterized by absence of diarrhea, deeper kidney damage, slower recovery and hypertension.

P - 256 RELATIONSHIP BETWEEN PROTEINURIA AND DECREASE OF ESTIMATED GLOMERULAR FILTRATION RATE IN LONG TERM OUTCOMES OF CHILDREN WITH SHIGATOXIN-ASSOCIATED HEMOLYTIC UREMIC SYNDROME

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Introduction:
In long term outcomes, 20-40% of patients with hemolytic uremic syndrome (HUS) can result in chronic kidney disease (CKD). Additionally, the appearance of proteinuria after the acute phase can be one of the poor prognostic factors in HUS patients. Shigatoxin-associated hemolytic uremic syndrome (STEC-HUS) is accounting for about 90% of pediatric HUS. There has been no long-term study revealing the process of development of CKD in children with STEC-HUS. In this study, we assessed long-term process of renal function in children with STEC-HUS focusing in attention on the appearance of proteinuria and the decrease of estimated glomerular filtration rate (eGFR).
Material and methods:
We investigated the clinical courses of the children with STEC-HUS who were followed up in our institution over one year between 1975 and 2014, retrospectively. The Kaplan Meier method was used to evaluate the long-term process of renal function. We defined the endpoint of their long-term follow-up as the appearance of proteinuria or the decrease of eGFR below 90ml/min./1.73m^2 after the acute phase. Proteinuria was evaluated with urine dipstick test, and eGFR was calculated based on serum creatinine.
Results:
Forty two patients were enrolled (male female ratio, 1:1.5). The median age of the onset of STEC-HUS was 3.5 years (range, 0.7-13.1), and the median age of follow-up was 5.9 years (range, 1.2-26.0). Twenty one patients (50.0%) received the dialysis on acute phase, and two of them needed to the transition to maintenance dialysis. Sixteen patients (38.1%) reached to the end point in their follow-up period, and the median survival time was 11.1 years. In only one patient of them (6.2%), the appearance of proteinuria preceded the decrease of eGFR.
Conclusions:
In long term follow-up of children with STEC-HUS, it can be important to evaluate the renal function with blood test in tandem with urine test.

P - 257 ATYPICAL HEMOLYTIC UREMIC SYNDROME ASSOCIATED WITH ANTIBODIES TO FACTOR H

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Introduction:
Atypical hemolytic uremic syndrome (aHUS) due to the production of antibodies to factor H (CFH-Ab-HUS) is diagnosed in 6-25% cases of aHUS.
Material and methods:
CFH-Ab-HUS (7,1 ± 3,2 years) was diagnosed in 9(32%) among 28 patients with aHUS. Anti-factor H antibodies were determined by ELISA.
Results:
Manifestation of CFH-Ab-HUS associated with gastro-intestinal symptoms in 33,3%(n=3) of the cases, acute respiratory infections in 22, 2%(n=2), cytomegalovirusinfection in 1(11.1%)case, vaccination against influenza in 1(11.1%)patient and trauma in 1(11.1%)patient. All patients presented with microangiopathic hemolysis (Hb65,0±3,39g/l; schistocytosis, LDH 4613,2±4334,9U/L, Coombs negative), thrombocytopenia(81,8,0 ± 46,3h10^9/L), reduction of C3(65,0±19,2mg/dL), creatinine increase(288,4±112,8mmol/l). ADAMTS-13 activity was higher than 5%(81,3±20,4%). The homozygote deletion of the CFHR3-CFHR1 was revealed in 4 patients.Oligoanuria and proteinuria was diagnosed in 5(55.5%) patients, arterial hypertension - 4(44.4%), hematuria - 6(66.6%). In the acute phase in 2(22.2%) patients hadseizures, cardiomyopathy - in 1 case, myocardial infarction in 1 patient, in 4(44.4%) dialysis was necessary. Plazmatherapy was the initially therapy, in 22.2%immunosuppressive therapy was conducted, in 6(66.6%) cases eculizumab was used. 1 child achieved remission after plazmatherapy. Dilated cardiomyopathy was formed in 2(22.2%) cases, proteinuria persisted in 1(14.3%) children. Hematological remission without organ dysfunction reached in 33,3%(n=3) of the cases. Relapses CFH-Ab-HUS were diagnosed in 5(55.5%) patients before the start of eculizumab therapy.
Conclusions:
Frequency of CFH-Ab-HUS among children living in Russia, is higher in comparison with statistical data. In 77.7% cases CFH-Ab-HUS is provoked by infectious agents. Heart disorders and hematuria in children with CFH-Ab-HUS occur more frequently in comparison with publication.

P - 258 PERINATAL MANIFESTATION OF AN ATYPICAL HEMOLYTIC UREMIC SYNDROME (AHUS) IN A PRETERM INFANT

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Introduction:
Atypical HUS is a rare life-threatening disease, caused by uncontrolled activation of the complement system. Typical signs are a triad of hemolytic anemia, thrombocytopenia, and acute renal failure. In many aHUS cases genetic mutations in the alternative pathway and in the coagulation pathway can be identified. Onset of the disease may vary from the neonatal period up to adulthood.
Material and methods:
None
Results:
We report a case of a female preterm infant, born by sectio in the 31st week of gestational age. She had an intrauterine growth retardation (birthweight: 940

gr) and an oligohydramnion. After birth she presented with multiple hematoma and petechial haemorrhages. At this time thrombocytopenia (13000 thrombocytes/μl) and a hemoglobin level of 13.1 gr/dl were found. Anemia and thrombocytopenia persisted and were treatment-resistant. Furthermore she had two episodes of acute renal failure at age 4 and 8 weeks and concomittantly elevated LDH. At that time fragmentocytes were detected. Global markers for complement activation did not show any abnormalities (C3 0.89 mg/ml, C4 0.21 mg/ml, CH50 142%, APH50 89% and C5b-9 184 ng/ml). We then performed a C5b-9 deposit test on rested and activated human microvascular endothelial cells (HMEC), which finally showed a complement activation on endothelia cell surface with a value of 414% and 417%, respectively (norm <150%). We started treatment with the C5-antibody Eculizumab at age 4 month. The preliminary results seem to be favorable as thrombocyte level rose to 160000/μl and kidney function normalized.

Conclusions:

Even though aHUS is a rare disease which may already manifest in neonates, in this case the onset may have been directly postnatal, or prenatally. Circulating complement abnormalities may not be found in all patients. Nevertheless, the typical clinical signs, here especially the treatment resistant anemia, may lead way to further testing (if possible complement deposition on HMEC) and thus to start treatment.

P - 259 ATYPICAL HEMOLYTIC UREMIC SYNDROME UNRESPONSIVE TO ECULIZUMAB THERAPY

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Introduction:

Atypical hemolytic uremic syndrome (aHUS) is characterized by uncontrolled activation of alternative complement pathway. Mutations in diacylglycerol kinase-□ (DGKE) causes activation of protein kinase C leading to prothrombotic state.

Material and methods:

We report a child with aHUS who has mutation in *DGKE*.

Results:

A four year-old boy, third child of a second degree cousin marriage, presented with vomiting, abdominal pain, decrease of urine volume. Hemolytic anemia, thrombocytopenia, hypertension and renal failure were detected. Complement levels, ADAMTS13 were normal. Hemodialysis and fresh frozen plasma were initiated. During the following day hemolytic parameters got better, LDH levels decreased and urine volume increased but severe hypertension required multiple antihypertensive drugs continued. Eculizumab was started one week later. Renal function did not recruit and renal biopsy could not be performed due to risk of bleeding. Eculizumab treatment has continued every two weeks. On follow-up, he was treated with antibiotics for sepsis and pneumonia. Despite eculizumab treatment over five months, the patient remained on chronic hemodialysis program.

Conclusions:

aHUS is a disease requiring immediate intervention to avoid irreversible organ damage or death. Therapies that target the complement cascade will be probably ineffective in patients with *DGKE* mutations so new therapeutic regimens should be sought for these patients under the light of pathophysiology of the disease.

P - 260 OCCURRENCE OF ATYPICAL HEMOLYTIC UREMIC SYNDROME FOLLOWING INFLUENZA B INFECTION

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Introduction:

Hemolytic uremic syndrome (HUS) is a disease characterized by thrombotic microangiopathy with a triad of non-immune hemolytic anemia, thrombocytopenia and renal impairment. Approximately 10 % of cases of HUS are classified as atypical (aHUS). While today many genetically forms of aHUS pathology are known, only about 50% of carriers precipitate the disease. The reason remains unclear, and triggering events like intercurrent infections have been postulated. In rare cases influenza A is the known trigger of aHUS, however no cases of influenza B have been reported.

Material and methods:

We describe retrospectively for the first time a series of 3 patients with aHUS triggered by influenza B virus infection within the same flu season 2012- 2013.

Results:

Three patients with a known primary hereditary complement disorder presented with a first episode or recurrence of aHUS triggered by influenza B virus infection. They were 9, 10 and 15 years old. The first patient recovered spontaneously over one week without need of dialysis or plasma exchange. The 2 following patients were treated with plasma exchanges (six times in total) with improvement of diuresis and renal function. There was no need of dialysis. Full recovery was seen in all the patients. All three patients were infected with the same B-strain within the same flu season (2012- 2013), namely the B/Massachusetts/2/2012-like virus. The three children received further follow-up and with the upcoming 2 influenza season they were administrated an inactivated trivalent influenza vaccine as protection. No recurrence of aHUS occurs following vaccination.

Conclusions:

Influenza viruses are an uncommon trigger of aHUS. Influenza A viruses have been recognized as a trigger for aHUS in the past. We describe for the first time that influenza B strain is also capable of triggering aHUS in children with a primary hereditary forms. We also showed in our 3 cases that immunization appears to be save, however this needs to be confirmed in larger cohort.

P - 261 FIRST-LINE AND LONG TERM ECULIZUMAB THERAPY IN ATYPICAL HEMOLYTIC UREMIC SYNDROME; SINGLE CENTER EXPERIENCE

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Introduction:

We present four patients with atypical hemolytic uremic syndrome (aHUS) that were treated with eculizumab therapy. In three of them eculizumab was used as a first-line therapy. Follow up period was >2 years in two patients.

Material and methods:

The records of patients who were treated with eculizumab for presumptive diagnosis of aHUS (microangiopathic hemolytic anemia, thrombocytopenia, and renal failure with hypocomplementemia [low C3] and normal plasma ADAMTS13 activity) were reviewed.

Results:

Between March 2012 and March 2015, we encountered 4 cases of aHUS (age range:14 months-11 years). Plasma exchange couldn't be performed in any patient. Fresh frozen plasma infusions were only used in patient-1 (14-month-old boy) for 8 days, he didn't respond and eculizumab was started at 11th day after admission in patient. Patient-2 (16-month-old boy), patient-3 (11-year-old girl) and patient4 (32-month-old girl) were treated with eculizumab as first-line therapy and started 2-4 days of admission. Hematologic parameters and C_3 were recovered in all patients. Since the patients 1, 2 and 4 were admitted with anuria, peritoneal dialysis

was also performed. The time interval between initiation of eculizumab and to achieve a normal urine output was 2 days in patient1, 12 days in patient2 and 14 days in patient4. Patient-3 also had reflux nephropathy with bilateral grade III vesicoureteral reflux and renal scars. Her creatinine clearance returned to baseline value after eculizumab. Although patient-1 developed stage II chronic kidney disease, complete renal recovery was occurred in patient-2 and patient-4. Genetic analysis (Hacettepe University Nephrogenetic Laboratory) revealed a mutation of CFH gene in patient-1, a variation of CFI in patient-2 and four variations of C_3 and MCP genes in patient-3. Eculizumab was ceased after 6 dozes in patient-2. Follow up period of the patients without complications and relapses were 32, 25, 15 and 7 months, respectively.

Conclusions:

Eculizumab can be successfully used as a first-line therapy in aHUS patients. It seems that early initiation of eculizumab was associated with complete recovery of renal functions.

P - 262 TWO BOYS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME: A SINGLE CENTER EXPERIENCE

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Introduction:

Atypical hemolytic syndrome (aHUS) is a life threatening disease characterized by hemolytic anemia, thrombocytopenia and renal failure.

Material and methods:

Two boys of neonatal age were treated with aHUS after exclusion of infective aetiology and hematologic and metabolic diseases with clinical presentation alike HUS.

Results:

Laboratory tests revealed hemolytic anaemia, thrombocytopenia, elevated serum urea, creatinine and LDH alongside with low haptoglobin. C3 was low in one child but normal in another. Serum ADAMTS 13 concentration was normal, no serum inhibitors were found.Tests for EMA, ANCA, methylmalonic aciduria, hyperhomocysteinemia, flow cytometry and "cold" antibodies were negative. The boys were treated with fresh frozen plasma, plasmapheresis and hemodialysis. Hypertension and seizures alongside with right femoral vein thrombosis developed in one child and life threatening incident requiring resuscitation in another. Kidney biopsy was performed in one child, revealing histopathological finding compatible with thrombotic microangiopathy. Eculizumab was administered in both children after fall od renal function below 0.5 ml/kg/hr. Normalisation of clinical and laboratory finding followed. Genetic analysis in both children revealed aHUS compatible mutations

Conclusions:

Appropriate clinical assessment is still crucial for successful treatment of aHUS. Close monitoring of complement blockade, antibiotic prophylaxis and vaccination are necessary. The boys are now healthy with no signs of the disease.

P - 263 TYPICAL HEMOLYTIC UREMIC SYNDROME: LONG TERM FOLLOW-UP AT THE CHILDREN UNIVERSITY HOSPITAL REINE FABIOLA OF BRUSSELS (HUDERF)

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Introduction:

The aim of this study is to evaluate the relationship between clinical and laboratory data of children with typical hemolytic syndrome (HUS) on admission and the severity of the disease as well as the outcome of kidney function after long-term follow-up.

Material and methods:

Retrospective study on data of 50 children with typical HUS at HUDERF from January 1992 to December 2012.

Results:

The presence of the 3 main criteria of the definition of HUS were lacking in 24% of patients. Renal replacement therapy (RRT) was necessary in 84% of cases with a median duration of 5 days. Infection with STEC was confirmed in 75% of cases and it was not associated with the need of RRT or its duration. Initial natremia (p:-0.029), glutamic pyruvic transaminase serum (p:0.038), hematocrit (p:0.013) were associated with the need of RRT. Anuria and RRT duration were related to the presence of proteinuria (p:0.01 and 0.009 respectively) and chronic renal failure (CRF) (p:0.009 and 0.014 respectively) after 1 year follow-up. Initial hematocrit was related to the presence of proteinuria (p:0.05) and initial natremia to the presence of CRF (p:-0.025) after 1 year follow-up. Initial C3 serum was not related to the need of RRT (p:-0.044). However, it was associated to a longer duration of RRT (p:-0.06) and a higher risk of CRF (p:-0.04) after 1 year of follow-up. After a median follow-up of 6 years, 34% of patients presented proteinuria, 4% hypertension, 12% CRF (mainly grade 2).

Conclusions:

A diagnosis of HUS cas be posed even in the absence of the 3 main criteria of its definition. Hyponatremia and long lasting anuria are correlated with the risk of CFR. Hypocomplementemia (C3) is related to the duration of RRT and to the risk of CRF.

P - 264 HEMOLYTIC-UREMIC SYNDROME THROUGH 18 YEARS IN TWO TERTIARY HOSPITALS

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Introduction:

HUS is the most common cause of acute renal failure in children. We try to asses mortality, morbidity, recurrences and renal function at the end of follow-up in children with haemolytic uremic syndrome.

Material and methods:

Multicentre retrospective study. We collect from the medical records of patients diagnosed of HUS from 1996 to 2014: epidemiology, diarrhea or other infections, renal replacement therapy needed, mortality, morbidity, presence of recurrences, follow-up and final outcome.

Results:

Preliminary results. Mean age at onset was3.7 years (range 0,2 to 14); eighty-three percent of patients had diarrhea before HUS with mean free interval of 4.4 days, it was absent in six patients. E. coli was detected in 25% patient's stools culture and one in blood culture; Streptococcus pneumonia grew in three blood cultures. Three patients were diagnosed of atypical HUS, a case with C3 low (30 mg/dl) and another with anti-H factor. Hypertension was detected in 45% patients. Maximum mean serum creatinine 3.8 mg/dl (range: 0.4 to 15.2). Maximum mean serum urea 180 mg/dl (range: 51-631). Minimum mean Hb 6.4 g / dl (range: 4.4 to 12). Minimum mean platelets 48,830 (range: 5000-150000). Renal replacement therapy was necessary in 58%. Mean days in PICU were 14

(range: 0-66) and in paediatric nephrology ward 9.4 days (0-43). Mean follow-up was 7.8 years. Eighteen percent of patients had renal consequences (proteinuria, microalbuminuria, hypertension and chronic renal failure). We had two familiar cases and one patient died due to fulminant sepsis with C3 low (12 mg/dl). There were no recurrences.

Conclusions:

Mortality was low despite being a serious illness but the acute morbidity was high with non-negligible incidence of chronic consequences. There were no recurrences. The number of atypical HUS was low because it is an historical review; however, some data suggest a higher incidence (familial cases and low complement levels).

P - 265 THROMBOELASTOGRAPHY IN CHILDREN WITH HEMOLYTIC UREMIC SYNDROME

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Introduction:

Hemolytic-uremic syndrome (HUS) is a form of thrombotic microangiopathy that characterized by massive microvascular thrombosis due to the formation of platelet thrombi followed by the activation of the coagulation cascade. Thromboelastography (TEG) enables complete evaluation of the process of clot initiation, the structural characteristics of the formed clot, its stability and fibrinolysis.

Material and methods:

We conduct thromboelastography and coagulation analysis in 16 patients with severe HUS (mean age 2,2 ± 1,3 years) in the anuria stage (1st point) and the stage of diuresis recovery (2nd point).

Results:

In the 1st point we revealed significant increasing of K-time (time taken to achieve a certain level of clot strength, normal range - 1-3 min) to 3,9±2,9 min, $p<0,05$ and reduction of maximum amplitude (reflecting the strength of the clot, normal range - 51-69 mm) to 49,3±11,5 mm, $p<0,05$. The angle α (represents the thrombin burst and conversion of fibrinogen to fibrin, normal range - 55-78°) decreased to53,2±16,2°. D-dimer elevated to 2767,4±2438,6 ng/ml, activated clotting time (ACT), thrombin clotting time (TCT) and fibrinolysis time (FT) was also increased. In the 2nd point all of TEG parameters normalized while D-dimer, TCT and FT remained elevated.

Conclusions:

The identified changes indicates the activation of platelet and plasma coagulation cascade. TEG indices are normalized by the time of diuresis recovery, despite the absence of complete resolution of the pathological process, due to the initiation of plazmatherapy and low molecular weight heparins in the early stages of the disease. TEG can be used in patients with HUS to assess the severity of hemostaticdisturbances, efficiency and duration of blood substitute.

P - 266 MIDDLE EAST EXPERIENCE OF ECULIZUMAB AMONG PEDIATRIC PATIENTS WITH AHUS: CASE SERIES

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Introduction:

Atypical hemolytic-uremic syndrome (aHUS) is a rare disease caused by uncontrolled complement pathway activation resulting in thrombotic microangiopathy (TMA). The main objective of the present study was to describe the demographic and clinical data of our patients and outcomes after treating with eculizumab.

Material and methods:

Description of efficacy with long-term eculizumab treatment in 8 patients with aHUS at one referral centre.

Results:

Mean age (range) at diagnosis was 13 (3-28) months, all patients were of Arabic origin with familial aHUS and 2/8 with a genetic mutation identified. This was the first clinical manifestation of aHUS in 5 patients , while three had had previous manifestations (2-6). At presentation, all but one patient had reduced eGFR, 5/8 had serious renal dysfunction, 4 of which were on dialysis. Mean time (range) to initiation of eculizumab from diagnosis was 23 (0.1-72) months.

Mean duration (range) of eculizumab treatment in cohort is 20 (4-46) months. With eculizumab treatment 7/8 patients had significant renal recovery; at 3 months eGFR had increased by mean (range) 52 (0-103) min/mL/1.73m^2 and dialysis was discontinued in 3/4 patients. In the one patient who continued to be dialysis dependant, eculizumab had been started 2 months after diagnosis. After start of eculizumab only one patient had TMA manifestations, this patient had interrupted treatment and had nephrotic range proteinuria. Adverse events during eculizumab treatment included neutropenia.

Conclusions:

The long-term efficacy of eculizumab in treating aHUS was confirmed and treatment was well tolerated. Eculizumab was effective irrespective of identification of a genetic mutation, highlighting that a complement mutation is not always found in patients with aHUS. Better outcomes (greater improvement in eGFR) was seen in patients in which eculizumab was initiated rapidly after first TMA manifestation, suggesting that eculizumab should be initiated as soon as possible to maximize renal outcomes.

P - 267 LEVELS OF COMPLEMENT C3, C4 AND VITAMIN D IN CHILDREN WITH STX-HUS

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Introduction:

The aim of our study was to assess the changes of complement and vitamin D levels during acute Shiga toxin-associated HUS (Stx-HUS).

Material and methods:

The study group included 41 children with acute Stx-HUS (median age 2,08 years (0,75-9,42); control group – 72 children after recovery of HUS (median age 6, 17 y (1,58-16,08), follow-up 4,34 y (0,5-9,17). Complement C3, C4, 25(OH)D total were measured prospectively at baseline (admission to hospital) (1) and after normalization of blood creatinin (2), and in control group (3).

Results:

Median levels of complement C3 were in (1) 0,73 (IQR 0,65-0,89 g/l), in (2) 1,18 (1,09-1,29) and in (3) 1,06 (0,94-1,19) (p_{1-2}, $p_{1-3} < 0,001$; $p_{2-3} < 0,01$), levels less normal range were in 80%, 4% and 18,4%, respectively.

Median levels of complement C4 were in (1) 0,21 (IQR 0,19-0,24 g/l), in (2) 0,35 (0,31-0,39) and in (3) 0,27 (0,24-0,3) (p_{1-2}, p_{2-3}, $p_{1-3} < 0,001$), not noted low levels in all groups.

Median levels of vitamin D were in (1) 6,22 (IQR 3,76-11,85 ng/ml), in (2) 11,18 (5,83-13,44) and in (3) 24,05 (19,65-30,69) (p_{1-3}, $p_{2-3} < 0,001$), low levels (<30 ng/ml) were in 100%, 100% and 33,8%, severe vitamin D deficit (<5 ng/ml) were in 25,7%, 12,1% and 0%, respectively.

Not correlation between levels of complement C3, C4, vitamin D and duration of anuria, dialysis and normalization of creatinin levels were found.

Conclusions:

Acute phase of Stx-HUS accompanied with decreasing of levels complement C3 as activation of alternative pathway and severe deficiency of vitamin D.

P - 268 A NOVEL MUTATIONS OF CFB GENE IN CHILD WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME

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Introduction:
Atypical hemolytic uremic syndrome (aHUS) is a rare, life-threatening condition with uncontrolled activation of the complement system. Mutations of Factor B (CFB gene) are founded in 1-4% cases of aHUS.
Material and methods:
A 8-years old girl had onset of aHUS with stomach ache, vomiting, jaundice, elevated serum creatinine 530mkmol/l, LDH 1261MU, decreased C3 58mg/dl, anemia Hb 53g/l, thrombocytopenia 79x10*9/l, proteinuria 2g/l, hematuria. Hemodialysis and plasma exchange were done with full recovery effect. During three years the girl had three relapses with severe kidney failure and malignant arterial hypertension in the last year. Short courses of hemodialysis and plasma exchange or/and plasma infusion had positive effect on renal function.
Levels of ADAMATS 13 and antibody to complement H were normal and Eculizumab treatment were started after the 3d relapse. After 6 months creatinine level decreased from 197 to 146mkmol/l and levels of thrombocytes, Hb, C3 were normal. Despite positive effect on kidney function, malignant hypertension and proteinuria 5-1g/l have still existed.
Next-generation sequencing with Roche 454 platform was used for analysis of selected regions of genes CFH, CFI, CFB, MCP and THBD, mutations in which lead to the development of aHUS. Direct sequencing was applied to confirm these mutations. Bioinformatic analysis was performed to determine the clinical significance of found genomic replacements using Alamut Visual software.
Results:
Next-generation sequencing revealed two novel nucleotide substitutions of CFB gene: c.1169-108A>G in the 8th intron in heterozigous state and c.672C>T in 5th exon, causing synonymous aminoacid polymorphism p.Tyr224Tyr. Both mutations were confirmed by direct sequencing. According bioinformatic analysis by Alamut Visual these mutations may influence on splycing and may be clinical significant.
Conclusions:
A novel mutation of CFB gene c.1169-108A>G may be pathogenic and may causes atypical hemolytic uremic syndrome. Eculizumab improved kidney functions in this patient.
Supported by Russian Science Fund, grant №14-15-00994.

P - 269 SINGLE-DOSE PHARMACOKINETIC STUDY OF AZILSARTAN MEDOXOMIL AND DERIVATION OF APPROPRIATE DOSE FOR USE IN CHILDREN

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Introduction:
Azilsartan medoxomil (AZL-M) is a new angiotensin II receptor antagonist approved for the treatment of hypertension in adults. This Phase 1, first-in-child, open-label, multicenter, single-dose study characterized the pharmacokinetics and short-term safety of AZL-M in children aged 4–16 years.
Material and methods:
Boys or girls with hypertension (12–16 years [Cohort 1a; n=9]; 6–11 years [Cohort 2; n=8]; 4–5 years [Cohort 3; n=3]) received one dose of AZL-M according to body weight (20–60 mg tablet, Cohorts 1a/2; 0.66 mg/kg granule suspension, Cohort 3). Gender-matched healthy adults (Cohort 1b; n=9) received AZL-M 80 mg. Blood samples were collected pre-dose and at 0.25, 0.5, 1, 2, 4, 6, 8, 12, and 24 hours post-dose for Cohorts 1 and 2, and pre-dose and at 0.25, 1, 6, 12, and 24 hours post-dose for Cohort 3. Model-based simulations were also performed to guide dosing, especially in younger subjects (1–5 years).
Results:
Exposure to AZL, measured by dose- and body weight-normalized C_{max} and $AUC_{0-\infty}$, was ~15–30% lower in children compared with adults. In simulations, exposure with 0.66 mg/kg AZL-M in children weighing 8–25 kg approximated to AZL-M 40 mg (a typical starting dose) in adults. The simulations also suggest that those weighing 25–50 kg require only half the adult dose, whereas children weighing 50–100 kg can use the same dosing as adults. Only two subjects (both in Cohort 1a) experienced an adverse event that was considered to be related to study medication (1 headache, 1 migraine). There were no reports of post-treatment serious adverse events.
Conclusions:
This dosing strategy should be safe for further clinical evaluation in children, as AZL exposure would not exceed that seen in adults with the highest approved AZL-M dose (80 mg).

P - 270 AMBULATORY ARTERIAL STIFFNESS INDEX, BLOOD PRESSURE VARIABILITY AND BLOOD PRESSURE DIPPING IN CHILDREN WITH IGA AND SCHOENLEIN-HENOCH NEPHROPATHY

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Introduction:
Aim of the study was to evaluate blood pressure, arterial stiffness, pulse pressure (PP), BP variability (SBPV, DBPV), and BP dipping in children with IgA and Schoenlein-Henoch nephropathy (IgAN/SHN).
Material and methods:
In 48 children (34♂, 14♀) aged 14.04±3.76 years with IgAN (n=29), SHN (n=19), we evaluated: in ABPM - 24h systolic and diastolic blood pressure (SBP, DBP 24h), ambulatory arterial stiffness index (AASI), PP, SBPV, DBPV, SBP, DBP dipping; BMI Z-score, medications, and biochemical parameters. Control group (CG): 20 healthy children (14♂, 6♀) aged 13.38±4.12 years.
Results:
In the study group GFR ac. to Schwartz was 102.8±29.1mL/min/1.73m^2; 18 had CKD II, 1 CKD III; 30 pts were treated with prednisone; proteinuria was present in 21 (nephrotic proteinuria in 6); hypertension (HT) in 22 (IgAN 13, SHN 9); poor HT control in 13 (IgAN 8, SHN 5). Patients with HT had higher ($p<0.05$) BMI Z-score, cholesterol, and triglycerides. AASI was 0.37±0.10 in IgAN, 0.32±0.17 in SHN, 0.30±0.07 in CG; significantly ($p=0.009$) higher in IgAN vs. CG. PP was higher ($p=0.04$) in IgAN vs. SHN children (53.9±5.5 vs. 49.2±7.07mm Hg); there were no differences in BPV and dipping between the groups; disturbed circadian BP rhythm was found in 10 (34.5%) IgAN and 5 (26.3%) SHN children. In 48 children with IgAN/SHN DBP 24h correlated with proteinuria ($r=0.46$, $p=0.001$), total and LDL cholesterol ($r=0.49$, $p=0.001$; $r=0.52$, $p=0.01$), triglycerides ($r=0.33$, $p=0.04$), and prednisone dose ($r=0.39$, $p=0.007$); BMI Z-score with SBPV, DBPV, and PP ($r=0.35$, $p=0.01$; $r=0.36$, $p=0.02$; $r=0.36$, $p=0.01$).

Conclusions:

1. Children with IgAN have higher arterial stiffness compared to healthy peers.
2. In children with IgAN/SHN proteinuria and hyperlipidemia are risk factors for elevated diastolic blood pressure, whereas obesity for increased blood pressure variability and pulse pressure.
3. Pediatric patients with IgAN/SHN require regular ABPM evaluation for early detection of poor pharmacological control of hypertension.

P - 271 MEASUREMENTS OF LEFT VENTRICULAR MASS IN CHILDREN: COMPARISON OF TWO-DIMENSIONAL (2D) VOLUMETRIC AND M-MODE ECHOCARDIOGRAPHY METHODS

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Introduction:
Children with chronic kidney disease (CKD) exhibit greatly increased mortality and morbidity from cardiovascular disease (CVD). Left ventricular mass (LVM) has prognostic value for many CVD states. The aim of this study was to evaluate the agreement of LVM estimation by 2D volumetric versus M-mode echocardiography.
Material and methods:
Ninety-two children (51 boys) aged 11.6 ± 4.0 (mean ± SD) years including 62 with CKD and majority of white caucasin were studied. Transthoracic echocardiographic imaging of the left ventricle was performed and endocardial and epicardial volumes obtained from Tomtec wall tracking analysis. 2D LVM was derived from end-diastolic myocardial volume from an apical 4-chamber view and ten studies were reassessed by the same observer on a separate occasion. M-mode measurements were made from a long-axis view. LVM was indexed by height raised to a power of 2.7 as g/m. Left ventricular hypertrophy (LVH) was defined as LVMI higher than 38.6 g/m$^{2.7}$.
Results:
The median (range) for LVM and LVMI by 2D and M-mode was 85g (26-198), 30.1g/m$^{2.7}$ (16.4-45.7) and 90g (37-217), 31.8g/m$^{2.7}$ (19.4-68.5), respectively. Correlation of LVM between methods was high (R^2=0.80, p<0.0001) with a systematic difference of 4.3±16.3g. Ten children (10.9%) by 2D and twelve (13.0%) by M-mode were found to have LVH. The intra-observer coefficient of variation by 2D method was 7.0%.
Conclusions:
The 2D volumetric method, which makes fewer assumptions in regarding to ventricular geometry, correlates with M-mode method and is reproducible. It also is easier to perform in children in comparison with 3D echocardiography.

P - 272 TRENDS OF ANTIHYPERTENSIVE MEDICATION USE IN CHILDREN WITH CHRONIC KIDNEY DISEASE: FINDINGS FROM THE CARDIOVASCULAR COMORBIDITY IN CHILDREN WITH CHRONIC KIDNEY DISEASE (4C) STUDY

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Introduction:
Hypertension is a detrimental complication of chronic kidney disease (CKD). Due to their anti-proteinuric effect, renin-angiotensin system (RAS) antagonists are recommended as first-line antihypertensive therapy. The longitudinal 4C Study allows to investigate trends of hypertension management as CKD progresses.
Material and methods:
In 296 patients with at least 8 six-monthly follow-up visits, the use of antihypertensive drug classes was analyzed with respect to CKD stage and renal replacement therapy (RRT). Potential causes of medication withdrawal (blood pressure, serum potassium, albuminuria and annual glomerular filtration rate (GFR) loss) were analyzed within 6 months before drug withdrawal.
Results:
While the overall use of antihypertensive medications and diuretics was stable (percentages in table), RAS antagonist use decreased significantly with CKD progression accompanied by an increase of calcium-channel blocker (CCB) and beta-blocker (BB) use. Annual GFR loss and albuminuria differed significantly between patients who continued and withdrew RAS antagonists (-2.4±3.5 vs. -5.0±7.2, p=0.001, and 224 (664) vs. 326 (1665), p=0.01, respectively).

	CKD2	CKD3	CKD4	CKD5	CKD-D	CKD-T	p
Any antihypertensives	*67.9*	*58.8*	*65.9*	*58.4*	*66.8*	*63.5*	*0.074*
Any RAS antagonists	*67.9*	*50.0*	*46.7*	*30.1*	*29.9*	*16.4*	*0.0001*
ACE inhibitors	53.6	42.1	40.5	26.6	27.2	15.1	*0.0001*
AT1 receptor antagonist	17.9	10.7	9.5	7.5	5.3	4.5	*0.0015*
CCB	10.7	18.8	26.1	40.5	49.2	48.6	*0.0001*
BB	17.9	6.1	12.8	16.8	18.3	21.7	*0.0001*
Alpha-blockers/ vasodilators	7.1	3.72	4.6	6.4	11.3	7.6	*0.0001*
Diuretics	7.1	10.5	11.4	12.1	9.0	10.6	*0.824*

Conclusions:
We observed a significant decrease in the use of RAS antagonists with a concomitant increase of CCB and BB use with the progression of CKD. The reasons underlying the decision to change treatment are possibly multifactorial and more rapid CKD progression with failure to control proteinuria may play a role.

P - 273 INTIMA MEDIA THICKNESS IN OBESE ADOLESCENTS

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Introduction:
Cardiovascular disease is the leading cause of morbidity and mortality in adults. Although, cardiovascular disease is generally rare in childhood, vascular injury is not. Carotid intima media thickness (cIMT) is often used as a marker of vascular injury. The aim of this study was to assess the independent predictors of cIMT in obese adolescents.
Material and methods:
Obese patients referred for ambulatory blood pressure monitoring (ABPM) were enrolled in the cross-sectional study. A fasting blood sample was obtained for glucose, insulin, creatinine, uric acid, triglycerides, cholesterol, HDL, LDL. ABPM measurements were obtained on outpatient basis (SpaceLabs 90217). Ambulatory hypertension was defined as mean BP index ≥ 1 or daytime BP load ≥ 25%. Carotid intima-media thickness measurements were performed by an experienced radiologist using a high-resolution ultrasound. A mean value of six measurements at a distance 1 cm proximal of the bifurcation was used for further analysis. Treadmill exercise test was performed using modified Bruce protocol.
Results:
A total of 96 obese patients (66 males) aged 14.1±2.1 years were analyzed. Variables included in stepwise regression analysis to investigate the independent predictors of IMT were age, body mass index, waist circumference, hip circumference, night systolic blood pressure, and peak diastolic blood pressure on exercise test. Age, waist circumference, and peak diastolic blood pressure were the independent determinants of cIMT (adapted $R^2 = 0{,}192$, $p < 0{,}001$).
Conclusions:
Our results suggest that age, waist circumpherence and peak diastolic blood pressure on treadmill exercise test may facilitate the recognition of obese adolescents with higher cIMT.

P - 274 PREVALENCE OF HYPERTENSION IN CHILDREN AND ADOLESCENTS WITH UNCLASSIFIED HEADACHE

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Introduction:
According to the criteria published by International Headache Society (IHS), headaches in children and adolescents are classified as primary headaches (migraine, tension-type headache), secondary headaches (those attributed to brain tumors, increased intracranial pressure, inflammatory diseases, etc.), cranial neuralgia, primary facial pains and unclassified headaches. This study aims to determine the prevalence of hypertension in patients reporting an unclassified headache, comparing the prevalence of hypertension between clinical blood pressure measurements and ambulatory blood pressure monitoring (ABPM).
Material and methods:
We retrospectively evaluated a total of consecutive 124 patients (65 females, 59 males) aged 5-18 years, who presented to the pediatric neurology clinic of Baskent University Faculty of Medicine, Adana Teaching and Medical Research Center between in 2012 and 2014 with unclassified headache according to IHS criteria and were monitored by 24-hour ABPM.
Results:
The blood pressure measurements in the outpatient clinic detected hypertension in 27 of 124 patients (21.8%), while ABPM readings showed no hypertension in 17 of them (13.7%). These cases were identified as having white coat hypertension. On the other hand, ABPM readings showed that 30 of 124 patients (24.2%) had hypertension, with 21 of 97 patients (21.6%) having normal blood pressure, as determined by outpatient clinic measurements. The patients diagnosed with stage 1 hypertension by ABPM were only prescribed a salt-free diet and exercise, whereas those with stage 2 hypertension were given pharmacological therapy, along with a salt-free diet and exercise. By three-month follow-up, symptoms of headache had improved in all patients.
Conclusions:
Based on the findings of this study, we suggest that hypertension may be responsible for the etiology of unclassified headache. The ABPM procedure detected hypertension in the 21.6% of the children with unclassified headache who had normal blood pressure in the outpatient clinic. It is therefore concluded that a single blood pressure measurement in the clinic does not provide sufficient data for the evaluation of hypertension in these patients, so the ABPM method should be employed to confirm the diagnosis of hypertension.

P - 275 ALDOSTERONE AND PLASMA RENIN ACTIVITY IN OBESITY-RELATED CHILDHOOD HYPERTENSION

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Introduction:
To investigate if there are any differences in values of aldosterone and plasma renin activity (PRA) between overweight and normal-weight children and adolescents with essential hypertension.
Material and methods:
51 children and adolescents, diagnosed with essential hypertension in our Nephrology Unit, have been prospectively included in the study. All secondary causes of high blood pressure have been excluded. There were 22 girls and 29 boys included. In all of them anthropometrical measurements have been performed and aldosterone and PRA determined according to standard methods. Basic statistical methods have been used for statistical analysis.
Results:
The mean age of included hypertensive children and adolescents was 14.2 ± 4.1 years. 22 (43.1 %) of them were overweight. Body mass index (BMI) was found to be 23.42 ± 4.39 kg/m2. The mean value of aldosterone was 0.31 ± 0.19 nmol/l and PRA 0.97 ± 1.00 μg/l/h, respectively. There were no statistically significant differences in values of BMI, aldosterone and PRA between included boys and girls (p=0.66 for BMI, p=0.88 for aldosterone and p=0.70 for PRA). The value of aldosterone was 0.38 ± 0.27 for overweight hypertensive patients compared to 0.26 ± 0.08 nmol/l for patients with normal weight, reaching the statistical significance (p=0.03). In addition, values of PRA were higher for overweight hypertensive patients (1.12 ± 1.09 vs. 0.86 ± 0.94 μg/l/h), although not reaching the statistical significance (p=0.36).
Conclusions:
Our pilot study found out that overweight hypertensive children and adolescents have higher values of both aldosterone and PRA compared to hypertensive patients with normal weight, although the latter has not reached the statistical significance. The results have to be confirmed in larger study population and their role in diagnostic procedure determined.

P - 276 ARTERIAL COMPLIANCE MEASUREMENT IN OVERWEIGHT AND HYPERTENSIVE CHILDREN AND ADOLESCENTS

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Introduction:
The purpose of this study is to investigate the pulse wave velocity (PWV), a measure of arterial stiffness, in connection with two main risk factors for cardiovascular disease - hypertension and obesity. We are also interested in whether applanation tonometry is an adequate tool for non-invasive assessment of the cardiovascular system in children and adolescents.
Material and methods:
PWV, body mass index (BMI) and mean arterial pressure (MAP) of two groups of subjects were analyzed (group 1 - 31 subjects with arterial hypertension and group 2 - 85 overweight subjects), and compared with the control group (50 healthy individuals). Subjects in group 1 and 2 were recruited according to diagnostic criteria for hypertension and obesity, respectively. Subjects (total N=166, 94 male, 72 female) were sampled by opportunity sampling at Department of Paediatrics, University Medical Centre Maribor. Informed consent form was signed by their parents. Data was collected by applanation tonometry technique using SphygmoCor, SCOR-Vx, Australia. Statistics was done with IBM SPSS Statistics 20.
Results:
Using Pearson correlation test we compared PWV and subjects age, BMI and MAP. In control group the results show a significant correlation between PWV and age ($r=0.461$, $p=0.001$), whereas no correlation was obtained between PWV and BMI or MAP. In group 1 PWV correlated solely with MAP ($r=0.496$, $p=0.005$). A significant correlation was found in group 2 between PWV and both age and BMI ($r=0.484$, $p<0.001$ and $r=0.347$, $p=0.001$, respectively).
Conclusions:
Overweight and hypertensive children and adolescents have less compliant arteries than the healthy ones. In addition, aging increases arterial stiffness in the pediatric population. According to our pilot study, applanation tonometry presents a valuable tool for cardiovascular risk assessment and follow-up.

P - 277 FGF23 IN URINE OF HYPERTENSIVE CHILDREN AND ADOLESCENTS.

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Introduction:
Hypertension (HT) is an emerging condition in young population. In recent years, there has been an increasing amount of literature on the role of calcium – phosphorus imbalance in its pathogenesis, however the role of fibroblast growth factor 23 (FGF23) in this condition has not been adequately studied. The objective of this study was to assess urinary FGF23 excretion in relation to blood pressure values and calcium – phosphorus metabolism.
Material and methods:
The study was conducted on a random sample of 42 hypertensive subjects (17 girls) and 46 healthy children (17 girls) aged 6-18 years. FGF23 in the urine was measured using Human Intact FGF-23 ELISA Kit (Immutopics Inc.) according to the manufacturer instruction.
Results:
We observed significantly higher urine FGF23/creatinine (FGF23/cr.) values in hypertensive subjects in comparison to reference group (8.65 v 5.59 RU/mg cr., $p<0.01$). We also found a positive correlation between urine FGF23/cr. and systolic blood pressure ($r= 0.28$, $p<0.05$). Additionally, in hypertensive patients a positive correlation between urine FGF23/cr. and serum calcium and negative correlations with serum 25(OH)D, urinary calcium, phosphorus and magnesium were noted.
Conclusions:
FGF23 may play an important role in the pathogenesis of HT in children and teenagers. However this research should serve as a base for future studies in this field.

P - 278 EVALUATION OF RENOVASCULAR HYPERTENSION IN 13 CHILDREN AFTER ANGIOPLASTY

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Introduction:
Explore catamnesis 13 children with renal artery stenosis (RAS) and renovascular hypertension (RVH).
Material and methods:
A retrospective case review of 13 pediatric patients with RVH, age from 4 years to 17 years. Etiological diagnoses were: Mid-aortic syndrome (MAS) (2); neurofibromatosis type I (2); renal-coloboma syndrome (1) and neuroblastoma (1). The diagnosis of renal artery stenosis established at duplex ultrasound (DUS), pre- and post-captopril DMSA (captopril renography), magnetic resonance angiography (MRA), computed tomography angiography (CTA) and angiography.
Results:
13 patients (7 boys and 6 girls) examined with RVH. In accordance with the classification Flynn et. al., 2014; 11 had Ambulatory hypertension (>95th percentile) and 2 had severe ambulatory hypertension (at risk for end-organ damage) (>95th percentile); came to our hospital. Of the 13 patients, 7 had medical therapy with 1 antihypertensive agent (3); with 2 antihypertensive agents (3) and with 3 antihypertensive agents (1), and 6 without therapy. After the passage of a comprehensive diagnosis, 8 children have unilateral renal artery stenosis and 5 children have bilateral renal artery stenosis. MAS diagnosed in 2 patients with severe ambulatory hypertension (at risk for end-organ damage) characterized by severe narrowing of the abdominal aorta and bilateral renal artery stenosis. 13 children underwent endovascular intervention: balloon angioplasty (12) and stenting (1). After angioplasty 6 children have normal blood pressure and 7 have decrease of blood pressure. After angioplasty 5 had medical therapy with 1 antihypertensive agent (2); with 2 antihypertensive agents (2) and with 3 antihypertensive agents (1) and 8 without medical therapy. Because of restenosis of renal artery in one patient, repeated endovascular intervention (balloon angioplasty).
Conclusions:
At renovascular hypertension used balloon angioplasty and stenting permit to normalize or decrease in blood pressure and the reduction or elimination of antihypertensive therapy.

P - 279 PREVALENCE OF HYPERTENSION AMONG CHILDREN WITH ATTENTION DEFICIT-HYPERACTIVITY DISORDER (ADHD)

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Introduction:
Attention deficit/hyperactivity disorder (ADHD) is an increasingly common neurobehavioral childhood disorder that frequently continues into adulthood. Most affected children are treated with psycho-stimulant agents which are known to be associated with a modest but significant increase in blood pressure and heart rate, however the clinical significance of this adverse effect is considered negligible. Our objective was to define the prevalence of hypertension detectable at single office visits, combined with 24h ambulatory blood pressure monitoring (ABPM), in a sample of otherwise healthy children with ADHD, treated by community pediatricians with any medication indicated for ADHD.

Material and methods:
Three collaborating community pediatricians in Calgary, provided lists of all children in their care, with documented histories of ADHD. Candidate subjects from the compiled list were randomly contacted; children aged 5 – 18 years receiving ongoing treatment with any type of medication indicated for ADHD were eligible for inclusion. Consenting participants had a full medical history and physical examination, anthropomorphic measurements and initiation of 24h ABPM. The Sleep Disturbance Scale for Children (SDSC) questionnaire was also applied.
Results:
One hundred and forty five of 240 potential candidates were contacted; 55 children completed the study (47 males), average age 11.6 (± 2.5) years, average BMI z-score -0.37 (±1.22). Most children, (82%) were treated with various formulations of short or long acting stimulant agents. Office blood pressure was greater than the 95th percentile in 3 (5.5%) children and in an additional 4 (7.3%) - greater than the 90th percentile. All 7 children who had elevated office BPs, had entirely normal ABPM results suggesting "white coat" hypertension however 15 (27.3%) children were found to be "non-dippers" on ABPM tests;91% of all participants had SDSC scores suggestive of disturbed sleep.
Conclusions:
Prevalence of white coat hypertension may be higher among children with ADHD medicated for their condition, however true hypertension and prehypertension, based on current definitions, does not appear to be frequent in this population. Highly prevalent non-dipping on ABPM may be related to common sleep disturbances in children treated with stimulant medications for ADHD.

P - 280 INFLUENCE OF CONTROLLED PHYSICAL ACTIVITY ON SERUM ADIPOKINES CONCENTRATION IN OBESE CHILDREN.

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Introduction:
The number of obese people is increasing, and its negative impact on the people's health is significant. Therefore, fight against overweight and obesity in children and adolescents has become one of the biggest global challenges of the twenty-first century. The relationship between physical activity and obesity is still under investigation. One of components responsible for the metabolism are adipokines such as adropin or adiponectin. The purpose of this study was to investigate, whether the controlled physical activity affects the concentrations of adipokines and may play role in treatment of obesity in children.
Material and methods:
34 obese children aged 5-18 years were involved to the dynamic prospective study. The reference group consisted of 16 healthy children. The participants were informed about recommended physical activity, adjusted for sex, age, and degree of overweight. They were equipped with exercise recorder for a period of 8 weeks. Before start of the study and after 8 weeks of effort, has been made anthropometric measurements, electrical bioimpedance and blood serum was collected. Adropin and adiponectin concentrations in serum were determined by ELISA.
Results:
In the study group, 22 children decreased BMI Z-score. Average BMI Z-score has decreased from 2.75±0.43 at baseline to 2.51±0.31 at the end of the study ($p<0.05$). In the whole study group, there was no statistical significant differences in the concentrations of adiponectin and adropin compared between study points and the control group. In contrast, significantly increase the concentration of adropin after 8 weeks, in group of patients who have lowered their BMI Z-Score (38.84±20.29 vs. 64.54 ±40.45 pg/ml, $p<0.01$).
Conclusions:
Controlled physical activity leads to reduction of obesity in children and increases serum adropine concentration, which may play role in prevention of obesity complications.

P - 281 DECREASED ARTERIAL ELASTICITY IN CHILDREN WITH NON-DIALYSIS CHRONIC KIDNEY DISEASE RELATES TO BLOOD PRESSURE AND NOT TO GFR

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Introduction:
We compared large artery mechanical properties in children with non-dialysis stages of chronic kidney disease (CKD) to those in children with normal renal function, examining the potential impact of blood pressure (BP) components and level of renal dysfunction.
Material and methods:
Single centre cross-sectional study, measuring common carotid artery mechanical properties, carotid-femoral pulse wave velocity, carotid and peripheral BP.
Results:
Of 226 recruited children, there were n=188 with non-dialysis CKD with a mean age of 11.9±3.7 years; 26%, 25%, 30%, 16% and 3% in CKD stages 1, 2, 3, 4 and 5 respectively) and healthy controls (n=38, 11.5±3.3 years). In children with non-dialysis CKD when compared with healthy controls, at similar levels of peripheral and carotid BP, carotid artery diastolic diameter and wall thickness were similar. In those with sub-optimal blood pressure (>75th percentile) indices of arterial elasticity indicated greater stiffness than in healthy normotensive controls (distensibility: 92±31 vs. 114±33 kPa^{-1} x 10^3, $p=0.03$; compliance: 2.1±0.7 vs. 2.6±0.7 m^2 kPa^{-1} x 10^6, $p=0.02$; Young's elastic modulus: 0.151±0.068 vs. 0.109±0.049 kPa x 10^{-3}, $p=0.02$; and wall stress: 83.6±23.5 vs. 68.7±14.9 kPa, $p=0.02$). In all children, mechanical properties were independently related to central and peripheral BP components but not to estimated glomerular filtration rate (GFR).
Conclusions:
In children with non-dialysis CKD, changes in elastic properties of the carotid artery relate primarily to blood pressure and not to GFR.

P - 282 ENDOVASCULAR MANAGEMENT OF RENOVASCULAR HYPERTENSION IN THE PAEDIATRIC POPULATION – A 12-YEAR SINGLE-CENTRE EXPERIENCE

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Introduction:
Our objective in this retrospective study was to review our recent experience of RVD as a cause of hypertension, to identify characteristics of the patient population, findings at angiography and early angiographic outcomes following endovascular treatment.
Material and methods:
Records of all patients < 18 years who underwent DSA over the past 12 years were analysed with demographic, medical history, procedural details, adverse events and early outcome data collected.

Results:
63 patients underwent DSA during the study period, of whom 25 (40%) had confirmed renovascular disease including 12 boys, 76% were White Caucasian. The mean age at initial diagnosis was 7.3 years (range 4 weeks-16.8 years). 36% (9/25) had an underlying syndrome, (6 Neurofibromatosis type 1, 2 William's syndrome, 1 Tuberous sclerosis).
Of the 90 DSA studies performed, there were 41 (46%) with evidence of RVD with a total of 52 renovascular lesions; lesion '*laterality*' included 37% (15/41) right, 39% (16/41) left and 24% (10/41) bilateral; lesion '*location*' 13% (7/52) osteal, 67% (35/52) proximal main stem, 4% distal main stem, 6% segmental branch and 10% having other vascular abnormality. 28 interventions performed, included PTA 86% (24/28, normal pressure balloon 18, high-pressure balloon 3 and cutting balloon 3), renal artery stent insertion 7% (2/28), aortic angioplasty 3.5% (1/28) and aortic stent insertion 3.5% (1/28). There were three access-site complications (vessel thrombosis), two anaesthetic complications and one stent displacement.
Conclusions:
DSA remains the gold-standard tool for evaluating renovascular disease causing hypertension in children. PTA offers a safe and effective therapeutic option.

P - 283 LIPIDAPHERESIS IN 3 SISTERS WITH FAMILIAL HYPERCHOLESTEROLEMIA

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Introduction:
Familial hypercholesterolemia (FH) is the most common and a severe monogenic form of hypercholesterolemia. It is an autosomal codominant disease characterized by an increased low density lipoprotein (LDL)-cholesterol plasma concentration and carries the risk of premature coronary heart disease (CHD). As the atherosclerotic burden is dependent on the degree and duration of exposure to raised LDL-cholesterol levels, early diagnosis and initiation of effective treatment is imperative. Statins are presently the mainstay in the management of these patients. Lipoprotein-apheresis as a treatment to remove LDL-cholesterol in patients with severe dyslipidemia becomes recently more established. Together these treatments have notably improved the prognosis of FH. A majority of children fails to attain targeted lipid goals owing to persistent shortcomings in diagnosis, monitoring, and treatment. This work aims to highlight the necessity of result monitored LDL-apheresis dose as well in treated plasma volumes as in treatment frequency.
Material and methods:
Three siblings with a LDLR mutation (p.Trp577Arg) undergoing a therapy with statins (20 mg/d Atorvastatin) and Ezetimib (10 mg/d) for 12 months with still LDL-cholesterol plasma concentration of above 300-500 mg/dl (7,8-12mmol/l) started once weekly a double filtration plasmapheresis (DFPP) using a plasma separator, Plasmaflo OP and a plasma component separator, Cascadeflo EC-50W (Asahi Kasei Medical, Tokyo, Japan) with a single plasma volume to be treated.
Results:
A good response to each LDL-apheresis was evident with LDL-cholesterol plasma concentration of 100-150 mg/dl (2,6-3,9 mmol/l) after treatment. (66-70% reduction). Nevertheless after 6 months plasma volume to treat was doubled because of a rebound within 7 days with LDL-plasma concentration up to 300-350 mg/dl (7,8-9,1mmol/l). But though after each session LDL-plasma concentration decreased to 50-100 mg/dl (1,3-3,9 mmol/l) the rebound was still evident after 7 days of therapy pause. With a new treatment regime with twice plasma volume every 3-4 days the children finally attained a stable pre-treatment LDL-plasma concentration of 120-170 mg/dl (3,1-4,4 mmol/l). Another 2 months later statin therapy was stopped because of underlying mutation with assumed non receptor function. Neither the effectiveness of each apharesis nor the LDL-C concentration after 4 days showed any change.
Conclusions:
In pediatric FH patients with very high levels of LDL-cholesterol plasma concentration it might be necessary to treat with apheresis in high frequency and with high plasma volumes instead of non-effective conservative medication to reach a durable decrease in LDL-cholesterol plasma concentration. The use of cholesterol uptake-inhibitors should be considered.

P - 284 A RARE CAUSE OF SYSTEMIC HYPERTENSION IN A CHILD: LIDDLE'S SYNDROME

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Introduction:
Pediatric hypertension is usually secondary to an underlying identifiable cause, most often renal. In these cases plasma rennin activity (PRA) is usually elevated. However, hypertension with low PRA is often underdiagnosed and an important cause of resistant hypertension. A few conditions are associated with this type of hypertension. One of those rare conditions is Liddle's syndrome. This syndrome results from hyperactivation of the epithelial Na channel (ENaC), resulting in sodium retention and urinary potassium and hydrogen ion wasting, causing hypokalaemic alkalosis with severe hypertension and low PRA and aldosterone level.
Material and methods:
We report a case of a 10 month old patient with the diagnosis of Liddle's syndrome.
Results:
A 10 month old girl admitted to our hospital for the evaluation of hypokalemia. During hospitalization of patient, hypertension was detected and she was consultated to pediatric nephrology clinic for the evaluation of hypertension. Her past medical history revealed that she was a premature and small for gestational age baby. There was no family history of hypertension. On physical examination, her blood pressure was 130/90 mm Hg. Femoral pulses were bilaterally equal and well palpable. The labarotory investigations revealed hypokalemia, metabolic alkalosis, low serum aldosterone level and low PRA.Urinary steroid profiles for the exclusion of hypertensive endocrine causes and renal doppler ultrasonography for the exclusion of renal artery stenosis were normal. Her blood pressure did not respond to a combination of amlodipine, enalapril, propranolol, spironolactone, doxazosin treatment. After starting of triamterine, hypertension was controlled and hypokalemia resolved with potasium supplementation.
Conclusions:
We report this case to increase awareness of physician about Liddle's syndrome, because treatment differs from other forms of hypertension. So early detection and appropriate treatment may help to improve the long term morbidity and mortality in children with this disorder.

P - 285 RENAL VASCULAR HYPERTENSIONCAUSED BY UPPER LEFT BRANCH RENAL ARTERY STENOSIS COMPLICATED WITH MULTIPLE THROMBOSIS AND CARDIAC HYPERTROPHY

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Introduction:
Hypertension is not rare in children and can occur in neonates. The broad spectrum of causes includes potential life-threatening renal arterial stenosis. A severe hypertension was found in 9 month old boy with signs and symptoms of severe arterial hypertension.
Material and methods:
A standard laboratory tests with RAP and aldosterone blood determination alongside with Doppler kidney ultrasound, multislice CT renal angiography and kidney scintigraphy (Tc-99m MAG3, Tc-99m DMSA) were performed.
Results:
An upper left branch renal artery stenosis complicated with multiple thromboses and cardiac hypertrophy was diagnosed. Precise location of single arterial stenosis was the key support for our decision of surgical heminephrectomy and removal of just upper pole of the left kidney instead of total nephrectomy Heminephrectomy was successful in blood pressure normalization with significant improve of cardiac function and thrombosis recanalization.
Conclusions:
A difficult decision between total nephrectomy and rational sparing *primum non nocere* approach has to be made in such children. Our successful clinical restitution serves as an encouragement for clinical decision of partial instead of total nephrectomy in carefully selected neonatal patients. It is also important to acknowledge that persistent restlessness or changes in childs behavior is important for early diagnosis of neonate hypertensive crisis.

P - 286 HYPONATREMIC HYPERTENSIVE SYNDROME – A NOT SO UNCOMMON PRESENTATION

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Introduction:
Hypertension presenting as severe hyponatremia is rare.
Material and methods:
We report a series of 3 children with unilateral renal artery stenosis who presented as hyponatremic hypertensive syndrome characterized by hypertension, hyponatremia secondary to salt diuresis, hypokalemia and metabolic alkalosis.
Results:
All 3 children had features of activation of rennin aldosterone axis secondary to renal artery stenosis which were confirmed by imaging. Despite this all of them had hyponatremia as characteristic in HHS.
Conclusions:
Although deemed to be rare these 3 children presented with HHS over a span of 18 months and prompt diagnosis and renal re-vascularisation produced excellent results.

P - 287 AMLODIPINE DOUBLE-EDGED SWORD

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Introduction:
Choice of antihypertensive for children depends upon clinician discretion and a balance between the safety profile and the efficacy. Amlodipine, a calcium channel blocker with a long half-life (35±50 h), seems to be an attractive option as it could be given once daily. Such regimen is reflected positively on the compliance. However, a close eye should be kept on the potential adverse effects and drug interactions. Lower limb edema has been reported among the possible untoward effects .
Material and methods:
Here by we present a case series of five children with amlodipine-induced edema. The edema was generalized in three patients while the other two patients experienced lower limb edema with puffiness of the eyes. The dose of amlodipine ranged from to 2.5-10 mg/day. Edema resulted in significant weight gain (1to 2.2 kg). The interval between drug initiation and onset of edema varied widely from few days to 16 months. The rate of edema resolution after cessation of the drug depends upon the type of edema. Anasarca took 2 weeks to resolve while lower limb edema regressed in a matter of 2-3 days. Concomitant use of drugs possibly raising the serum concentration of amlodipine was observed in two of our patients. Fluconazole was used in one patient whereas ciclosporin, magnesium and fluconazole were utilized in the other.
Results:
The mechanism of Amlodipine-induced edema is not clear. Yet, it was postulated that arteriolar dilatation with inhibition of pre-capillary vasoconstriction which promote interstitial edema.
Conclusions:
Edema could be a troublesome adverse effect of amlodipine but it fortunately resolves in most cases within 2 weeks of drug stoppage.

P - 288 SEVERE HYPERTENSIVE ENCEPHALOPATHY POST BILATERAL NEPHRECTOMY IN A CHILD WITH SENSENBRENNAR SYNDROME

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Introduction:
Hypertension is reported to occur in 85-95% of patients with end stage renal disease. Most patients require multiple antihypertensive agents to achieve normal blood pressure (BP) and in some cases control is only achieved with bilateral nephrectomy. We present the case of a five year old boy with Sensenbrenner syndrome and refractory hypertension despite bilateral nephrectomy.
Material and methods:
A 23 month old presented in established renal failure, with systolic BP of 140mmHg. Ultrasound scan demonstrated small dysplastic kidneys and echo showed left ventricular hypertrophy. He was initially commenced on peritoneal dialysis but switched to haemodialysis following peritonitis. He required multiple antihypertensive agents including captopril, minoxidil, atenolol and amlodipine. Despite these, he developed hypertensive encephalopathy, requiring a labetalol infusion, followed by bilateral nephrectomy. Amlodipine, atenolol and minoxidil were discontinued and he remained on a small dose of captopril.
Results:
A month post nephrectomy he represented, encephalopathic with a systolic BP of 175mmHg. He required a Hydralazine infusion and antihypertensive agents were changed tophenoxybenzamine and atenolol. Four months later antihypertensive medications were weaned to stop due to hypotension. Two days after complete cessation he again represented,

encephalopathic with BP 180/110mmHg. Labetalol infusion was required and minoxidil and atenolol recommenced. In the last month, he has received a living related donor transplant for his father, following transplant his BP is controlled below the 90th percentile with only Amlodipine 1mg once daily.

Conclusions:

Bilateral nephrectomy causes a decrease in both BP and total peripheral resistance (TPR), with most anephric patients having a normal BP at dry weight. Few patients post bilateral nephrectomy have persistent hypertension. Our case is unusual with the post nephrectomy patient requiring two separate admissions to intensive care due to hypertensive encephalopathy. We are hopeful that the reduction in TPR following transplantation will enable our patient to remain normotensive with minimal antihypertensive medication.

P - 289 AN UNCOMMON CAUSE OF NEONATAL HYPERTENSION

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Introduction:

Neonatal hypertension is exceedingly uncommon with a reported rate of 0.2% to 3% percent. Adrenal hematoma with renal artery compression leading hypertension is rare as an acquired cause of neonatal hypertension. Herein, we report a case of neonatal hypertension associated with adrenal hematoma.

Material and methods:

A baby boy was immediately transferred to neonatal intensive care unit after delivery because of meconium aspiration. He had mechanical ventilation support. At that time, his blood pressure was normal. On the 15 days of discharge, he was found to have hypertension and admitted to pediatric nephrology Clinic. Physical examination was normal except irritability. Screening of hypertension was normal except the right renal agenesis, grade two dilatation in the collective system of the left kidney, and a heterogeneous cystic, round, measuring 46*28 mm adrenal hematoma with no blood flow in left suprarenal region by ultrasound. Renal scintigraphy showed right renal agenesis, prolonged retention of the injected material in the left kidney and a mass on the left kidney. He was started antihypertensive therapy; the adrenal hematoma was examined by US weekly. Its sizes gradually got smaller and his blood pressure returned to normal for his age.

Results:

In our patient there was a complicated delivery history and as a possible cause of adrenal hematoma, on the second week of the life serious hypertension was observed. We could only detect an adrenal hematoma as a cause of hypertension. His blood pressure gradually decrease with gradual decrease in the size of the adrenal hematoma, transient compression of the left kidney was thought as a possible mechanism of hypertension.

Conclusions: We think that neonates with hypertension accompanied the history of complicated delivery should be evaluated for adrenal hematoma to clarify the reason of hypertension.

P - 290 FIBROMUSCULAR DYSPLASIA AS A CAUSE OF STROKE AND PERSISTENT HYPERTENSION IN AN 8-YEAR-OLD GIRL

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Introduction:

Fibromuscular dysplasia (FMD) is a noninflammatory, nonateromatous, systemic disease of unknown etiology that mainly affecting medium and small arteries and rarely seen in children. We report a child with stroke and resistant hypertension in whom extensive FMD of intracranial vessels and renal artery were established.

Material and methods:

A previously healthy 8-year
old girl admitted with decreased level of consciousness, weakness in left side of the body and a prior headache and left focal seizure. She was lethargic and a glascow coma scale of 13, blood pressure was 165/102 (>99p/ >99p) mmHg. Neurological examination revealed left facial paralysis, muscle strength on the left was found 3/5 in the lower, 1/5 in the upper extremities.

Results:

Brain magnetic resonance imagination (MRI) revealed an acute right middle cerebral artery territory infarct and the same localization diffusion limitation were observed in diffusion MRI. Cranial MRI angiography showed that focal
segmental stenosis and irregularity of the right MCA M1 - M2 segments. Renal Doppler US and Renal MRI angiography performed for resistant hypertension were revealed focal narrowing on the renal artery. Conventional angiography and balloon angioplasty were performed without complications in the same setting. In the sixth month of followup, she was able to walk, no seizure and stroke was observed and her muscle strength was 4/5 on the left upper and lower extremities and blood pressure has been kept under control
with two antihypertensive drugs.

Conclusions:

In conclusion, stroke is an unusual condition in childhood. FMD should be kept in mind in a case of resistant hypertension accompanying stroke.

P - 291 COMPARISON BETWEEN OFFICE BLOOD PRESSURE AND AMBULATORY BLOOD PRESSURE MONITORING (ABPM) PARAMETERS IN CHILDREN; EVALUATING CASES USING THE UPDATED ABPM GUIDELINE.

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Introduction:

Ambulatory blood pressure monitoring (ABPM) has a superior ability to distinguish patients at higher risk for target-organ damage than office BP measurement. Our purpose was to compare the office blood pressure with ABPM parameters in patients with prediagnosis of primary hypertension and interpretation of the data according to the recommendations of American Heart Society on the use of ABPM in the pediatric population reported in 2014.

Material and methods:

The medical records of the patients who received ABPM due to their office BP levels >90th percentile were reviewed retrospectively. The patients who had secondary hypertension and those receiving antihypertensive medication were excluded. The ABPM data of the patients were

interpreted retrospectively according to the recommendations of American Heart Society on the use of ABPM in the pediatric population reported in 2014. The demographic findings, body mass indexes (BMI), BMI-standard deviation scores and ABPM results of the patients were statistically compared.

Results:

Thirty one boys and 26 girls were included in the study. The mean age of the patients was 14,42±2,14 years. BP was categorized based on office and ABPM results into pre- (5.3%, n: 3), white-coat (63%, n: 36), masked (3.2%, n: 2), ambulatory (15.7%, n: 9) and severe ambulatory (12.2%, n: 7) hypertension. Two of 3 patients with prehypertension and 10 of 18 patients with ambulatory/severe ambulatory hypertension were obese. Forty percent (n: 10) of non-dippers (n: 25) were owerweight or obese. Positive correlation was found between 24 hour mean systolic BP and diastolic BP. BMI positively correlated with 24 hour mean systolic BP, night systolic BP, 24 hour mean arterial BP, respectively.

Conclusions:

The children with high office BP measurement and those who had high risk for hypertension should be evaluated with ABPM.

P - 292 ACTINOMYCOSIS IN A CHILD WITH SYSTEMIC LUPUS ERYTHEMATOSUS.

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Introduction:

In our hospital we observed a case of systemic lupus erythematosus complicated by the development of pulmonary actinomycosis in a child of 17 years old.

Case description:

The child has been sick from the age of 13 when SLE started. Hospitalization in our clinic is associated with the development of sore throat, arthralgia, fever, throat ache, a decrease in urine output. During the examination the native DNA antibody and LE-cells. In smears of mucus from the throat and nasal fungi of the genus Candida were found. The childs condition was extremely severe. Child received nessesary treatment. On the third day of the childs stay in the hospital a syndrome of multiple organ failure developed which was fatal.

Complications: Pulmonary actinomycosis with the defeat of the walls of the bronchi and peribronchial extension to the pulmonary parenchyma, acute renal failure. A sample of lung tissue. Bronchial wall and surrounding veins are densely infiltrated by leukocytes karyorrhexis phenomena; there is filaments actinomycete mycelium the gaps in branching; the integrity of the structures in place infiltrative growth of the fungus is damaged.

Conclusions:

Actinomycetes are not allocated with phlegm. Their identification is possible with transbronchial biopsy. Pathogenis no spore-forming rods that are beginning to grow from the 5th day. A specific feature of this case was the emergence and rapid progression of actinomycosis, which was not diagnosed for a short child′s stay in the hospital.

P - 293 LONG-TERM OUTCOMES OF DIFFUSE PROLIFERATIVE LUPUS NEPHRITIS AND THE SIGNIFICANCE OF GLOBAL AND SEGMENTAL SUBCLASSES IN CHILDREN

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Introduction: Data on global (IV-G) and segmental (IV-S) subclasses of diffuse proliferative lupus nephritis (DPLN) based on the 2003 classification in children are lacking.

Material and methods: To determine clinicopathology and prognosis, 56 children aged <18 years (36 IV-G, 64.3%; 20 IV-S, 35.7%) from 2004 to 2014 were analyzed. The median follow-up was 6 years (range 1–11). Every patient received corticosteroids plus cyclophosphamide (77%) or mycophenolate mofetil (23%). Clinical endpoints were 1) complete remission (CR), 2) chronic kidney disease (CKD) defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m2 or end-stage renal disease (ESRD), and 3) death.

Results: Proteinuria and activity index was higher in IV-G ($p<0.05$). The chronicity index was similar. Global endocapillary proliferation and leukocyte exudation were predominate in IV-G whereas segmental endocapillary proliferation was predominate in IV-S ($p<0.005$). Hyaline deposits, fibrinoid necrosis/karyorrhexis and crescents did not differ between subclasses. Treatment regimens were similar in both subclasses ($p=0.50$). The CR rate was 53.6% (IV-G, 50%; IV-S, 60%; $p=0.47$). Four of 16 patients with CKD had ESRD (3 IV-G, 1 IV-S). ESRD-free rates were 94.4 at 1, 5 years and 87.9% at 10 years for IV-G and 95% at 1, 5 and 10 years for IV-S, and similar in both subclasses ($p=0.64$). Renal survival rates, defined as eGFR ≥60 mL/min/1.73 m2 of IV-G vs. IV-S at 1, 5 and 10 years were similar at 91% vs. 95%, 85 vs. 70% and 63% vs. 70%, respectively ($p=0.66$). Three deaths occurred (all in IV-G). Patient survival rates (95% CI) at 1, 5 and 10 years were 98% (88–100), 96% (85–99) and 91% (71–97), respectively and similar between both groups ($p=0.18$).

Conclusions: IV-G and IV-S displayed some clinical and histopathological disparities but rendered similar outcomes in children. Majority of children with DPGN reached adulthood but accrued significant renal damage. Thus, treatment regimens which can slow the progression of CKD are needed.

P - 294 EVALUATING THE OXFORD CLASSIFICATION FOR IGA NEPHROPATHY IN A UK PAEDIATRIC COHORT

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Introduction:

The objective of this study was (i) to describe findings on renal biopsy as per the Oxford classification for IgA nephropathy (IgAN) and (ii) to establish if findings on biopsy predict medium term outcomes

Material and methods:

Single centre, retrospective review of all children aged <18 years, with biopsy proven IgAN over a recent 10 year period. The biopsies were reviewed and scored as per the Oxford classification by single histopathologist. Data regarding clinical characteristics including glomerular filtration rate (eGFR), proteinuria, blood pressure and any specific treatment were analysed at presentation, 1, 3 and 5 years and at the time of last follow-up.

Results:

Seventy one children (80% boys), presented at a mean age of 12.1 years. Of whom 62 (87%) Caucasian. Macroscopic haematuria was the commonest presenting symptom and the most common indication for proceeding to renal biopsy.

Overall, the MEST score of the cohort was as mesangial hypercellularity M0 was in 61% (43/71), M1 in the remaining; endocapillary proliferation, E0 in 56% (40/71), E1 in remaining; segmental glomerulosclerosis, S0 in 60% (43/71), S1 in remaining; tubular atrophy >25% (T1) was seen in 1, tubular atrophy >50% (T2) in 2 (3%) with T0 in remaining. Active crescents >30% (cellular/ fibrocellular) were seen in only 6% (4/71) of cases. Immunosuppressant medications were used in 8.5% (6/71), often in those with acute renal dysfunction associated with active crescents. 21% (15/71) were treated additionally with anti-proteinuric agents.

At the time of last follow up 4 patients were in stages 3 or worse of chronic kidney disease (CKD). Their MEST scores on presentation are described in Table below

Age	M	E	S	T	Active crescents
9.2	1	1	1	0	30%
16	0	0	0	1	None
16.8	1	1	1	1	50%
17.5	1	1	0	0	22%

Conclusions:
Oxford classification in children with IgAN provides a precise description of histological findings. The predictive ability of the classification for clinical outcomes in children remains to be shown.

P - 295 MYCOPHENOLATE MOFETIL (MMF) IN THE TREATMENT OF HENOCH-SCHONLEIN PURPURA NEPHRITIS (HSPN)

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Introduction:
HSP is the most frequent childhood vasculitis with kidney involvement in 45-50% of patients and progression to renal insufficiency in 1- 2 %. In patients with significant proteinuria it was suggested the use of MMF. The aim of the study was to evaluate the efficacy of Mycophenolate Mofetil (MMF) for treating children affected by Henoch-Schonlein purpura nephritis (HSP-N).
Material and methods:
We observed 237 cases of HSPN: in 75 patients (31%) we performed renal biopsy. Fourthy-five patients were categorized as grade II and 23 as grade III HSPN according with Emancipator classification. Tweenty-two children, 3 patients with grade II and 19 with grade III, were treated with MMF (17 males and 5 females, mean age of 7±3 years). In 72% of the cases renal involvement occurred within 1 month from the clinical onset, within a range of 2-24 months in other patients. One third of grade II patients and 58% of grade III patients had macroscopic hematuria (MA). Proteinuria >1 g/24h was present in 2 patients with grade II and 11 patients with grade III nephropathy. One patient (grade III) had acute renal injury. All patients had normal values of blood pressure, C3 and IgA levels. All patients received methyl-prednisone pulses iv (1 g/1.73 m2 for 3 consecutives days) and subsequently oral Prednisone with gradual withdrawal in six months, and MMF at dose of 10-20 mg/kg/12 h for 24 months.
Results:
After six months of therapy all patients but one had persistent microscopic hematuria (ME), only 3/11 patients had recurrent MA. Patients with grade II HSPN showed significant reduction or normal proteinuria. Only 3/11 patients with grade III HSPN had proteinuria still >1gr/24 h, 4/11 patients had proteinuria <1g/24 h, in 4/11 proteinuria was normal. Mean period of follow-up was 3 years. After one year, only 1 patient had recurrent MA, 10 patients showed persistent ME. Two patients with persistent proteinuria >1 g/24 h showed a significant reduction (< 1g/24 h in 2 pts, normal in 1 pt). Proteinuria did not reappear in all patients. The effect persisted after 2 years and after therapy withdrawal. No side effects was recorded.
Conclusions: Our experience shows the efficacy and safety of MMF in HSPN and has to be confirmed by larger controlled studies.

P - 296 ANTI-INTERLEUKIN 1 TREATMENT IN SECONDARY RENAL AMYLOIDOSIS ASSOCIATED WITH AUTOINFLAMMATORY DISEASES

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Introduction:
Amyloidosis may complicate autoinflammatory diseases (AID). We aimed to evaluate the renal biopsy findings and clinical and laboratory parameters in patients with amyloidosis secondary to AID who have responded to the anti-interleukin 1 (IL1) treatment.
Material and methods:
Two children with systemic juvenile idiopathic arthritis and one with cryopyrin-associated periodic syndrome diagnosed as AA type amyloidosis were treated with anti-IL1 drugs and we have evaluated the course and management of these patients for a follow-up of median 56 (41-56) months. The renal histopathological findings at the time of diagnosis of amyloidosis and after the onset of anti-IL1 treatment were evaluated according to the amyloid scoring/grading system.
Results:
The median age of disease onset and diagnosis of amyloidosis were three years and 12 years of age respectively. The patients previously used nonsteroidal anti-inflammatory drugs, corticosteroid, methotrexate, azathioprine, infliximab, and intravenous immunoglobulin treatments. Anakinra was started in all; however, canakinumab was commenced in patient 3 since anakinra caused local cutaneous reaction. Proteinuria improved in patients after anti-IL 1 treatment. Control renal biopsies were performed a median of three years later than the diagnosis of amyloidosis. At the renal biopsy level, the renal amyloid prognostic score did not improve in patient 1 and progressed in patient 2 and 3. The renal amyloid grade has also progressed in patient 2.
Conclusions:
To the best of our knowledge, this is the first series showing progression of renal tissue damage after the improvement of proteinuria with anti-IL 1 treatment in AID-associated amyloidosis. Although anti-IL1 drugs are important to control inflammation effectively and prevent further amyloid accumulation in inflammation-associated amyloidosis, new treatment strategies are needed to target the amyloid deposits for patients with severe organ involvement.

P - 297 C3-MEMBRANOPROLIFERATIVE GLOMERULOPATHY AND ECULIZUMAB: A REPORT ON 4 PAEDIATRIC CASES

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Introduction:
The use of the C5 blocker eculizumab may be interesting in C3-membranoproliferative glomerulopathy (MPGN), a rare but severe glomerulopathy.

Material and methods:
We report on four paediatric cases with MPGN receiving eculizumab.
Results:
Patients 1 and 2 are a 9 year-old brother (Pt1) and a 13 year-old sister (Pt2), who presented with proteinuria (nephrotic range in Pt2), microscopic hematuria, normal renal function and alternative complement pathway activation (very low C3 and CH50 levels, positive C3nef). Renal biopsy showed MPGN with C3 deposits in both, although clinical phenotype was more severe in Pt2. No mutations of the complement pathway were found. Eculizumab therapy (900mg every 2-3 weeks) initially enabled a decrease of proteinuria. However, no histological improvement was observed in Pt2 (second biopsy performed after 9 months of eculizumab), and proteinuria re-increased in a context of bad compliance to ACE inhibitors.
Patient 3 is a 12-year old boy who presented with nephrotic proteinuria, gross hematuria and renal failure (maximal serum creatinine 176 μmol/L); C3nef was present. Renal biopsy showed MPGN with IgA-G-M, C3 and C1q deposits. In addition to corticosteroids and mycophenolate mofetil, eculizumab therapy (900mg every 2-3 weeks) stabilized renal function within five months; proteinuria progressively decreased, from 2046 to 80 mg/mmol after 6 months of eculizumab.
Patient 4 is a girl with C3membranoproliferative glomerulopathy diagnosed at 9 years of age, with ESRD within two years and a first R-Tx. She lost the first graft in 39 months, and was referred to us for a second R-Tx, after which she rapidly presented with biological and histological recurrence (biopsy performed 6 weeks after R-Tx). Eculizumab was then started, with no effect on proteinuria after five months. A second biopsy revealed a combination of recurrence, humoral rejection and BK nephritis.
Conclusions:
Our results balance previous observations of eculizumab efficacy in C3 membranoproliferative glomerulopathy.

P - 298 IGG4-RELATED ACUTE TUBULO-INTERSTITIAL NEPHRITIS (TIN) IN A 14 YEAR OLD GIRL: SYMPTOMATOLOGY, DIAGNOSIS, TREATMENT AND CLINICAL COURSE

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Introduction:
IgG4-related disease is a presumed autoimmune disease, predominantly described in elderly males.
Case description:
A 14 year old female presented with a 3 week history of fever, fatigue, abdominal pain, anorexia, weight loss, arthralgia and mild acute kidney insufficiency (p-creatinine = 133 micromole/l). On examination she was normotensive, pale and generally unwell. Renal ultrasound showed enlarged (13cm long) and edematous kidneys. Hemoglobin was 5,4mmol/l, C-reactive protein 52 mg/L, ESR was 65; immunoglobulins and IgG subclasses were normal and urine dipstick revealed 1+ proteinuria. No underlying cause for acute tubular-interstitial nephritis was identified.
Renal biopsy showed normal glomeruli, prominent interstitial fibrosis (with rare areas of storiform fibrosis), tubular atrophy and prominent acute interstitial inflammation consisting mainly of lymphocytes and plasma cells; 10-20% of the latter stained positive for IgG4 on immunofluorescence.
She responded quickly to prednisolone (2mg/kg/day). Her p-creatinine normalized and all her symptoms disappeared within days. Upon tapering of prednisolone, her p-creatinine rapidly rose. Prednisolone was subsequently increased and Mycophenolatmofetil (MMF) was added to the regimen in a dose of 900mg/m^2/day, thus allowing us to taper her glucocorticoids completely over 3 months. After 24 months treatment, MMF has successfully been discontinued. The patient is with stable p-creatinine (60micromol/l) and without evidence of recurrence.
Conclusions:
We postulate that this patient might have IgG4-related kidney disease even though she does not fulfill the diagnostic criteria for this disease (>40% IgG4 positive plasma cells). IgG4-related kidney disease has not previously been described in children, but should be considered causative in children with TIN of unknown origin.

P - 299 MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS IN CHILDHOOD: A 30-YEAR EXPERIENCE

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Introduction:
We report our 30 year experience of patients less than 18 years with a diagnosis of membranoproliferative glomerulonephritis (MPGN) presenting to a tertiary paediatric nephrology centre between January 1985 and December 2015.
Material and methods:
Data from 1985 to 2015 detailing presenting features, immunological findings and long term outcome was collected from an electronic renal database and case notes.
Results:
Data in 34 of 42 patients was available for analysis: 14 male, 20 female. Median age at presentation: 10.5 years (3.8 - 15.7 years). Median follow up: 4.4 years (0.7- 29.4 years). Histological type: MPGN I - 18; MPGN II/Dense Deposit Disease (DDD) - 15; MPGN III - 1. Clinical features at presentation: 50%- nephritic; 46% - nephrotic; 59% - hypertensive. Mean creatinine: 84μmol/L (28-357). In the 31 with complement levels measured at presentation: 28 (90%) low C3; 13 (42%) low C4. Further immunological and genetic measures of complement dysregulation are presented. Treatment included prednisolone in 29 (85%) patients; azathioprine- 4; ciclosporin - 5; tacrolimus - 5; mycophenolate mofetil - 9. 2 underwent plasma exchange; 1 FFP infusions; 3 received rituximab infusions and one eculizumab. 33/34 patients received treatment with an angiotensin converting enzyme inhibitor. 9 (26.4%) patients progressed to end stage renal disease (ESRD). 6 patients were transplanted. 3 were re-transplanted: 2 MPGN II/DDD, 1 MPGN I. 3/18 (16.6%) patients with MPGN I, 5/15 (33.3%) with MPGN II/DDD and 1 patient with MPGN III developed ESRD. Current CKD stages by eGFR in the 25 patients with renal survival are CKD 1: 17; CKD 2: 6; CKD 3: 1; CKD 4: 1. Mortality is 8.8% (1 ESRD and 2 transplant patients).
Conclusions: Long term clinical follow up using renal registries and local renal databases remains important in tracking how prognostic factors, including immunological and genetic markers, guide treatment selection and modify disease outcomes.

P - 301 INFLUENCE OF IGA AND C3 DEPOSITS IN RENAL BIOPSY FOR DISEASE SYMPTOMS AND FOLLOW UP IN CHILDHOOD IGA NEPHROPATHY

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Introduction:
Assessment the significance of IgA and C3 deposits intensity and location in kidney childhood IgA nephropathy (IgAN) for the symptoms of the disease and the follow up
Material and methods:
Study population consisted of 81 children, average 11.45±3.99 years. IgAN was recognized based on renal biopsy, performed 1.2±1.84, median 0.5 years after the onset. We used Oxford classification (OC) to assess the severity of histopatological lesions. In renal biopsy IgA and C3 deposits were found in immunofluorescence in mesangium or in vessels of glomeruli or both, and intensity was defined 0 to +4.We analyzed: proteinuria (mg/kg/day), hematuria, creatinine, GFR (in Schwartz formula) two times, at the onset of the disease (OOD) and at the follow up (FU). Patients were treated with: ACEI/ARB or steroids alone or with imunossupresion drugs: azathioprine (AZA), cyclophosphamide (CYC), cyclosporine A (CsA), mycopnenolate mophetil (MMF). The follow up was 3.31±2.88 years. We divided the patients into two groups, depending on the intensity of IgA deposits: G1 n=29 (+1/+2), G2 n=52 (+3/+4); depending on the locations of these deposits, we analyzed 3 groups: A n= 39 (mesangium), B n= 15 (glomeruli vessels), C n=27 (both). Statistical analysis: linear correlation, Chi2 Pearson test, Kruskal-Wallis test, ROC curve
Results:
At OOD and FU we not found any differences in G1vsG2 for: age, proteinuria, GFR and OC in renal biopsy; at FU GFR<90ml/min FU was observed more frequently in G2vsG1 (p=0.02). Number of children with FU GFR <90ml/min treated ACEI/ARB was higher than AZA (p=0.016; ROC curve sensitivity 0.8, specificity 0.5) and to immunossupresive group (p=0.01; ROC sensitivity 0.78, specificity 0.5). Any differences for IgA, C3 in A,B,C were not found.
Conclusions:

1. Poor prognosis in childhood IgAN may also depend on the intensity of IgA deposits in kidney, independently of their location.
2. Early immunosuppressive therapy in children with IgAN may influence on decrease of disease progression.

P - 301 NEW CLASSIFICATION OF PAEDIATRIC MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS CASES IN LITHUANIA

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Introduction:
Depending on deposition of complement and immunoglobulin (Ig) in the glomerular mesangium and capillary walls found on immunofluorescent (IF) microscopy membranoproliferative glomerulonephritis (MPGN) has been reclassified into two groups: immune complex mediated (ICM) and complement mediated MPGN (C3 glomerulopathy) which is further subdivided into dense deposit disease (DDD) and C3 glomerulonephritis (C3GN). The aim of our study was to re-evaluate paediatric MPGN cases according to the new classification.
Material and methods:
The records of 23 children diagnosed with MPGN between 1994 and 2014 at Paediatric Center of Vilnius University Hospital and Department of Pediatrics of Lithuanian University of Health Sciences – the two main tertiary paediatric nephrology centers in Lithuania were studied retrospectively. Renal biopsies assessed as MPGN in National Centre of Pathology were re-evaluated. C3 glomerulopathy was defined when isolated C3 deposits or predominant glomerular C3 intensity of ≥2 levels of magnitude greater than any combination of IgG, IgM, IgA was found on IF. C3GN and DDD were distinguished depending on the appearance of electron-dense deposits on electron microscopy (EM).
Results:
23 cases (11 girls, 47,8 %) were analysed, with mean age of 11,8 (± 4,7) years. After re-evaluation 14 cases (60,9 %) were classified as ICM, 8 (34,8 %) as C3 glomerulopathy, 1 case could not be reclassified as IF was uninformative. Mean plasma C3 level was 0,26 (± 0,29) g/l in a group of C3 glomerulopathies.One of 8 C3 glomerulopathies was confirmed as DDD, one as C3GN on EM. EM was not performed on other C3 glomerulopathy cases.
Conclusions:
The retrospective re-evaluation of MPGN cases during 20 year period revealed that ICM MPGN dominates - counts for approximately 2/3 of all paediatric MPGN. For fully applying new classification and distinguishing MPGN into separate pathogenetic groups the evaluation of EM is essential.

P - 302 CLINICAL PROFILE AND OUTCOME OF ACUTE NEPHRITIC SYNDROME

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Introduction:
Objectives of study: To analyze retrospectively clinical profile of acute nephritic syndrome in hospitalized children and to correlate various clinical and laboratory parameters with the outcome.
Material and methods:
91 children (56 boys and 35 girls) with age of 8,5 years (±4,86) were hospitalized from 2012 till 2014 with features of acute nephritis (hematuria, oedema, arterial hypertension, ± renal failure). History of precedent infection was noted. Duration of symptoms, presence of systemic features (skin or joint involvement) and complications-(hypertensive encephalopathy, congestive heart failure and acute renal failure) were recorded. Full blood count, biochemistry, immunological investigation, urine analysis and ultrasound were performed. Renal biopsy was done if there was either nonresolution, progression or if presentation was atypical.
Results:
70 children (76,9%) had macroscopic hematuria, 65 children (71,4%)-proteinuria, 26 (28,5%) -hypocomplementemia, 67 (73,6%)- a preceding infection, 29
(31,9%) - pharyngitis and 3 (3,3%)- pyoderma, in 15,8%-elevated AST levels. Nineteen children (20,9%) were with I-st stage of renal failure, 7 (7,7%)- with II-nd stage and 5 (5,5%) with III-rd stage. 29 children (31,9%) were with hypertension. Hyperechogenisity of the kidneys- in 61 (67%), in 3-pleural effusions and ascites. Renal biopsy was performed in 19 (20,9%) and in 5(5,5%)- IgA nephritis was found, in 3 (3,3%) –Henoch-Shönlein, in 1-membranoprolipherative glomerulonephritis type I, 6- (6,6 %) with mesangioproliferative glomerulonephritis, 4- (4,4%) with lupus nephritis.
Conclusions:
In our study, nephritic syndrome in children is associated mostly with acute post-infectious glomerulonephritis, with hematuria, hypertension ± renal failure. The prognosis, in most of the cases, is favorable with complete recovery in three months. Bad prognostic factors are associated with: short latent period, presence of extrarenal features, normal C3

levels, persistent proteinuria > 6 months and hematuria > 18 months and persistent hyperechogenisity of the kidneys.

P - 303 HENOCH-SCHöNLEIN PURPURA NEPHRITIS: EVALUATION OF A NEW CARE PROTOCOL

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Introduction:
There is no consensus for the management of Henoch-Schönlein purpura (HSP) nephritis in France. Kidney biopsies (KB) are often performed to evaluate kidney impairment but histologic lesions may not correlate with long term evolution. A care protocol was adapted in the western region in 2011 : HSP nephritis with proteinuria >1g/day, without nephrotic syndrome or acute kidney injury (called « important nephritis ») was treated with corticosteroids (CS) bolus without KB (whereas KB was systematically performed before CS before 2011). The aim of the study is to assess the impact of this protocol.
Material and methods:
This retrospective observational study included all patients aged <18 years at diagnosis of HSP nephritis, between 01/01/2008 and 31/09/2013, in 5 university hospitals. We compared patients treated according to the new protocol (P+) or not (P-). CS and renin-angiotensin system inhibitors (RASI) administration was evaluated. Renal sequelae at one year were defined as a significant proteinuria or microalbuminuria or RASI use. Fischer and Mann Withney tests were performed, $p<0.05$ was considered as significant.
Results:
88 patients were included, one third had severe HSP nephritis (nephrotic syndrome or acute kidney injury) and more than half of them had important nephritis. 60 patients were treated according P+. The protocol reduced the number of KB (41,7% in P+ *vs* 91,7% in P- for patients with important nephritis, $p = 0.0005$). There were no significant differences for the administration of CS (75% *vs* 85,7% in P+ and P- respectively, $p = 0,4$), for the use of RASI (63% *vs* 50%, $p = 0,25$) and for the risk of renal sequelae at one year (46,6% *vs* 37%, $p = 0,64$).
Conclusions:
The management of « important » HSP nephritis without systematic KB before starting CS may be a good alternative. This analysis has to be extended to assess long-term renal prognosis.

P - 304 CLINICAL VALUE OF DETERMINATION MARKERS OF IMMUNE SYSTEM ACTIVATION IN CHILDREN WITH GLOMERULOPATHIES

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Introduction:
The purpose of the study was to clarify the clinical significance of determining chemokines CCL5/RANTES and BAFF in the blood serum of children with primary and secondary glomerulopathies(GP).
Material and methods:
25 patients with secondary nephritis (lupus nephritis(LN), Henoch-Schonlein pupura nephritis(HSPN)), 22 patients with primary GP (IgA-nephropathy, FSGS, minimal change, MPGN), 28 healthy children were examined, 13 patients during followup. Test systems R&D Systems Quantikine ELISA were used.
Results:
In patients with LN RANTES was 450-870U (median (med)-530, 539,4 ±22,9), in HSPN 470-540U (med-525, 515,0±9,06), in healthy 260-510U(med-460, 432,9±15,08). BAFF concentration in LN 125-600U (med-360, 349,7±40), in HSPN 240-1000U (med-400, 452,5±84,2), in healthy 62,5-250U (med-162.5, 173,8±11,76). Significant differences in RANTES and BAFFconcentration between LN and healthy, HSPN and control($p<0.05$) were obtained.
Conclusions:
The participation factors activation of T- and B-lymphocytes in the development of secondary GP($p<0.05$) compared with healthy and primary GP was shown. In secondary GP concentration of chemokines correlated with the severity of the pathology(hypertension, creatinine, proteinuria, hematuria, morphological and laboratory signs of high activity). In case of positive clinical and laboratory dynamics reduction of BAFF and RANTES and, conversely, increasing during the disease exacerbation revealed, which allows their use in clinical practice as an additional immunological markers for the diagnosis and evaluation of the therapy effectiveness.

P - 305 THE BRUCELLA VASCULITIS IN THE KIDNEY : A CASE REPORT

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Introduction:
Brucellosis can be associated with hematuria, proteinuria, and renal failure in endemic areas although renal involvement is uncommon**.** Many diverse etiologies can play a role in the renal involvement like membranoproliferative glomerulonephritis, chronic tubulointerstitial nephritis associated with vasculitis, immune complex nephritis, acute tubuler necrosis due to drugs.
Case description:
A nine years old boy was admitted to our department with macroscopic hematuria and arthritis in ankles for two days. In his history he has had maculopapuler rashes especially on lower extremities periodically for a year and have been treated like allergic urticeria. Additionally his father had brucellosis treatment two years ago. In his physical examination there were maculopapuler rashes and arthritis on ankles . In routine laboratory tests microscopic hematuria and proteinuria (11mg/m2/h) were detected. His complements, immunglobulins, ANA, ANCA tests were negative.The serological tests were negative except brucella aglutination test (1/640). Brucella tests was confirmed twice by western blot. Bilateral edema and increased echogenity in renal cortex were seen by ultrasonography and leucocytoklastic vasculitis was detected in skin punch biyopsy. brusellosis treatment (rifampin,tetracycline,gentamycine) was given to him.On the 15 th day of treatment macroscopic hematuria reproduced and then renal biyopsy was performed. Because of mesangioproliferatif glomerulonephritis in biyopsy prednisolone was added to therapy and enalapril was started due to proteinuria. After eight weeks, Brusellosis treatment was stopped aglutination was 1/320. The patient has been still followed with microscopic hematuria and proteinuria was dissappeared. Brucellosis is a common multisystemic infectious disease with a variety of clinical manifestations like skin lesions including vasculitis, which is another unusual clinical manifestation . It may occur due to immunological reactions. Although mild proteinuria is commonly observed during the course of Brucellosis, biopsy-proven glomerulonephritis is quite rare likewise our patient .
Conclusions:
Brucellosis should be considered in the differential diagnosis of vasculitic diseases especially in endemic areas.

P - 306 ADDITIONAL CRITERIA FOR DIAGNOSIS AND PROGNOSIS OF IMMUNE-MEDIATED GLOMERULOPATHIES IN CHILDREN

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Introduction:
The aim of the study was to determine the concentrations of growth factors TGF-1β and VEGF in the blood serum of patients with secondary glomerulopathies(GP)-lupus nephritis(LN, n=16), Henoch-Schonlein pupura nephritis(HSPN, n=8), 1girl with Wegener's granulomatosis, and children with primary GP(n=22). As a control group 28 healthy children were examined. 13 children surveyed in the dynamics.
Material and methods:
The study was performed on the basis of the Department of Nephrology and laboratory of Research Institution of Epidemiology and Microbiology. Test systems R&D Systems Quantikine ELISA were used.
Results:
In patients with LN TGF-1β was 112,0-280,0U (median (med)-165, 189.6 ±13.5), in HSPN 140,0-240,0 U(med-187,5, 183,8±14,35, in healthy 100,0-160,0U (med-140.0,137.5 ± 2,9). In patients with LN VEGF was 70-1850U(med-425, 501,5±110,0), in HSPN 215-880U (med- 477.5, 483,8 ±74,2), in healthy 65,5-415U (med-140, 174,2±13,9). Significant differences in concentration of TGF1b and VEGF obtained between LN and healthy, HSPN and control, LN and FSGS ($p<0.05$). In secondary GP and primary FSGS concentration correlated with the severity of the pathological process in the kidneys: creatinine, hypertension, proteinuria, morphological signs of chronic damage (glomerulosclerosis, tubulointerstitial fibrosis, fibrous crescent), and resistance to standard therapy.
Conclusions:
Significant increase in serum concentrations of factors of progression of vascular disorders VEGF and TGF1β in patients with LN, HSPN and FSGS compared with healthy and their correlation with markers of severity/chronic damage allows to use these molecules in predicting prognosis of secondary GP and FSGS.

P - 307 MOLECULAR MEDIATORS OF DEVELOPMENT AND PROGRESSION OF SECONDARY GLOMERULOPATHIES IN CHILDREN

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Introduction:
Among secondary glomerulopathies(GP) in pediatric practice the most common are lupus(LN) and Henoch-Schonlein purpura nephritis (HSPN). Renal involvement usually determines the prognosis of these diseases. Immune disorders play a key role in the development and progression of GP. The aim of the study was to determine the concentration of proinflammatory molecules-caspase-1, IL1β and TNFα in blood serum of patients with GP and clarify their role in the development of diseases.
Material and methods:
Patients with LN(n=16), HSPN(n=8) and 1 with Wegeners granulomatosis,comparison group with primary GP(n=22) and 28 healthy children were examined, 13 surveyed during followup. Test systems R&D Systems Quantikine ELISA were used.
Results:
In LN patients caspase-1 concentration 25-400U (median (med)-90, 131, 8±29,5), in HSPN 45-350U (med-162.5, 186,3±41,9), in healthy 12.5-80U (med-50, 48,66±4,07). In patients with LN TNFα was 40,0-120,0U (med–60, 67,2±5,4), in HSPN ranged 31.2-80.0U (med-61.25, 56,4±5, 45), in control 31,2-62,5U (med-40.0, 42,1±1,8). IL-1β in LNpatients15, 6-95,0U (med-26, 40,56±6,74), in HSPN 15,6-31,3 U (med -25), in healthy 5-27,0U (med-15.6, 3,74±1,15). Significant differences in caspase-1, TNFα, IL1β between LN and healthy, HSPN and control were found($p<0.05$). Concentrations of cytokines correlated with the severity of the disease (proteinuria, hematuria, creatinine, hypertension, morphological and laboratory signs of high activity).
Conclusions:
Significant increase in the concentration of proinflammatory cytokines caspase-1, IL1β, TNFα in secondary GP, changes during the treatment or alternatively, relapse disease, evidence of their involvement in the pathogenesis of GP and allows use them as an additional criteria in the diagnosis and assessment of the adequacy of therapy.

P - 308 A 13-YEAR-OLD CHILD WITH PERSISTENT LUPUS NEPHRITIS AND 22Q11 MICRODUBLICATION SYNDROME

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Introduction:
Microduplication 22q11 syndrome has been recently characterized as a new genomic syndrome having only few overlapping features compared with the classic DiGeorge/ velocardiofacial syndrome. The 22q11 syndrome shows a wide phenotypic variability ranging from normal to multiple congenital defects including heart defects and urogenital abnormalities.
Case description:
A 13-year-old Caucasian male was admitted due to prolonged macroscopic painless hematuria, without having any recent history of trauma or infection. The child was hemodynamically stable, with elevated blood pressure (Stage I). The patient's medical history revealed congenital heart disease, common patent ductus arteriosus, repaired at the age of 9 months with valvuplasty. The child presented five years later subsequent graft stenosis and aortic valve insufficiency. At seven years of age, the child was hospitalized due to staphylococcal endocarditis which was successfully treated with antibiotics. On admission initial laboratory and clinical findings excluded hemolytic phenomena and infection, but revealed mild anemia, hypocalcemia, hematuria, albuminuria, impaired renal function, elevated ESR, D-Dimers and positive ANA autoantibodies. Complement/ASTO were within the normal range. Due to gradual deterioration of the nephritic syndrome, renal biopsy was performed. Genetic testing was also preformed due to his history and mild dysmoprhic features.
Biopsy indicated proliferative SLE nephritis (class IV) with active lesions. Within six months the child showed additionally thrombocytopenia, leucopenia, positive autoantibodies (anti-DNA /ANA/acL) and decrease of C3/C4. Based on the above findings, a lupus nephritis was confirmed. Therapeutic approach consisted of corticosteroids and mycophenolate mofetil. Molecular karyotype with CGH array revealed microdublication of the distal 22q11 region.
Conclusions:
This case illustrates the importance of reporting unusual 22q11.2 duplications to further evaluate the incidence of these rearrangements and to improve genotype-phenotype correlations and genetic counseling.

P - 309 HYPOURICEMIA AND HYPOPHOSPHATEMIA MAY BE INDICATORS OF DISEASE ACTIVITY IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction:
Systemic lupus erythematosus (SLE) is a relapsing autoimmune disease with clinical manifestations that affect multiple organ systems. Despite advances in medicine, diagnosis of active SLE remains as a major challenge. There are not cheap and practical markers available for recognize of active SLE.

Case description:
In this paper, we report decreased serum uric acid and phosphate levels in 4 children with active SLE.

The serum anti-DNA and CRP levels and sedimentation rate were increased, while serum complement C3, uric acid and phosphate levels were reduced in active disease. In active stage, serum PTH levels and tubular phosphate reabsorption rate were normal. The serum CRP, complement C3, uric acid and phosphate levels were return to normal after successful immunosuppressive treatment in all patients. Our patients were not treated with phosphate contain drugs during the active stage of SLE.

Table I. Clinical and laboratory characteristics of 4 patients with SLE in active stage.

Patients	1	2	3	4
Gender	Female	Male	Female	Female
Age (year)	18	16	17	17
Age at SLE onset	15	13	14	15
Disease duration	3	3	3	2
Clinical manifestations	Cytopenia SLE nephritis	Pericardial effusion, Cytopenia	Cytopenia SLE nephritis	Fever, arthritis, Pleural effusion
Therapy	corticosteroids CYC HCLQ	Corticosteroids MMF	corticosteroids CYC MMF	corticosteroids CYC MMF
Thrombocyte count (mm^3, 150000-10000)	142000	367000	89000	111000
Leukocyte count (mm^3,4000-10000)	2760	7200	2780	2200
Phosphate (mg/dl, 2.7-4.5)				
-Active stage	2.1	1.4	2.6	2.0
-Remission stage	4.2	3.2	4	4.2
Uric acid (mg/dl, 3.4-7)				
-Active stage	3.1	1.2	2.7	3.3
-Remission stage	5.9	6.3	4.3	6.2
CRP (mg/dl, 0-0.8)	10.5	11.5	5.6	17
Sedimentation rate	27	116	91	149
PTH (pg/ml, 15*65)	27.1	63.7	33	47
ANA	(+)	(+)	(+)	(+)
Anti DNA (0-1.1)	2.07	3.8	15.7	4.09
C3 (mg/dl, 90-180)	47.5	39.4	27.3	39.4
C4 (mg/dl,10-40)	11.6	3.46	5.8	6.18
Tubular phosphate reabsorbation rate (%)	92	86	88	94

Conclusions:
The mechanism of hypophosphatemia and hypouricemia may be relate elevated cytokines levels such as TNF and IL-6 in patients with active satge of SLE. In conclusion, we suggest that serum uric acid and phosphate assay may reflect the disease activity of SLE and may be used as biomarkers for SLE. Further studies are needed to assess of these findings.

P - 310 HENOCH SCHöNLEIN PURPURA NEPHRITIS: DESCRIPTION OF TWO CASES AND THERAPEUTIC CONSIDERATIONS

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Introduction:
describe two cases of HSP nephritis with nephrotic range proteinuria.

Cases description:
two five years old children (one male, one female) were seen for palpable skin purpura. None had intestinal involvement. At onset both children had an increasing hematuria and proteinuria up to nephrotic range. GFR was normal. Renal biopsies showed < 50% crescents with focal mesangial proliferation (II/a ISKDC classification) in male and diffuse mesangial proliferation in female (III/b). Six weeks from onset children were commenced on Methylprednisone pulses 1g/1,73 mq for three consecutive days at month 1,3 and 5, followed by oral Prednisone 0,5 mg/kg on alternate days for six months. Simultaneously was added oral Cyclophosphamide (CyP) 3 mg/Kg for eight weeks.

One month after starting therapy satisfactory improvement of proteinuria and hematuria was obtained in both children. Complete remission of proteinuria was reached in the next four weeks. No relevant side effects were noted. No relapses occurred in four months follow-up.

Conclusions:
at present no strong prognostic evidences support the choice of the best treatment of HSP nephritis, especially in absence of severe histological pattern at onset. Although in many cases a spontaneous resolution was observed, the possibile long term progression to ESRD should be taken in account. The use of ACE-I drugs, as provided by KDIGO guidelines, might delay the beginning of an effective treatment.

These two reports aim to underline the importance of an early treatment of HSP nephritis especially in case of persistent high range proteinuria irrespective of histological classification. Six months of steroids with Methylprednisone pulses on alternate months effectively improve proteinuria rather than oral steroid alone (as already reported in previous studies). Although with not proven efficacy, is reasonable the addition of immunosoppressor drugs as CyP. It is recommended that a multicentre international prospective study about HSP nephritis will be planned.

P - 311 NOVEL MUTATION AMONG 9 ADFNDI KINDREDS IDENTIFIED IN SLOVAK AND CZECH POPULATION

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Introduction:
Familial neurohypophyseal diabetes insipidus (FNDI) is a rare hereditary diseased manifested by progressive tendency to polyuria from early childhood. We report the results of the molecular testing and clinical presentation of the disease in nine apparently unrelated kindreds of Slovak or Czech origin.
Material and methods:
Each family provided clear evidence of the disease symptoms in at least two consecutive generations consistent with autosomal dominant inheritance. Six kindreds are presented for the first time; the remaining three have been previously reported in a large international study. Symptomatic individuals and their healthy relatives were tested for *AVP* gene mutations.
Results:
In 9 kindreds we found 34 affected individuals, which predict, in the population of 16 millions, a prevalence of 1:450 000 for the Central European region. Six various mutations of the AVP gene were identified including a novel one (c.298G>C). The remaining five were repetitive and were described earlier (c.3G>A, c.55G>A, c.173G>T, c.276C>A, c.310T>G). Affected individuals developed polyuria and thirst between their 2nd and the 17th birthday with large inter- and intrakindred age variation. One subject was presented by nocturnal enuresis, another one had chronic hypernatremia and psychomotor delay. We also report a monozygotic twin pair, who presented by partial diabetes insipidus at age of 17 years and DNA analysis was needed to confirm the diagnosis. One child was diagnosed presymptomatically at the age of 1 year.
Conclusions:
The non-uniform clinical phenotype and the risk of secondary complications from polyuria make the early molecular diagnosis of FNDI reasonable. Water deprivation test can be misleading in cases of partial diabetes insipidus. We suggest that all first degree relatives of patients with clinical diagnosis of FNDI should be tested for AVP gene mutations.
This work was supported by Ministry of Health of the Slovak Republic under the project registration number 2012/5-UKBA-5.

P - 312 HYPOMELANOSIS OF ITO AND RENAL CYSTIC DISEASE

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Introduction:
Hypomelanosis of Ito is a syndrome characterized by hypopigmented streaks and patches with neurologic, skeletal and ocular involvement; renal involvement is unusual. The syndrome occurs generally as a sporadic trait, but autosomal dominant, recessive or X-linked inheritance have been described. We report the case of a female infant with Hypomelanosis of Ito associated to advanced degree of chronic kidney failure (stage 3 by KDOQI) and glomerulocystic kidney disease.
Case description:
Our patient was born preterm by caesarean section in premature rupture of membranes. At birth the baby showed hypo- and hyper pigmented patches of the lower limbs and the thoracic and lumbar spine, suspected for Hypomelanosis of Ito, and the diagnosis was confirmed by examination with the Wood lamp. At the age of two months the baby had manifested seizures.The girl had run regular follow-up checks, during which it has been performed abdominal ultrasounds that highlighted the hyper echoic renal cortex and several further blood tests showed over time increasing creatinine and azotemia, macrocytic anemia and hypovitaminosis D. So we submitted the patient to paediatric nephrology evaluation that showed a reduction of glomerular filtration rate (GFR 40 ml/min by Schwarz formula). Abdominal ultrasound showed hyper echogenicity of the renal cortex, with absent corticomedullary differentiation and minute cortical cysts.
Kidney involvement in Hypomelanosis of Ito has been described in five other cases; in two of them, as our case, it has been reported cystic renal changes.
Conclusions:
Our case report demonstrates the importance of follow-up in these patients, in order to identify a possible renal involvement and to develop appropriate conservative treatment.

P - 313 A FRENCH COHORT OF PATIENTS WITH CYSTINOSIS : VARIABILITY IN THE COMPLIANCE TO TWO FORMULATIONS OF CYSTEAMINE, USE OF ELECTRONIC MONITORING DEVICES.

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Introduction:
Cystinosis is an inherited autosomal recessive disease. Our objectives are (i) to describe the profiles of compliance to cysteamine treatment and the White Blood Cell (WBC) cystine levels in cystinosis patients followed-up for one year in the CrYSTobs study; (ii) to describe patients characteristics at baseline and their evolution in terms of renal function, disease and cysteamine treatment; and (iii) to explore the differences in compliance profiles under delayed release or short acting cysteamine.
Material and methods:
CrYSTobs is a French cohort of patients with cystinosis. Thirty patients are expected in the study. Subjects are seen every 3 month for 2 years. All subjects receive oral cysteamine. A descriptive analysis is performed on subjects followed-up for at least a year in the study. Compliance is decribed as a continuous variable, using an electronic monitoring system. Level of observance and white blood cell cystine level are represented graphically. Level of compliance is calculated as the number of opening / number of theoretical opening. Mean of compliance and delays are presented.
Results:
Seventeen patients have already been enrolled in the study; two patients have terminated the follow-up.Twelve patients (Mean age: 18.2 years, 58% female) followed-up for at least one year were analyzed. Seven patients were transplanted and 2 under dialysis. GFR rates remained stable over time: mean of 72.14 at D0 and 73.92 ml / min / 1.73m² at 12 months. WBC levels remained under 1 µmol / ½ cystine / g protein over the year. Four patients had a mean period of 42 days under short acting cysteamine followed by a mean period of 278 days under RP103.
Conclusions:
First results confirm a great variability of compliance profiles of cysteamine whatever the formulation used. Complementary results will be presented.

P - 314 COMPANION DIAGNOSTICS BY COMPREHENSIVE TARGETED NGS WITH EVIDENCE FOR A THRESHOLD MODEL IN A COHORT OF 605 PATIENTS WITH ATYPICAL HAEMOLYTIC UREMIC SYNDROME AND HEREDITARY GLOMERULOPATHIES

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Introduction:
Genetic defects are responsible for the majority of primary renal diseases leading to end-stage renal disease. The risk of recurrence after transplantation depends on the genotype. Genetic testing becomes increasingly important for proper clinical management and therapeutic and prognostic issues, but there is a need for novel comprehensive, time- and cost-efficient strategies.
Material and methods:
By Next Generation Sequencing (NGS) we established a multi-gene panel for the parallel analysis of 347 genes for atypical haemolytic uremic syndrome (aHUS) and hereditary glomerular disorders (nephrotic syndrome, FSGS, Alport syndrome, MPGN, C3 glomerulopathies) which often show clinical and genetic overlap.
Results:
In total, we analysed 605 unrelated patients by a customized NGS-panel targeting 347 genes. The alternative complement pathway is typically overactivated in aHUS and C3 glomerulopathies, but genes implicated in coagulation and haemostasis play a pivotal role too. Secondary triggers (e. g., hypertension, pregnancy, transplantation, infection) and predisposing polymorphisms lower the threshold for disease onset. We will present new disease genes and demonstrate that variations in more than one gene contribute to the phenotype with variable expressivity and incomplete penetrance. We show that detailed information on the genotype is crucial for decisions on transplantation, recurrence risk and treatment such as when and how long an expensive drug like the monoclonal antibody eculizumab should be given. The diseases discussed represent an interesting model that may help to explain basic genetic principles not confined to aHUS and related disorders.
Conclusions:
Overall, our study represents the by far largest cohort analysed by comprehensive genetic testing. We demonstrate that genetic testing assists in the decision-making process to treat patients adequately while handling public resources responsibly.

P - 315 GENETIC TESTING IN PATIENTS WITH TUBULOPATHIES

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Introduction:
Genetic testing can provide certainty of the diagnosis, informs prognosis and clinical management and allows precise genetic testing. At Great Ormond Street Hospital for Children NHS Foundation Trust, we have a specialised clinic for patients with mostly inherited tubular disorders. Genetic testing for most of these disorders had not been available within the National Health System. Recently, we obtained a comprehensive testing kit called MULTIPLICOM TUBMASTR through the EU FP7 grant EURONOMICS. Here we describe the results, focusig on patients with a clinical diagnosis of salt-wasting tubulopathies (SWT) and distal renal tubular acidosis (dRTA).
Material and methods:
The TUBMASTR kit allows testing of 37 known tubulopathy genes. These genes are divided in 751 amplicons, which are amplified through 9 multiplexed PCR. Amplicons from individual patients were pooled and "barcoded" via a second PCR reaction, according to manufacturers instructions. Amplified DNA from 23 patients and one negative control was simultaneously sequenced on a Illumina MiSeq 2X300 bp reads and data were reviewed with an in-house analysis pipeline (using open-source software).
Included was DNA from 7 patients with previously identified 8 mutations in tubulopathy genes as positive controls and from unaffected patients as negative controls.
Results:
Amplification was successful in all but 2 GC rich amplicons (99.7%) and sequencing yielded >30x coverage in all. Causative mutations were identified in 48/52 (92%) patients with a clinical diagnosis of SWT and in 18/23 (78%) with clinical diagnosis of dRTA. In addition, causative mutations were identified in one patient each with Dent disease, isolated hypomagnesaemia and Familial Hypomagnesaemia with Hypercalciuria/Nephrocalcinosis, respectively. All identified mutations were confirmed by Sanger sequencing.
All 8 positive control mutations were identified and no disease-causing variants in the negative controls.
Conclusions:
Next generation sequencing with the TUBMASTR kit allows cost efficient and comprehensive genetic testing in renal tubulopathies.
Further review of clinical and genetic data in those patients without causative mutations is needed to assess the accuracy of the clnical diagnosis and the potential for novel disease gene discovery.

P - 316 AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE (ARPKD) AN OVERVIEW WITH LOCAL PERSPECTIVE

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Introduction:
polycstic kidneys a group of cilia related disorder, it constitute a major cause of ESRD in children and adults .many pediatric disorders demonstrate renal cysts or cystic dysplasia.the major distinction of enlareged cystic echogenic kidneys mainly between ARPKD and ADPKD.the gene mutation of both diseases is well known to the world, because of different cultural and envirnomental variablity between reces and countries, esp. the prevelnce of consanguinity in some countries including our country with very high prevelence of concanguity and inherited disease with no clear study to evaluate such problems.
Material and Methods:
objective: 1) to identify families from several saudi regions with suspected ARPKD, 2) to establish a data base for the nature of mutations present in saudi populations
inclusion criteria: 1) family history of consanguinity or normal parnts with affected sibling 2) ultrasound diagnosis of nephromegaly or antenatal history of oliguhydramnion3)associated findings of hypertension, renal failure, or portal hypertension 4) confirmatory CT/MRI or liver biopsy (not mandatery)

exclusion criteria: 1) affected parents with different cystic disease (ADPKD), 2) normal size, normal echogenic kidney with normal kidney function, 3) refusal to contribute.
method and material:
1) sample collected in a accordance with research Ethics committees regulation, 2) signed consent 3) 63 unrelated ARPKD clinicaly diagnosed were recruited for the gentic screening from all regions in saudi arabia 3) 2-5ml of whole preferal blood in EDTA tube and sent to umm al-qura university laboratory by commercial carrier for storage and further analysis
mathodology: 1) DNA isolation 2) Exons sequencings (Sanger sequencing) 3) whole gene sequencing by (NGS)
ARPKD mutation detection algorith developed
Results:
results: the study still in progress
so far we stusied 21 cases and capillary sequencing for known exons of the PKHD1 gene
we found by conventional sequencing novel causative missense varient at the exon 21 of PKHD1 gene and known silent varients, with known missense mutations
NGS sequencing done for negative cases by the conventional sequencing tested for PKHD1, PKD1, PKD2 again from different regions in saudi arabia
we found one novel missense varient at the exon 61-3 of PKHD1 gene and four known missense varient in the exons 19, 21, 32-6, and 35
one varient was found in 8 patents and all were homozygous
Conclusions:
Total samples collected were 63 cases representing different regions in saudi arabia, we have established and optimized DNA sequencing testing, we have identified 5 known deleterious mutations and 2 novel mutations in PKHD1 gene
We hope by the end of this study our target of establishing genetic data base for the ARPKD in saudi population

P - 317 IDENTIFICATION OF A NOVEL, DE NOVO MUTATION IN THE ACTN4-GENE IN A 12-YEAR OLD GIRL WITH END-STAGE RENAL DISEASE

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Introduction:
Children presenting as sporadic cases with end-stage renal disease (ESRD) benefit from Next-Generation-Sequencing (NGS) techniques that allow the rapid identification of causative mutations in established or new genes. In case of novel potentially pathogenic variants a detailed functional work-up is mandatory to definitely confirm the diagnosis.
Material and methods:
We here illustrate a novel pipeline for a genetic, translational work-up of rare kidney disease by an exemplary case: A 12-year-old girl presented with symptomatic arterial hypertension, ESRD (GFR 6 ml/min/1,73m2), proteinuria of 2 g/m2/d and small hyperechogenic kidneys to our service. Family history as well as extensive immunological analyses were unremarkable.
Results:
Mutations in NPHS2 (Podocin) and HNF1ß were excluded by Sanger-sequencing prior NGS-sequencing of a panel of disease-associated genes (TruSightOne, 4813 genes, "Mendeliom"). Mendeliom analysis revealed a novel, potential pathogenic variant c.584G>A (p.Gly195Asp) in the ACTN4-gene (alpha-Aktinin 4) in heterozygous state. The variation was not found in any SNP databases (ExAC browser etc.), predicted to be pathogenic, and segregation analysis demonstrated absence of the variant in both healthy parents. To further characterize the mutation, we isolated primary renal cells from the urine of the patient and of normal healthy controls. Mass spectometry (MS) of these cells showed significant differential expression of cytoskeletal proteins due to the mutation and decreased ACTN4-expression in the patient´s cells. In addition, we cloned human ACTN4 and introduced the patient mutation by PCR mutagenesis. Immunofluorescence of transfected podocytes revealed an abnormal aggregation of ACTN4 and a severely disturbed actin-cytoskeleton which is in line with the MS findings
Conclusions:
Dominant mutations in the actin-crosslinking ACTN4 are known to cause a rare type of late-onset FSGS. NGS techniques and subsequent functional work-up of patient-derived cells will help not only to expand the phenotypic spectrum like in this case of ACTN4-associated FSGS but also to better understand the molecular pathogenesis of rare kidney diseases.

P - 318 RESULTS OF TURKISH MULTICENTRIC NATIONAL CYSTINOSIS REGISTRY

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Introduction:
In cystinosis, defective lysosomal transport leads to widespread accumulation and crystallization of cystine in many organs including the kidney.
Material and methods:
Clinical and genetic features of cytinosis patients in national registry system were investigated.
Results:
A total of 102 cystinosis patients (47 girls, 55 boys) were included in the study. Median age of diagnosis was 18 months (IQR; 12 months-48

months). Consanguinity between parents and family history for cystinosis was present in 74 (72.5%) and 40 (39.2%) patients, respectively. Genetic analysis still continue for all patients, at the moment genetic data was available for 43 patients (42.1%). Analyses revealed c.1015G>A (p.G339R) and c.681G>A (p.E227E) as the two most common CTNS mutations. None of the patients had 57 kb deletion on CTNS gene. Clinical data is available for all patients. Median duration of follow-up was 5.37 years (IQR; 2.35-9.87 years). At last visit; mean age was 10.8 ±6.9 years and 29 patients (28.4%) were under renal replacement therapy (13 patients dialysis, 16 patients renal transplantation). Median GFR of transplant patients at last visit was 74.2±45.5 ml/min/1.73 m2 after a median follow-up of 5.9 years. Mutation on CTNS did not have an effect on renal outcome. At diagnosis, X-bein/O-bein and rickets was present in 24 patients (23.5%) and in 47 patients (46%), respectively. As extrarenal complications, hypothyroidism and gastrointestinal system (GIS) involvement was present in 14 and 8 patients at diagnosis, respectively. Most common GIS finding was hepatosplenomegaly.

Conclusions:

This cohort showed that rickets is a common finding at diagnosis and should be not overlooked. None of the patients in this national registry system had 57 kb deletion affecting ~76% of northern European alleles. Screening for 57 kb deletion is not recommended in our country.

P - 319 GENETIC, PATHOLOGICAL AND CLINICAL BACKGROUNDS IN AUTOSOMAL DOMINANT ALPORT SYNDROME

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Introduction:

Alport syndrome is a group of inherited, heterogeneous disorders involving chronic kidney disease, sensorineural hearing loss and ocular abnormalities. Autosomal dominant Alport syndrome (ADAS) is caused by heterozygous mutations in either *COL4A3* gene or *COL4A4* gene encoding type IV collagen α3 or α4 chain, respectively. ADAS is rare mode of inheritance and it's character is still unclear. In addition, recently, these genes are focused as causative for familial focal segmental glomerulosclerosis (FSGS). Our objective is to clarify genetic, pathological and clinical backgrounds for ADAS.

Material and methods:

A retrospective analysis for 21 genetically diagnosed patients with ADAS and their affected family members who showed renal symptoms was conducted (n=35).

Results:

Median renal survival time by Kaplan Meier method was 57 years. All patients showed hematuria and the mean age at first detection of proteinuria was 15.8 years. No patient had hearing loss or ocular lesions. Renal biopsy was performed in 10 patients. With light microscopy, four of them showed diffuse mesangial proliferation, three showed minimal glomerular change and three showed FSGS. Molecular analysis revealed *COL4A3* gene mutations in four families, COL4A4 gene mutations in five families and two families had mutations in both *COL4A3* and *COL4A4* genes. Four mutations were reported as causative mutations for autosomal recessive Alport syndrome (ARAS) in the previous studies. Intra-familial variability of clinical features were observed such as the age at reaching ESRD.

Conclusions:

The present study showed that clinical features in ADAS patients were much milder than X-linked Alport syndrome or ARAS patients. Pathological analysis suggested some of ADAS patients might be diagnosed as familial FSGS as reported recently. Genetic analysis indicated secondary factors such as existence of modifier genes or environmental factors might affect severity of renal phenotypes in ADAS.

P - 320 EGYPTIAN GROUP FOR ORPHAN RENAL DISEASES (EGORD): UNIQUE REGIONAL RARE KIDNEY DISEASE BODY

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Introduction:

With the changing nephrology landscape and rapidly advancing basic science, the Egyptian Group for Orphan Renal Diseases (EGORD) was established with the vision of creating a body to care for the commonly overlooked inherited kidney diseases in Egypt.

Material and methods:

Patients with familial and/or syndromic kidney disorders as well as patients with unidentified primary etiology for their chronic kidney disease were reviewed by EGORD team. Detailed history taking and deep clinical phenotyping (clearly identifying both renal and extrarenal phenotypes) were the basic tools to spot and categorize inherited kidney disease in this subset of patients. Moreover, mutational genetic analysis through collaborative research work with expert centers managed to unravel the underlying molecular defect in many of these patients.

Results:

Databases were created for cystinosis, inherited Podocytopathies, ciliopathies, primary hyperoxaluria type 1 and congenital anomalies of the kidney and urinary tract as a nucleus for future national registries. Clinical and molecular characterization of these patients also resulted in many publications documenting these data for the first time in Egyptian children.

Conclusions:

EGORD is committed to identifying patients/families affected by an inherited kidney diseases through programs of awareness, education/training, and advocacy. Promoting awareness and diagnosis of these previously overlooked diseases is expected to improve clinical outcomes (particularly in potentially treatable diseases) in the highly consanguineous Egyptian community.

P - 321 COMPREHENSIVE GENETIC TESTING IN PATIENTS WITH RENAL TUBULOPATHIES BY NGS MULTI-GENE PANEL

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Introduction:

Primary tubulopathies comprise a group of clinically and genetically heterogeneous disorders that affect proximal and distal tubular transport systems and lead to inappropriate loss of organic and anorganic solutes. Alterations in ion and water homeostasis often result in systemic complications and chronic kidney disease. Targeted and early management of patients is crucial to prevent severe clinical manifestations. Although several clinical entities have been described for years, recent advantages in our understanding of transepithelial ion transport, energy metabolism and regulation of both processes revealed a phenotypic spectrum with considerable clinical and genetic overlap. In addition, some of the phenotypes such as nephrolithiasis or hypophosphatemic rickets are a common feature of a wide spectrum of renal tubulopathies and a variety of

underlying genetic causes are known. Genetic testing becomes increasingly important for proper clinical management, but there is a need for comprehensive, time- and cost-efficient strategies.

Material and methods:

We designed a customized NGS (next-generation sequencing) based panel for genes involved in renal tubulopathies (currently targeting 122 genes) including all known genes described for different salt-wasting syndromes (Bartter syndrome, Gitelman syndrome and related disorders), renal tubular acidosis, hypomagnesemia, proximal tubulopathies and pseudoaldosteronism. All coding exons as wel as the corresponding exon-intron boundaries were enriched using the Roche/NimbleGen sequence capture technology, amplified and sequenced simultaneously on an Illumina MiSeq or HiSeq platform with an average coverage of more than 200x.

Results:

In the majority of patients, causative mutations could be detected in one of the genes targeted by our NGS multi-gene panel that allows the parallel analysis of all disease genes that are usually discussed for differential diagnosis. Moreover, high-coverage NGS enabled the detection of copy-number variations.

Conclusions:

We demonstrate that NGS-based testing can considerably accelerate and improve genetic diagnostics in renal tubulopathies, especially in patients with singular and more unspecific symptoms or a milder clinical presentation. Comprehensive characterization of the genotype enables genetic counselling and improved clinical management of patients with different tubulopathies.

P - 322 CLINICAL AND GENETIC PRESENTATION OF NEPHRONOPHTHISIS AND ASSOCIATED CILIOPATHIES

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Introduction:

Nephronophthisis (NPH) is among the most important ciliopathies and a major cause of end-stage renal disease in childhood. The clinical and genetic presentation is highly variable. Due to clinical and genetic overlap, establishment of the correct diagnosis may be challenging.

Material and methods:

In 2011 we established an online-based patient registry (www.nephreg.de), to assess the clinical course of NPH and associated ciliopathies in a standardized longitudinal manner focusing on extrarenal organ manifestations.

Results:

We present the data of 133 pediatric patients, 50% of them suffering from NPH associated ciliopathies: Joubert/COACH syndrome (n=23), Senior-Løken syndrome (n=15), congenital oculomotor apraxia (n=5), Bardet-Biedl syndrome (n=4), skeletal disorders (n=5), Meckel-Gruber syndrome (n=1). Ciliary gene defects were identified in 61% of cases with homozygous deletions of NPHP1 being the most frequent mutation (n=50).

While in most NPHP1 patients the clinical picture was restricted to a renal phenotype only, many of the non NPHP1 patients showed hepatic (31%), ophtalmologic (50%) or cns (38%) pathologies. Due to small numbers a clear-cut genotype-phenotype correlation is not possible yet, but some trends seem to emerge: While NPHP3 patients presented an obligatory congenital hepatic fibrosis with chronic kidney disease, NPHP5 mutations caused congenital blindness and late onset renal failure. All NPHP6 patients presented as Joubert syndrome without hepatopathy; in contrast NPHP11 mutations always resulted in hepatic involvement.

End-stage renal disease was noted in 80% of the NPHP1 and 50% of the nonNPHP1 group. Only 49% of patients showed typical cystic lesions.

Conclusions:

Mutations in NPHP genes cause a wide range of ciliopathies with multiorgan involvement and different clinical outcomes. Standardized assessment in clinical patient registries can provide the data that help clinicians in counselling affected families and hopefully allow a clear-cut genotype-phenotype correlation in the long run. To this end international collaborative effects will be needed.

P - 323 CYSTEAMINE HYDROCHLORIDE FOR NEPHROPATHIC CYSTINOSIS: OPEN-LABEL PHASE III STUDY

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Introduction:

To compare the efficacy and safety of cysteamine hydrochloride 0.55% viscous eye-drops solution (CH-0.55%) versus cysteamine hydrochloride 0.10% eye-drops solution (CH-0.10%) in cystinosis patients presenting corneal cystine crystal deposits.

Material and methods:

Open-label randomised phase-III clinical trial.bParticipants: Thirty-two cystinosis patients followed 90 days (visits at D30 and D90). Treatment: Patients were treated with one drop in each eye of study drug (CH-0.10% or CH-0.55%), four-times daily for 90 days. Main outcome measures: the total score of corneal cystine crystal density measured by in vivo confocal microscopy (IVCM) in 7 corneal layers, photophobia, Corneal Cystine Crystal Score and crystal thickness.

Results:

Thirty-two patients (mean age (± SD) at inclusion: 17.1±13 years) were randomized in the study: 15 patients randomized to CH-0.55% treatment arm and 17 to CH-0.10% treatment arm. Thirty-one patients (62 eyes) received study drug, underwent assessments and completed the study (mean duration: 89.6±14.5 days).

Twenty-three patients underwent IVCM and 9 did not. The IVCM total score (±SD) decreased from baseline to D90 by a mean of 4.60±3.12 in the CH-0.55% arm and -0.455±3.38 in the CH-0.10% arm ($p<0.0001$). Difference in absolute change in IVCM total score between the two treatment arms (control minus CH-0.55%) at D90 was estimated as 3.8435 (±0.8853). The 95% confidence interval (CI) of the difference was (2.1083; -5.5786); the lower boundary was above zero, therefore the superiority of CH-0.55% compared to CH-0.10% can be concluded. A statistically significant difference between the two arms was also observed for investigator-assessed photophobia, Corneal Cystine Crystal Score and crystal thickness. During the study period, neither serious adverse events nor significant adverse events related to the study drug were reported.

Conclusions:

This study provides evidence that CH-0.55% is superior to CH-0.10% in terms of efficacy and is well-tolerated in pediatric and adult patients with cystinosis presenting with corneal cystine crystal deposits.

P - 324 GROWTH HORMONE TREATMENT IN HYP MICE: EFFECTS ON GROWTH PLATE AND BONE STRUCTURE

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Introduction:

Hyp-mouse is the most completely characterized animal model of X-linked hypophosphaptemia (XLH). Growth hormone (GH) administration has been shown to improve longitudinal growth rate of XLH pediatric patients. The aim of our study was to analyze the effect of GH

treatment on growth impairment, bone mineralization, growth plate and serum phosphate in the Hyp-mouse.

Material and methods:

Weaned male mice grouped (n=4-6) in wild type (WT); Hyp and Hyp + GH (3.33 mg/kg/day) (Hyp-GH). Animals were sacrificed after 7 days of treatment. Nose-tail length, tibia length, serum phosphate, femur growth plate histomorphometry and cell proliferation, bone mineralization by Von Kossa and tibia structure by micro-CT were analyzed

Results:

GH treatment improved hypophosphatemia (Wt=7.60±0.37, Hyp=3.75±0.38,Hyp-GH=5.62±0.06 mg/dl;p=0.03), nose-tail (Wt=14.30±0.27,Hyp=10.75±0.26,GH=11.54±0.05 cm;p=0.01) and tibia (Wt=1.4±0.02,Hyp=0.9±0.02,GH=1±0.01 cm;p=0.01) lengths. GH treatment did not normalize the marked abnormal appearance of growth cartilage and did not correct the enhanced height of the hypertrophic zone (Wt=48.8±0.7, Hyp=68.5±2.4, GH=68.7±3.7 % of total growth cartilage height; p>0.05). However, GH treatment increased both the terminal chondrocytes' height (W=48.7±1.5, Hyp=48.7±0.1, GH=51.9±0.4 μm;p=0.01) and the chondrocyte proliferation rate (Wt=63±1,Hyp=42±2,GH=66±2 per 100 cells; p=0.01).GH increased bone mineral density (Wt=0.26±0.01, Hyp=0.20±0.01,GH=0.23±0.0 g/cm^3;p=0.05), probably as a result of higher trabecula number (Wt=5.9±0.35, Hyp=5.4±0.14, GH=6.1 ±0.14;p=0.02), and enhanced cortical thickness (Wt=0.14±0.004, Hyp=0.07±0.03,GH=0.09±0.09 mm;p=0.02). Von Kossa staining fitted with micro-Ct analysis, and disclosed lower amount of osteoid in the Hyp-GH mice.

Conclusions:

GH treatment improves hypophosphatemia and growth of Hyp mice and ameliorates bone structure and mineralization but this positive effect is not associated with a correction of the profound growth plate morphological abnormalities caused by XLH. The persistence of these alterations with an increased growth velocity might lead to a higher risk of bone deformities in the GH treated XLH patient.

P - 325 PARTIAL NEPHROGENIC DIABETES INSIPIDUS CAUSED BY A NOVEL AQP2 VARIATION IMPAIRING TRAFFICKING OF THE AQUAPORIN-2 WATER CHANNEL

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Introduction:

Congenital nephrogenic diabetes insipidus (CNDI) is rarely caused by variations in the *AQP2* gene and only a small subset of those is dominantly inherited. We have investigated the genetic and molecular background underlying symptoms of diabetes insipidus in a Swedish family with autosomal dominant inheritance of the condition.

Material and methods:

The proband and her father were subjected to water deprivation test. Direct DNA sequencing of the coding regions of the *AQP2* and *AVP* genes was performed on family members. Using lentiviral gene delivery Madin-Darby canine kidney (MDCK) cells stably expressing AQP2 variant proteins were generated and analyzed for the localization of AQP2-R254W under stimulated and unstimulated conditions by means of immunostaining and confocal laser scanning microscopy. The intracellular trafficking of AQP2-R254W was studied using transient expression of mutant dynamin2-K44A-GFP protein and assessment of phosphorylation levels by means of Western blotting analysis.

Results:

Clinical and genetic data suggest that the proband and her father have partial nephrogenic diabetes insipidus caused by a variation (g4807C>T) in the *AQP2* gene, resulting in substitution of arginine-254 to tryptophan (p.R254W). Analysis of MDCK cells stably expressing AQP2 variant proteins revealed disabled phosphorylation, impaired trafficking and intracellular accumulation of AQP2-R254W compared to AQP2-WT. Notably, blocking of the endocytic pathway demonstrated impairment of AQP2-R254W to reach the cellular surface.

Conclusions:

The genetic and molecular data indicates that AQP2-R254W causes partial CNDI in the Swedish family by disabling AQP2-R254W to reach the subapical vesicle population as well as impairing S256 phosphorylation, rendering the AQP2-R254W protein unable to reach the plasma membrane to facilitate AVP mediated urine concentration.

P - 326 A NOVEL ASSOCIATION BETWEEN VAL2ALA MISSENSE MUTATION IN ATP6V0A4 GENE AND GLAUCOMA, PHACODONESIS AND CATARACT IN PATIENTS WITH DISTAL RENAL TUBULAR ACIDOSIS

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Introduction:

Vacuolar ATPases (v-ATPases) hydrolyze ATP to pump protons across cell membranes. Mutations in v-ATPase subunits are implicated in three disorders: distal renal tubular acidosis (dRTA), osteopetrosis and cutis laxa. Recessive dRTA is caused by loss-of-function mutations in either of 2 subunits of the V-ATPase; the B1 subunit of the V1 cytoplasmic ATPase complex and the a4 subunit of the V0 transmembrane pore complex.

Material and methods:

In this paper, we report Val2Ala missense mutation in Atp6v0A4 gene in a child with recessive dRTA, bilateral glaucoma and cataract and phacodonesis.

Results:

A 7 years old female patient was evaluated because of glaucoma. Her family history is unremarkable. She had short stature, enamel dysplasia, metabolic acidosis, hypokalemia, hypercalciuria and unilateral nephrolithiasis. Eye examination showed suspensory ligament laxity of lens, phacodonesis and cataract. There wasnt any dysmorphic appearance. The audiometric evaluation revealed normal hearing. Her urine pH was always above 5.5 in follow up period. We found a heterozygote Val2Ala missense mutation in ATP6V0A4 gene. To the best of our knowledge, this mutation is extremely rare. Only one Val2Ala mutation report has been published to date. Also, this is the first report describing a novel association between the ocular disorders and Val2Ala mutation in ATP6V0A4 gene.

Conclusions:

In conclusion, our findings suggest that Val2Ala missense mutation in ATP6V0A4 gene may influence elastic fiber formation of suspensory ligaments, lens and ciliary muscle in the eye. The glycosylation defects may be possible mechanisms in the same manner as the presence of ATP6V0A2 gene mutation in cutis laxa. Additionally, it has been shown that the V-ATPase complex is vital for production of aqueous humor in experimental study. Further investigations are necessary to elucidate this relation.

P - 327 PREVALENCE OF COMPLEMENT SYSTEM GENE MUTATIONS AND POLYMORPHISMS IN RUSSIAN CHILDREN WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME.

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Introduction:
Atypical hemolytic uremic syndrome (aHUS) is a thrombotic microangiopathy (TMA) mediated by disorders of complement system caused by mutations of complement regulatory factors genes.
Material and methods:
Twenty six pediatric patients aged 1-19 years with non-diarrheal HUS were included in the study. Other causes of TMA like lupus, thrombotic thrombocytopenic purpura, methylmalonic aciduria and hematologic disorders were carefully excluded. In 19 patients aHUS had an acute progressive course and in 7 –chronic course with decreased GFR and proteinuria, 12 were dialysis dependent.
Analysis of target regions, including all coding regions of *CFH*, *CFI*, *CFB*, *MCP* and *THBD* genes was performed by next-generation sequencing using the Roche 454 platform.
Results:
As a result of the study, ten (38,5%) patients had mutations in the targeted genes: *MCP*-5, *CFH*-3, *CFB*-2. We identified three previously described mutations in four patients with phenotype of AHUS: MCP:*c.307C>T* (*p.Arg103Trp*), CFH: *c.3148A>T* (*p.Asn1050Tyr*), CFB: *c.1697A>C* (*p.Glu566Ala*) and two novel mutations in MCP gene *c.848G>C* (*p.Cys283Ser*) and *c.735_736insC* (*p.Phe246Leufs*10*). Nine patients carried polymorphisms mostly of *CFH* gene associated with disturbances in complement system, whereas another four patients had very rare polymorphisms in *CFH* and *CFB* genes not described previously. In total, in 22 (84,6%) patients a genetic basis of aHUS was suggested. Because of heterogenous clinical data we did not find any genotype/phenotype correlations.
Conclusions:
Our results suggest that molecular genetic studies despite not necessary for diagnosis of aHUS may bring additional diagnostic value and indicate a high prevalence of complement system genes mutations and polymorphisms in the pathogenesis of the disease.
Supported with Russian Science Fund Grant 14-15-00994

P - 328 HYPERTENSION IN CHILDREN WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE.

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Introduction:
Hypertension is the main risk factor for progression of various nephropathies, including autosomal dominant polycystic kidney disease (ADPKD). The purpose of the study was to identify the frequency of hypertension and its association with the volume and renal function in children and adolescents in an early stage of ADPKD.
Material and methods:
40 children (16M/24F) with ADPKD and normal renal function (CKD 1 st) were examined. The median age was 14.0 (IQR: 9.5;15.0) years. We checked blood pressure with Office Monitoring Method (OBPM) and ambulatory blood pressure monitoring (ABPM) with estimate of the mean daily BP, mean pulse BP. Patients were divided into 3 groups according to three levels of BP: hypertension (HBP; greater than the 95th percentile for sex, age, and height), high normal BP (HNBP; 90–95th percentile), and normotension (NBP; less than the 90th percentile). Patients with < 10% decrease more than the daytime BP in the nighttime BP were considered to be non-dippers. Total kidney volume (cm3) assessed by ultrasound, corrected for standard body surface and estimation by centile tables.
Results:
Hypertension was found in 27.5% (11 of 40 children) of cases by OBPM and in 42.5% (17 of 40 children) by ABPM. By ABPM HNBP was in 25% (10 of 40 children) of cases, NBP was in 32.3% (18of 45 children). Non-dippers (27.5% of cases (11 of 40 children)) were detected more frequently in children with HBP compared with children with NBP: 53% vs. 0%, (p=0,003), RR=2.1 (95% CI:1.4-4.6) Children with HBP were detected more frequently increased renal volume ($cm^3/1{,}73m^2$) more than 97‰ compared with children with NBP: 80% vs. 44,4% (p=0.04), RR=2.3 (95% CI:1.2-5.6). A moderatecorrelation between mean daily BP (r=0.53, p=0.0002), mean pulse BP (r=*0.36*, p=*0.02*) and renal volume ($cm^3/1{,}73m^2$) was observed. HBP group had a significantly lower GFR than children with NBP (108 (103.1;125) vs. 140.5 (121;143.5), p=0.0008) and children with HNBP (108 (103.1;125) vs. 124 (111;138.5), p = 0.05). A moderate negative correlation between diastolic BP at night and GFR (*r=-0.38*, *p=0.01*) was found.
Conclusions:
ABPM is a more potent tool for detection of hypertension than the clinic BP. Children with ADPKD and hypertension have larger kidney volumes and a lower GFR as compared with their counterparts with normotension.

P - 329 DISEASE-CAUSING INF2 MUTATION IN AUTOSOMAL-DOMINANT FAMILIAL PROTEINURIA WITH PROGRESSION TO END-STAGE RENAL FAILURE

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Introduction:
In 2010 mutations in the *INF2* gene were identified to be causative for autosomal-dominant focal segmental glomerulosclerosis (FSGS) and were clinically associated with moderate proteinuria in adolescence. However, in the meantime more severe clinical courses have been described with rapid progression to end-stage renal failure (ESRD) during childhood– but with high phenotypic variability. *INF2* mutations in patients with isolated FSGS are clustered in exons 2 to 4. These exons encode the diaphanous inhibitory domain (DID) which is involved in the regulation of the actin cytoskeleton of kidney podocytes. Additionally, in patients with Charcot-Marie-Tooth neuropathy and associated FSGS *INF2* mutations were identified solely within exons 2 and 3.
Material and methods:
We report a large family with 14 affected individuals (autosomal-dominant mode of inheritance) who presented with nephrotic-range proteinuria, hypertension, and progressive renal failure. Four family members received a kidney transplant without recurrence of the disease. Two patients underwent renal biopsy with the histological result of minimal-change glomerulopathy and IgA mesangioproliferative glomerulonephritis, respectively. No affected family member had extrarenal manifestations. We analyzed the genes *ACTN4*, *CD2AP*, *COQ6*, *INF2*, *LAMB2*, *NPHS1*, *NPHS2*, *PLCE1*, *TRPC6*, and *WT1* in the index patient by next generation sequencing. Additionally, in six affected family members target diagnostics was performed.
Results:
The novel heterozygous mutation c.490G>C (p.(Ala164Pro), *INF2*, exon 3) was identified in the index patient. This mutation was also found in six additionally examined affected family members. In silico analysis

(PolyPhen-2 and Mutationt@ster) predicted its pathogenicity as "probably damaging".

Conclusions:

Mutations in *INF2* are associated with familial proteinuric diseases - irrespective of the presence of FSGS in renal histology. Clinical phenotype can manifest with high intrafamilial variability and predominance of severe courses with progression to ESRD. Therefore, mutational analysis should be considered also in patients with renal histology other than FSGS and with severe renal phenotype.

P - 330 RENAL INVOLVEMENT IN PAEDIATRIC AND ADULT PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER (FMF)

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Introduction:

Renal amyloidosis is considered as the most serious complication of FMF, almost inevitably leading to ESRF. However, renal diseases other than amyloidosis have also been described.

The aim of the study is to evaluate the spectrum of renal involvement in children and adults with FMF.

Material and methods:

From 1992 to 2014 a total of 619 biopsies of native kidneys were performed at the Arabkir hospital. 121 patients (19.5%) had FMF, 76 children (age 2-17) and 45 adults (age 18 – 71). Amyloid deposits were determined by Congo red stain (Yerevan). Other nephropathies were confirmed by light and electron microscopy and immunohistochemistry in 27 cases (Zurich).

Results:

Clinical findings were the nephrotic syndrome (in 18% of paediatric (P) and 29% of adult (A) patients), nephritic syndrome (7% P, 2% A) and proteinuria ± haematuria (75% P, 60% A); AKI and CKD were seen in 1 and 3 A patients, respectively.

Histological findings: Renal amyloidosis was found in 57 (75%) P and in 41 (91%) A patients. Other nephropathies were: Minimal change disease (7 P, 2 A), focal segmental glomerulosclerosis (4 P, 2 A), membranoproliferative glomerulonephritis (2 P) and Schoenlein-Henoch nephritis (2 P). Acute poststreptococcal glomerulonephritis, membranous glomerulopathy, thin basement membrane disease and IgA nephropathy were seen in 1 P patient each.

Conclusions:

Renal diseases other than amyloidosis are not rare in patients with FMF, especially in children. It is known that FMF predisposes to vasculitis; nevertheless the association with various forms of glomerulonephritis is not clear. The biopsy is important in patients with FMF and renal involvement, particularly in those with the nephrotic syndrome or isolated proteinuria mimicking amyloid nephropathy.

P - 331 TWO RENAL TRANSPLANTS IN TWO NEW UNRELATED CASES OF SENSENBRENNAR SYNDROME

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Introduction:

Sensenbrennar syndrome, or cranioectodermal dysplasia, is an extremely rare autosomal recessive ciliopathy, characterised by sagittal craniosynostosis, facial, ectodermal and skeletal anomalies. Patients frequently develop end stage renal failure due to nephronopthisis. There are 40 reported cases to date. We describe 2 new unrelated cases diagnosed at our centre, both of whom have undergone renal transplantation within the last two years.

Material and methods:

Child A is the third child of non- consanguineous parents. Rhizomelia was antenatally diagnosed and post-natally retinal dystrophy, frontal bossing and small teeth were noted. He presented aged 23 months in established renal failure, with small dysplastic kidneys on ultrasound scan. After a brief period of peritoneal dialysis, he developed peritonitis and was switched to haemodialysis. Genetic testing confirmed a homozygous defect in the IFT140 gene in keeping with Sensenbrennar syndrome. At 5 years of age he received a living related donor renal transplant from his father.

Results:

Child B is the second son of non-consanguineous parents. Antenatal scans were normal. Post birth oedema, narrow palpebral fissures, hypertelorism, micrognathia and thoracic hypoplasia were noted. MRI brain and initial genetics were normal. At 23 months of age he presented in end stage renal failure and was commenced on peritoneal dialysis. Biopsy demonstrated tubular atrophy, with severe interstitial fibrosis, in keeping with nephronopthisis. He received a living related donor transplant from his father at 4 years of age. At 5 years of age further genetic testing found two mutations in the IFT140 gene encoding for Sensenbrenner syndrome.

Conclusions:

Both children are new and unrelated cases from non-consanguineous parents. Both presented in renal failure at 23 months of age and both have homozygous mutations in the IFT140 gene. A ciliopathy such as Sensenbrennar syndrome should be considered as a potential underlying diagnosis for any child presenting with end stage renal failure and skeletal dysplasia.

P - 332 AREGPKD – A EUROPEAN ARPKD REGISTRY STUDY

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Introduction:
Autosomal recessive polycystic kidney disease (ARPKD) is among the most important causes for pediatric end stage renal disease and a leading reason for liver-, kidney- or combined liver kidney transplantation in childhood, although it is a rare disorder with an estimated incidence of 1 in 20.000 live births. The disease is characterized by massively enlarged, cystic kidneys and obligatory hepatic involvement in form of congenital hepatic fibrosis. ARPKD displays an enormous though unexplained phenotypic heterogeneity. As the pathophysiologic mechanisms for the various clinical manifestations remain poorly understood, current treatment lacks evidence-based management guidelines therefore remaining largely opinion-based and focussing on symptomatic treatment options. Therapeutic initiatives for ARPKD are facing the challenge of small and clinically variable cohorts for which specific clear-cut primary end points for ARPKD need to be established.
Material and methods:
ARegPKD is an international, mostly European, multicenter, pro- and retrospective, observational study in both pediatric and adult ARPKD cohorts aiming to deeply phenotype ARPKD patients. Using a web-based approach with detailed basic data questionnaires and yearly follow-up visits in combination with associated biobanking and reference histology ARegPKD will clinically characterize long-term ARPKD courses and set roots for future translational research.
Results:
ARegPKD is currently well pronounced with 56 registered centers in 16 mostly European countries. Here we present first clinical data following first data interpretation of more than 100 included patients regarding patient characteristics (sex, age at diagnosis, age at inclusion), genetic testing, surgical therapy (age at and indication of nephrectomy, renal replacement therapy, transplantations) as well as development during perinatal period and necessity of antihypertensive medication.
Conclusions:
ARegPKD aims to compare applied treatment options in a large European cohort of deeply characterized patients and will thus provide evidence base for clinical treatment decisions. In association with biobanking and reference histology ARegPKD addresses major scientific and clinical issues and contributes to the pathophysiological understanding of this severe inherited disorder.

P - 333 HOW TO VALIDATE RENAL HYPODYSPLASIA CANDIDATE GENES OBTAINED BY WHOLE-EXOME SEQUENCING.

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Introduction:
Whole-exome sequencing (WES) has become a privileged approach in unraveling the cause of rare genetic pathologies. However, WES strategy leads to the identification of large numbers of variants. Here we propose a novel strategy, fast and cost-efficient, to assess the functional and biological significance of renal hypodysplasia WES candidate genes.
Material and methods:
This strategy consists in knocking down a candidate gene in murine ex vivo kidney cultures using a specific vivo-morpholino, to recapitulate the renal phenotype observed in a patient. The presence of a renal phenotype is analyzed after culture in terms of branching and anomalies of nephron development, by whole-mount immunofluorescence and multiphoton microscopy.
Results:
Six WES candidate genes were tested, accounting for renal hypodysplasia in 7 unrelated families. One candidate gene was identified by the presence of a heterozygous frameshift variant segregating with renal cystic dysplasia in one family. Its expression in culture was decreased by 65% ($p < 0.001$). This was associated with cyst formation ($p < 0.001$). This phenotype recapitulated the patients renal phenotype. Another gene was a candidate to account for multicystic hypodysplasia because of the identification of a homozygous, predicted as damaging missense variant in 3 fetuses from 1 family. Its expression in culture was decreased by 60%. This was associated with cyst formation. Ureteric bud branching was decreased by 45%; renal volume was also reduced. Tubular cell thickness was increased by 28%. The phenotype observed after renal cultures matched the patients phenotype. No pathological phenotype could be identified for 3 WES candidate genes; one WES candidate gene is still being tested.
Conclusions:
This novel approach recapitulated the phenotype described in 2 unrelated families, confirming the functional and biological significance of 2 WES candidate genes. This strategy is fast and cost-efficient, especially when compared to generating transgenic mouse lines. Its expected to be powerful to recapitulate a phenotype caused by a frameshift or a loss-of-function missense mutation resulting in a decreased protein function in vivo. Together with cell cultures it is efficient to validate renal hypodysplasia WES candidate genes.

P - 334 A SINGLE-CENTRE RETROSPECTIVE REVIEW OF PATIENTS WITH A GENETIC DIAGNOSIS OF BARTTER & GITELMAN SYNDROME

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Introduction:
Bartter and Gitelman syndrome are rare autosomal recessive disorders of renal salt handling. They are characterized by disturbed electrolyte and acid-base homoeostasis with potentially severe complications. Currently little is known about the long-term disease course and best treatment is controversial.
We performed a retrospective case review to investigate the long-term disease course of patients with Bartter/Gitelman syndrome.
Material and methods:
Data was collected on presentation & gestational age and complications. Laboratory results were recorded at presentation, and ages 1,2,3,4,5,10,15.
Results:
42 patients with a confirmed genetic diagnosis of Bartter/Gitelman were reviewed with a median follow up of 7.85 years (Range 0 -18 Years)
Bartter 1&2 presented earliest with prematurity and deranged electrolytes. All of the Bartter 1 patients and 70% of Bartter 2 had evidence of nephrocalcinosis on their first ultrasound.
Growth at last follow-up was in the normal range.
Hypomagnesaemia (<0.7mmol/L) was seen in 11/14 Bartter 3 and 8/11 Gitelman patients; Hypomagnesaemia developed over time and was first seen earlier in Bartter 3 (3.8 years) than in Gitelman (7.9 years).
Obvious complications of hypokalaemia were only seen in one patient with Bartter 3 (despite potassium levels <2.5mmol/L in 10 patients) in the form of hypokalaemic paralysis: he was admitted twice at age 2 and 3 (Potassium 1.7 & 1.5 respectively); normal potassium levels were not achieved despite supplementation of potassium up to 16 mmol/kg/d.

One patient with Bartter 3 later developed proteinuric renal disease and biopsy evidence of Focal Segmental Glomerulosclerosis.

Conclusions:

The overall prognosis during childhood was good for these disorders. Most patients achieved growth in the normal range.

Interestingly, hypomagnesaemia is often absent at presentation and develops over time in both Bartter 3 and Gitelman.

Hypokalaemic complications only occurred in one patient and only with levels <2mmol/L.

P - 335 TUBULAR DISORDERS AND CARDIOMYOPATHIA - CASE REPORT AND RESEACH AT DATE

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Introduction:

We report a case study, of a girl of 13 months of age, presented with gastroenteritis and a severe electrolyte disturbances, classical symptoms of a renal phenotype, characterized by hypokalaemic alkalosis, hypomagnesaemia, hyperreninaemia, hyperaldosteronism, normal BP and bright kidneys, resembling Bartter Syndrome. Hypokaliemia by itself causes arrhythmia, also dilatative cardiopathy potentially can cause cardiac arrhythmias and unexpected death. Recomandations are for closely monitoring of QT interval and Potassium level should keep ≥3.0 mmol/L.

Material and methods:

She was hypotrophic, psycho-motoric retardated, spastic musculature. Polyuria even with diarrhea, 1500-2500ml. Urine pH:6, sw 1005-1010 and with no increase of urine sw during the desmopresin test, either improvement of the blood electrolytes. Urine electrolites Mg: 6.3, Ca:3.05, K: 12.3, Na: 58.0, Cl: 36.7. Blood electrolites were pH: 7.5, K: 2.5, Na:132, HCO3: 24.4, Ca: 1.15, Mg: 0.71, Cl: 96.5, iPTH: 40.5, Vit D: 36.7, Aldosteron: 19.1, Renin: 219.2, Cystic fibrosis test negative, celiac disease negative, TORCH neg, LDH: 640, Cre: 50. Molecular genetic examination done at "Great Ormond Street Hospital for Children" London, resulted no Bartter or Gitelman Sy mutacion. The girl had associated pathology Cardiomyopathia dilatativa congenita with LVID: 32.7%, LVIS: 28%.

Results:

Treatment was oriented to stabilize dehydration, electrolytes and heart function.We added indomethacin. She improved, polyuria decreased, electrolyte parameters were better.

Conclusions:

Conclusion. The risk was greater with those both problems. With adequate treatment we should modify function and decrease the risk of arrhythmia and heart failure. Latest genetic evidence data tell us for presence of functional mutations of ClC-K_a Gly83 on cardio-renal axis, present on patient with renal tubular disorders.

P - 336 GENOTYPE-PHENOTYPE CORRELATION OF TURKISH CHILDREN WITH AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE

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Introduction:

PKHD1gene mutations have been identified as a causative factor of autosomal recessive polycystic kidney diseases(ARPKD). However, evidence is still lacking with respect to the genotype to phenotype correlation. The aim was to determine the mutation distrubution of PKHD1 gene and genotype.phenotype correlation in Turkish patients with ARPKD.

Material and methods:

We evaluated 9 patients with ARPKD. Their clinical, biochemical and imaging data with PKHD1 sequencing results were analyzed. The presentation of the disease onset was defined as perinatal, neonatal, infantile and juvenile. Routine were covering of blood urea, creatinine, AST, ALT levels and urine analyses, osmolarity and culture. All patients had ultrasonography for renal and liver involvements. All 67 exons of PKHD1gene was firstly PCR amplificated then analyzed by direct DNAsequencing methods.

Results:

In all of 9 patients with ARPKD(7 boys, 2 girls with a mean age of 44±36 months), 3 patients were diagnosed by perinatal genetic analyses. There were 4 infantile ARPKD patients with different clinics; with one ESRD in infancy, with one ESRD and renal transplantation in adolescent and 2 patients both with normal renal functions. Portal hypertension was seen in only one patient with ESRD. The last patient displayed recurrent urinary tract infections and ESRD in late childhood. 2 patients were died with respiratory problems and malign hypertension with Potter face after delivery. Renal transplantation was achived in5 patients with one graft failure due to gastrointestinal bleeding. Recurrent urinary tract infections were the mostly found in the infantile onset. Ultrasonograhic findings were loss of differantation cortex-medulla, presentation of cysts.

The mutations reported in our study group were similar with literature whereas there was 1 novel mutation(c.779-12-13delTT) in the study group resulted with exitus after delivery.

Conclusions:

Characteristics of ARPKD varies by age and ethnic groups. This study displayed different features of ARPKD in

Turkish children with an intronic novel mutation.

P - 337 CLINICAL PRESENTATION OF PRIMARY HYPEROXLURIA TYPE1 IN PEDIATRIC AGE GROUP

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Introduction:

This descriptive cohort study of primary hyperoxaluria (PH1) in infants & children was performed to characterize the clinical presentation with respect to both renal and systemic involvement.

Material and methods:

The study included deep clinical phenotypying of 26 patients from 20 unrelated families with PH1 based on family history, clinico-radiological phenotype, infrared spectroscopy of stone and urinary oxalate.

Results:

Male to female ratio was 1.4:1 and median age at time of diagnosis was 6 years (age range 1.4-29 years). Consanguinity was confirmed in 20/26 patients (76.9%). Thirteen (50 %) were diagnosed before the age of 5 years. Two cases were asymptomatic and diagnosed by sibling screening of index patients. Uremia, gross hematuria, abdominal pain and stone passing were the most frequent manifestations reported in study patients. Seventeen cases (65.4%) had end-stage renal disease (ESRD) with infantile onset in 6 (23.1%) patients; early childhood onset in 4 (15.4%) patients (aged 1-5 years); whereas in the remaining 7 (26.9%) patients ESRD occurred after the age of 5 years. Systemic manifestations of oxalosis were elicited in two patients (7.7%). After 3 years follow up, normal renal functions were still maintained in 8/26 (30%) patients on pyridoxine therapy. Nephrolithiasis and/or nephrocalcinosis were

detected in all study patients. In 11 patients (42.3%) nephrocalcinosis was both cortical and medullary, whereas only medullary nephrocalcinosis was detected in the other 5 patients.

Conclusions:

PH1 is a clinically heterogeneous disease with wide spectrum of clinical presentation. Lack of awareness with low index of clinical suspicion play a major role in late diagnosis with increased ESRD. Timely diagnosis is therefore imperative particularly in communities with high rates of consanguinity.

P - 338 MOLECULAR GENETIC ANALYSES IN TURKISH CHILDREN WITH ALPORT SYNDROME

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Introduction:

Alport syndrome (AS) is a progressive renal disease characterized by haematuria and progressive renal failure. It is a well known hereditary nephritis with polygenic penetrance. Mutations in either COL4A4 or COL4A3 may be the causative factor of autosomal recessive or autosomal dominante form of AS. The aim of this study was to analyze the COL4A4 and COL4A3 gene mutations in Turkish children with AS.

Material and methods:

14 AS children were included [4 boys, 10 girls with mean age of (9,54±3, 82)]. All patients had admitted with hematuria, 6 patients both hematuria proteinuria with positive family history. Electrone microscopy findings had supported AS. None of the patients had hearing loss and eye involvement. End stage renal disease was not detected in our study group. Mutation analysis was performed in all exons and introns of COL4A4 and COL4A3 genes with direct DNA sequencing.

Results:

All patients were analyzed with both COL4A4 and COL4A3. 10/14 patients had mutations. COL4A4 gene mutations were detected in 7 patients with 2 novel mutations [IVS41+12 T>C, p.Gly545Ala]. COL4A3 gene mutations were detected in 3 patients with 1 frame shift (c.4887_4888delCA) and 2 missense forms.

Conclusions:

This study had pointed out 2 novel mutations one on the intron and one on the exon of COL4A4 gene. Other
mutations detected in the study were similar with the literature. Although renal biopsy is an occasional approach for nephritis, AS should be determined by molecular genetic tests in an algortyme due to the family history.

P - 339 SCL5A2 GENE MUTATIONS IN TURKISH CHILDREN WITH RENAL GLYCOSURIA

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Introduction:

The occurrence of glucosuria in the absence of hyperglycemia is distinctive for renal glucosuria. SCL5A2 gene mutations provoke familial renal glucosuria (RG) characterized by persistent glucosuria in the absence of any other renal tubular dysfunction. The aim was to analyze the SCL5A2 gene mutation distrubution in Turkish patients whom diagnosed as renal glycosuria clinically and to evaluate the phenotypic associations.

Material and methods:

10 RG children (3 boys, 7 girls with a mean age of [7,3±5,5]) were included who were incidentally diagnosed. Allpatients had renal tubulary tests, blood urea, creatinine, glucose, HbA1C, insulin and C-peptide levels. Family history and urine samples of parents were also analyzed. Mutation analysis was performed in all exons and intron-exon bounding regions of SLC5A2 gene with direct DNA sequencing.

Results:

All patients had normal renal tubulary tests and endocrinologic datas with normal growth percentiles. Only 3 children had unrelated parents. There was only one novel mutation (p.Gly225Arg) in two patients who were siblings. All patients had homozigot mutations where two patients displayed compound heterozygote mutation [p.Gly225Arg + p.Arg368Trp]. Only one patient had an intronic splice homozygote mutation (IVS7+5 G>A) with unrelated parents. The other mutations were all on Exon 4; Tyr128X nonsense (3 patients), Val116Met missense (3 patients), Arg368Trp missense (1 patient). All parents had normal urine samples and found to be healthy heterozygote carriers for SLC5A2 gene mutations.

Conclusions:

This study highlights RG is still a clinical entity which has no unfavourable effect on children growth and displays neither renal tubulopathy nor endocrinologic disorder. The mutations detected in the study were similar with reported in the literature with an exceptional novel (p.Gly225Arg) mutation.

P - 340 GENETIC MUTATIONAL TESTING FOR A CHINESE CHILD WITH FAMILIAL HAEMATURIA

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Introduction:

Pediatric haematuria remains a clinical dilemma.It is very important to make clear the causes of haematuria so that proper decisions are made.For this kind of patients, to date,we often make a diagnosis based on renal histology eventually,however,genetic testing can provide more information to the cases with familial history especially.Our study is to examine 18 genetic mutations known to be associated with FSGS in a Chinese child with isolated haematuria(her twin-sister with isolated haematuria, their father with chronic kidney disease) and a histological picture of FSGS.

Material and methods:

Peripheral blood samples were collected from the family(the child,her twin-sister,and their parents)and 20 people with normal urinalyses as controls. Genomic DNA was extracted from Peripheral blood leucocyte.,and mutation analysis was performed to sequence 18 genes(*NPHS1*, *NPHS2*, *CD2AP*, *PLCE1*, *ACTN4*, *TRPC6*,*INF2*, *WT1*, *LMX1B*,*LAMB2*, *LAMB3*,*GLA*, *ITGB4*,*SCARB2*,*COQ2*,*PDSS2*,*TNRL1*, *SMARCAL1*)using a PCR-based MassArray technology.

Results:

A homozygous mutation in *TNRL1*,which was novel and pathogenic by PolyPhen-2,was identified in two siblings,while it was not found in parents and control individuals. No mutation were detected in other 17 genes.

Conclusions:

Our data demonstrates that genetic testing is helpful for familial haematuria to make decision in a fast and cost-efficient way.We present for the first time mutational analysis of *TNRL1* gene in siblings with

familial haematuria,and there may be correlation between FSGS-proven familial haematuria and *TNRL1*.

P - 341 JOUBERT SYNDROME IN THREE SIBLINGS.

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Introduction:
Joubert Synddrome was named after Marie Joubert, who was the first to describe siblings from a French-Canadian family with hypotonia, ataxia, abnormal eye movement and agenesis of the cerebellar vermis presenting with episodic tachypnea. Several years later, a pathognomic midbrain-hindbrain abnormality, termed "molar tooth sign" was described via MRI of individuals with JS and JSRD. Mutations MK/TMEM67 in patients with nephronopthisis and associated liver fibrosis are rare.
Material and methods:
We present a family with three children of consanguineous Moroccan parents with the same genetic defect of Joubert Syndrome. The 14-year-old girl shows pancytopenia, due to hepatic fibrosis. The abnormal characteristics of this girl and her 3-year-old twin sisters correspond to the diagnosis of Joubert Syndrome. In all three patients a missense mutation c.1888 T>C in the gene TMEM67 on chromosome 8q22.1 was found, typical for JS type 6. Over the last 3 years the renal function of the oldest girl deteriorated to ESRF. Peritoneal dialysis was started, leading to improved quality of life. The renal function of both the twin sisters is still normal, but they have developed liver fibrosis over the last year.
Results:
In the paper of Ben-Salem et al. a list of pathogenic mutations responsible for JS in Arabs was described. Three different TMEM67 mutations have been reported in families from Morocco, Algeria and Egypt. We found the same DNA changes as were reported for families from Morocco described by Ben Salem et al. Otto et al. (2009) described 4 different MKS3/TMEM67 mutations in 5 families with nephronopthisis associated liver fibrosis.
Conclusions:
All 3 siblings were diagnosed with a missense mutation in the gene TMEM67, typical for JS type 6. The other ciliopathies with a mutation in the gene TMEM67 are the Meckel-Gruber syndrome type 3, COACH syndrome, nephronopthisis type 11 and Bardet-Biedl syndrome type 14.

P - 342 MUTATION IN THE HNF4α-GENE AS CAUSE OF TRANSIENT CONNATAL HYPOGLYCEMIA AND CONGENITAL FANCONI SYNDROME

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Introduction:
Mutations in the transcriptional hepatic nuclear factor 4A (HNF4A) are leading to an increasing failure of the ß-cells in the pancreas. This results in a rare form of diabetes mellitus (Maturity- onset of diabetes Type 1) in about 50 % of mutation carriers, usually beginning during the second or third decade of live. Recent studies showed that part of the subjects with mutations in this gene present after birth with macrosomia and transient hypoglycemia.
Material and methods:
We report about a boy who was precipitately born at home after 37 weeks gestation, birth weight 45010 g and length 51 cm. He was admitted to a Children's hospital for cardiovascular and respiratory monitoring, which was unremarkable. However, he showed severe hypoglycemia (glucose < 50 mg/dl), which was treated with intravenous glucose substitution for 2 days. Thereafter, blood glucose levels were stable with enteral feeding. However, a detailed work-up regarding the etiology of hypoglycemia was not done. Ultrasound of the abdomen showed one cyst beneath the liver. Follow-up showed glucosuria and tubular proteinuria, at the beginning without aminoaciduria; glucose and electrolytes in serum were in the normal range with the exception of elevated alkaline phosphatase. Therefore, we made the diagnosis of incomplete Fanconi syndrome. The most common causes of hereditary Fanconi syndrome were excluded by genetic or enzymatic analysis.
Results:
At the age of three years, molecular genetic analysis showed the mutation R76W in the HNF4α gene. This mutation was very recently described as a cause of congenital Fanconi syndrome in children with a history of transient hypoglycemia. Genetic analysis of the parents was without pathological findings.
Conclusions:
Our patient showed a specific mutations in the HNF4α gene with a mild phenotype of a congenital Fanconi syndrome. Mutations in this gene should be considered in the differential diagnosis in infants with otherwise inexplicable glucosuria and tubular proteinuria.

P - 343 DIAGNOSIS OF FABRY DISEASE IN EGYPTIAN CHILDREN: THE TIP OF THE ICEBERG.

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Introduction:
Fabry disease is a rare X-linked lysosomal storage disorder presenting usually in late childhood and adolescence. Main clinical features include renal, neurological and cardiac manifestations. In the current report we summarize the diagnostic experience of Fabry disease at Cairo University Childrens Hospital (CUCH), Egypt over the past five years.
Material and methods:
The enzymatic diagnosis for Fabry disease has been established at CUCH, the biggest referral pediatric hospital in Egypt, in 2010. All pediatric patients suspected for Fabry disease during the study period were referred to the inherited metabolic disease unit for clinical assessment and α-galactosidase enzymatic assay.
Results:
Only nine Fabry disease pediatric patients were confirmed enzymatically (8 males, 12±2.5y) out of 78 suspected children. Four more family members (4 males, 22±14y) of 3 pediatric patients were diagnosed later based on suspicious family history. Neurological pain in the form of acroparethesia was the most common presentation in childhood and adolescents (7/9 cases), while renal and cardiac manifestations were more common in adult relatives.
Conclusions:
We here describe the clinical spectrum of the first case series of Fabry disease to be ever reported from Egypt. Most Egyptian patients with Fabry disease still don't have access to proper diagnosis.

P - 344 A CHILD WITH PHENYLKETONURIA AND FOCAL SEGMENTAL GLOMERULOSCLEROSIS, THE BRIGHT SIDE OF PROTEINURIA

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Introduction:
Phenylketonuria (PKU) is the most common inborn error of amino acid metabolism. Only total of eight patients has been reported from Oman. PKU results in accumulation of phenylalanine in the blood. If left untreated, such increase of amino acid will lead to a serious mental damage. Nephrotic Syndrome is a renal disease characterized by heavy proteinuria and hypoalbuminaemia. Chronic nephrosis results in generalized hypoproteinaemia due to urinary loss of amino acids and albumin.
Material and methods:
We describe a three- year- male child who was referred to our hospital with generalized edema. Upon examination the child was found to have global developmental delay his developmental age was around 15 months.
Results:
Workup of generalized edema has yielded a diagnosis of nephrtoic syndrome while the global developmental delay turned out to be secondary to phenylketonuria as evidenced by tandam mass spectrometry and PKU profile. Subsequently, the nephrotic syndrome has proved to be steroid resistant. Renal biopsy unveiled that the child has focal segmental glomerulosclerosis (FSGS) with mild to moderate interstitial fibrosis and tubular atrophy, mild interstitial inflammation mainly in medulla. Sequence analysis for the patient's NPHS2 gene confirmed a homogenous pathogenic frame mutation c.467dup <p.(Leu156fs)>. Late diagnosis of phenylketonuria beyond the age of 2 years usually has drastic neurologic sequel as culminating in a vegetative state.
Conclusions:
We believe that the mild neurologic effect of phenylketonuria in our patient has been mitigated by the concomitant congenital nephrotic syndrome that rendered phenylalanine disposable through the urine. The coexistence between PKU and FSGS hasn't been described before.

P - 345 PNEUMOTHORAX AS A CLINICAL MANIFESTATION OF AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE IN NEONATES

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Introduction:
Autosomal recessive polycystic kidney disease (ARPKD) belongs to a group of congenital hepatorenal fibrocystic syndromes. The only gene known to be associated with ARPKD is PKHD1 and its mutations are for ARPKD diagnostic. Clinical manifestation depends on the severity of kidney and liver disease. The most common manifestation of ARPKD is the perinatal form.
Cases description:
We report 3 neonates with pneumothorax as a clinical manifestation of ARPKD.
Patient No.1 was a boy born in term. His antenatal screening tests were negative. He required resuscitation and mechanical ventilation immediately after delivery because of lung hypoplasia and bilateral pneumothorax. Extremely enlarged kidneys were detected on ultrasound and complete anuria was recorded in the clinical course. He expired during the first day of life due to refractory repiratory failure.
Patient No. 2 was a girl born in the 37th gestational week. After the birth she had tachydyspnea due to right-sided pneumothorax with improvement of the respiratory symptoms after single puncture. Postnatal ultrasonography revealed enlarged hyperechogenic kidneys. Glomerular filtration rate was normal. She required hypertension treatment and NaCl supplementation since day 3. Patient No. 3 was a boy from the second pregnancy monitored regularly for oligohydramnion since the 30th gestational week. He was born in term. Ride-sided pneumothorax was diagnosed shortly after birth with resolution after single puncture. Postnatal ultrasonography revealed enlarged hyperechogenic kidneys. The diagnosis of ARPKD was confirmed clinically and genetically also in his 6-year old brother.
Conclusions:
Spontaneus pneumothorax as the only respiratory problem was the first manifestation of ARPKD in two of our reported patients. Based on our experience, we recommend postnatal ultrasonographic evaluation of kidneys in all neonates and infants with the history of oligohydramnion or respiratory problems in neonatal period.
Supported by IGA MZČR NT/13090.

P - 346 UNUSUAL CAUSE OF SEVERE HYPOKALEMIA, HYPOMAGNESEMIA AND METABOLIC ACIDOSIS

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Introduction:
Kidneys have a major role in the regulation of the acidobasic balance. Renal tubular acidosis (RTA) is characterised by a normal anion gap (hyperchloremic) metabolic acidosis. Only patients with complete distal RTA have a urine pH > 5.3 during periods of metabolic acidosis. There secondary forms of RTA develop in the course of other renal diseases (nephrocalcinosis, genetic and autoimmune diseases, toxins and drugs).
Case description:
A 4-year old girl was admitted due to repeated vomiting. The laboratory results showed severe hypokalemia, hypomagnesemia, hypophosphatemia, increased urea and creatinine, anaemia and metabolic acidosis. In urinalysis there were mild proteinuria, hypercalciuria and alkaline pH with positive urine anion gap which suggested the distal type of RTA. The renal ultrasound scan showed enlarged kidneys with increased echogenity, multiple cysts and calcifications in the renal parenchyma. Bone X-ray showed osteoprosis. Familial hypomagnesemia with hyperkalciuria and nephrocalcinosis (FHHNC), nephronophthisis and primary hereditary forms of RTA were considered.
Molecular-genetic analysis of FHHNC (gene CLDN-16) did not find causal mutation (Prof. Konrad, Germany). Contrarily, a homozygous mutation of the gene NPHP-1 was identified (Prof. Hildebrandt, USA) and the diagnosis of type 1 nephronophthisis was confirmed. The treatment of metabolic acidosis and electrolyte supplementation were started, clinical symptoms disappeared and growth improved.
Conclusions:
This case report provides an example of a severe hypokalemia, hypomagnesemia and distal RTA as a rare manifestation of the type 1 nephronophthisis. The genetic result is important not only for optimal treatment and prognosis of the patient but also for possible diagnosis of other members of the family.

P - 347 HNF1B MUTATION IN A CHILD WITH CYSTINURIA AND RENAL HYPOPLASIA

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Introduction:
Kidney atrophy may be seen in children with nephrolithiasis and long-standing obstruction. Herein we report on a child who had cystine nephrolithiasis and congenital hypoplasia of the contralateral kidney.
Material and methods:
Clinical history, physical examiantion, ultrasound and X-ray imaging of the kidneys and urinary tract. Stone analysis with infrared spectroscopy and mutational analysis of the *SLC7A9* and *HNF1B* gene.
Case description:
An eight year old girl presented with gross hematuria and left renal colic. Ultrasound examination revealed a small non-obstructive calculus in the left kidney. The right kidney was small with regular contour and normal echogeneicity of the parenchyma (30% relative function on the Tc99mDMSA scan). Nitroprusside reaction was positive and analysis of the calculus confirmed cystinuria. In addition she was found to carry heterozygous *HNF1B* mutation (c.1024T>C; p.S342P).
Conclusions:
We present a rare association of two inherited renal disorders. Family relatives should be screened for cysitnuria and *HNF1B* mutation. Treatment of cystinuria should be lifelong and carriers of *HNF1B*mutation shoud be monitored for MODY5 diabetes, hyperuricemia and hypomagnesemia.

P - 348 RENAL HYPODYSPLASIA AND RMND1 MUTATION

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Introduction:
Mitochondrial disorders are a group of heterogeneous diseases implying various organs, which have in common respiratory chain complex defects. These diseases are most often precocious, serious and due to nuclear or mitochondrial genes mutations.
Case description:
We report on a brother and a sister, born 7 years apart, without familial consanguinity, who present with severe renal hypodysplasia, deafness and psychomotor delay, due to mutations in the *RMND1*(Required For Meiotic Nuclear Division 1) gene involved in mitochondrial transcription.
These two siblings were both born at 32 weeks of gestation, with intrauterine growth restriction and transitory neonatal respiratory distress. During the first year of life, they presented with hypotonia, psychomotor impairment, microcephaly, bilateral perception deafness and strabismus. Explorations pointed out rarefaction of brain white matter and increased lactate levels in blood and in cerebrospinal fluid. At 7 years of age, renal failure (GFR 36 mL/min per 1.73m^2), arterial hypertension, salt-losing tubulopathy and bilateral renal hypoplasia (<5thpercentile) were diagnosed in the first child: renal failurebecame terminal at 13 years of age. In this context, renal insufficiency was diagnosed earlier in the younger sister, i.e., at 1 year of age (GFR 41 mL/min per 1.73 m²), associated with arterial hypertension and salt-losing tubulopathy. Renal size was normal; at 6 years of age, GFR is currently 30 mL/min/1.73 m^2. Two compound heterozygous mutations of the nuclear gene *RMND1* were found.
Conclusions:
Five *RMND1* different mutations (homozygous or compound heterozygous) have already been described in 11 children. All had presented with precocious encephalopathy, and related symptoms were the following: perception deafness (N=6), tubular acidosis (N=2), and renal dysplasia (N=2). From our observation and the literature, it appears that *RMND1* mutations predispose to develop renal failure in mitochondrial disorders. However the heterogeneity between genotype and phenotype is significant and more studies are warranted.

P - 349 RECURRENT PANCREATITIS IN A GIRL WITH WT1 MUTATION

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Introduction:
WT1 mutations cause a wide spectrum of renal and extrarenal manifestations. Pancreatitis in childhood is a plurifactorial disease which can be caused by toxic, metabolic, infectious, genetic or anatomic factors.
Case description:
A 1-month-old girl presented with edema ,extreme hyponatriema and proteinuria. Due to rapid progression to terminale renal failure , renal replacement therapy was necessary and initially peritoneal dialysis was started. Kidney biopsy revealed diffuse mesangial sclerosis and genetic analysis revealed a de novo heterozygous mutation c.1323C>G or p.His441Gln substitution within the zinc finger-2 domain of the WT1 gene, confirming the diagnosis. Unless application of frequent exchanges with Physioneal PD solution(Baxter) there was insufficient clearance of the large molecules and ultrafiltration. Icodextrine (Extraneal Baxter) during the day was associated. she supported this regimen well and gained weight. However at the age of 16 months she was admitted with a first episode of severe acute abdominal pain. There were no signs of peritonitis. Biochemical investigations could not reveal any abnormality and ultrasound of the abdomen was normal. Explorative laparotomy was negative. No diagnosis could be made at that time.
Unfortunately one month later she developed a new episode of extreme acute pain crisis. Lipase was extreme high (1384 U/L) and ultrasound revealed signs of pancreatitis. Additional investigations could not detect any infection or anatomic abnormality with obstructive pathology. She used no toxic medications. In literature there were some case reports (in adults) about the association between the use of icodextrine and pancreatitis. The use of this peritoneal solution was stopped. Nevertheless she continued to experience recurrent episodes of severe painfull pancreatitis with a frequency of 1/8 weeks. Except for one episode (after vaccination) no other triggers were identified. We decided to stop treatment with peritoneal dialysis and started with hemodialysis. Since then one pancreatitis episode / 6 months occurred. Genetic analysis of SPINK1,PRSS1 and CFTR-gen did not show any mutation.
Conclusions:
This case shows an unusual association between a congenital nephropathy and recurrent pancreatitis. We hypothesize that this girl developed a first viral pancreatitis which lead to a severe inflammation of pancreas which made her vulnerable to recurrent episodes in addition to peritoneal dialysis, hypercalcemia and other viral triggers(HZV, CMV). Or the phenotypic expression of the recurrent pancreatitis in this girl might be due to an additional genetic modifier , associated with the known genetic mutation in WT1 gen.

P - 350 ENDOCRANIAL HYPERTENSION IN TWO PATIENTS WITH CYSTINOSIS

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Introduction:
Endocranial Hypertension is observed sometimes in patients with nephropathic cystinosis, but its real incidence may be underestimated. Cystinosis is a systemic and progressive lysosomal disease that

potentially involves central nervous system (CNS), in a subacute and severe manner. Routine retinal exams represent a key diagnostic tool.

Cases description:

We report two patients with nephropathic cystinosis and endocranial hypertension who presented with insidious and non-specific symptoms.

Characteristics	Case 1	Case 2
Age (months) at diagnosis	5	5
Genetic diagnosis	yes	Yes
Age (years) at Endocranialhypertension	9	10
Renal disease	Fanconi, CKD 1	Kidney Tx 11 months before, CKD 1
Medical treatment	cysteamine, 1alpha VitD, cholecalciferol, K and P supplement, thiazides, carnitine, omeprazole, losartan, rhGH	cysteamine, tacrolimus, mycophenolic ac, methylprednisolone, enalapril, omeprazole, rhGH
Adherence	good	Good
Risk factors	Arnold-Chiari anomaly	methylprednisolone reduction, rhGH initiation 2 weeks before, acute renal dysfunction
Previous retinal exam	Normal 1 year before	Normal 6 month before
Symptoms	Non-specific back pain, general discomfort, headache since few weeks before	Epigastric pain, morning nausea and reflux, malaise, and headache occasionally
Eye exam	Bilateral severe papilledema, retinal hemorrhages, retinal venous vessels ingurgitation and exudates,Bilateral reduced visual acuity (<10%), and campimetry	Bilateral Papilledema Visual acuity and campimetry preserved
Complementary exams	Normal cerebrospinal fluid MR: Arnold-Chiari anomaly Ventricular dilation severe endocranial hypertension	Normal cerebrospinal fluid High pressure (36 cm H2O) Absence of cystine crystals MR: endocranial hypertension
Treatment	Ventricular drainage	Corticosteroids, Acetazolamide (stopped due severe metabolic acidosis)
Outcome	Permanent reduced visual acuity	Global improvement

Conclusions:

Physicians treating patients with Nephropathic Cystinosis should be aware of endocranial hypertension occurrence and ensure ophtalmologic follow up, even in absence of symptoms, in order to prevent devastating consequences.

P - 351 JUVENILE NEPHRONOPHTISIS: A SINGLE CENTER EXPERIENCE

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Introduction:

Nephronophthisis NPHP (MIM 256100) is an autosomal recessive cystic kidney disease that leads to renal failure in childhood or adolescence. It is the most frequent genetic cause of renal failure in children,especially in countries with a high rate of consanguinity such as Tunisia. We report our single center experience of juvenile NPHP.

Material and methods:

Cinical, biological and genetic data of children presenting with CKD in the department of paediatrics of the university hospital of Sahloul (Tunisia), between 1998 and 2006.

Results:

There were 16 patients from 8 different families: 9 index cases and 7 screened family paediatric relatives. Consanguinity was found in 7 families. Mean age at diagnosis was 10.8 years for index cases and 6,4 years for the screened patents. Symptoms were diverse: polyuria in 2 patients and growth retardation in 5. Retinitis pigmentosa was found in 4 cases, hearing loss in 3 , and mental retardation in 3, 2 of whom showed vermien hypoplasia. All index cases and 2 screened presented ESRD at diagnosis and started a haemodialysis regimen. Kidney cysts were found in only 4 patients. Molecular testing showed mutations of NPHP1 in 6 families and NPHP4 in 2. 6 patients received a living donor transplantation, and 4 are still on haemodialysis, one of the screened relatives, aged 13 years, reached ESRD.

Conclusions:

NPHP is associated with a wide clinical spectrum; its early diagnosis is possible thanks to genetic screening, allowing an improved management before reaching ESRD.

P - 352 A NEW CLINICO-GENETIC FORM OF NEPHRONOPHTHISIS IN A BULGARIAN FAMILY

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Introduction:

Nephronophthisis (NPHP) is the most common genetic cause of end-stage renal disease in children and young adults. It is a genetically heterogeneous disorder and 9 genes were identified. Usually mutations in a specific gene correlate with clinical presentation, histological findings and extrarenal involvement.

Case description:

We observed 3 cases in one family.

The first and the third pregnancies resulted in a birth of boys with severe renal failure since first day, enlarged kidneys with cortical cysts, appearance of jaundice associated with liver fibrosis from second month of live, arterial hypertension. The first child died at 3 months of age and the second at 5 months of age. The second pregnancy with female fetus was terminated in 20 g.w. because of the same ultrasound kidney image. Genetic study of the two last children revealed compound mutation in NPHP3 gene. Heterozygous c.3608delC, leading to frame shift and not described in the literature and heterozygous c.1729C>T. The third child is bearing additionally heterozygous mutation c.7G>T in NPHP4 gene. Observed cases show clinical and histological patterns of infantile NPHP (type 2) and affected NPHP3 gene, which is associated with adolescent form of the disease (type 3). However, mice model has shown that complete loss of NPHP3 function results in situs inversus, congenital heart defects, and embryonic lethality.

Conclusions:

We assume, described for the first time mutation c.3608delC in NPHP3 gene, leading to frame shift, is responsible for a new clinico-genetic form of NPHP. It is characterized by severely presented clinical and histological features of infantile NPHP (type 2), combined with typical extrarenal involvement of adolescent NPHP (type 3) – liver fibrosis.

P - 353 HYPERECHOGENIC COLON FOR PRENATAL DIAGNOSIS OF CYSTINURIA

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Introduction:
Cystinuria (OMIM 220100) is an inborn metabolic disorder characterized by insufficient reabsorption of cystine and dibasic amino acids in the proximal renal tubule leading to cystine lithiasis. In 2006Brasseur-Daudruy et al. (Prenat Diagn 2006; 26: 1254–1255) reported that hyperechogenic colon may be useful ultrasound sign for prenatal diagnosis of cystinuria.
Material and methods:
Examination of the fetus by ultrasound, quantitative measurement of cystine and dibasic amino acids in the random urine sample, molecular diagnosis of cystinuria by sequencing *SLC3A1* gene.
Results:
Large bladder calculus was diagnosed in an 18 month old male infant from Roma ethnicity. The diagnosis of cystinuria was confirmed with quantitative measurement of urinary concentration of cystine and dibasic acid. Molecular analysis revealed typical Roma homozygous T216M mutation in *SLC3A1* gene. The both parents were heterozygous carriers. The family opted for prenatal diagnosis in the next pregnancy. Amniocentesis was performed in the 16 gestational weeks and mutational analysis of the *SLC3A1* gene detected homozygous T216M mutation. The family decided to continue pregnancy. In the 32 gestational week at the ultrasound fetal examination intensive hyperechogenicity of the colon was reported. There were no other abnormalities.
Conclusions:
Although hyperechogenic colon may be found in fetuses with cytomegalovirus infection, cystic fibrosis, ileal atresia, anorectal and urinary tract malformations it may be also suggestive sign for cystinuria as in our patient where molecular genetic diagnosis of cystinuria was established prenatally.

P - 354 A NOVEL FRAMESHIFT WT1 GENE MUTATION IN A CHILD WITH DENYS-DRASH SYNDROME

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Introduction:
The Denys-Drash syndrome (DDS) consists of a triad of nephrotic syndrome, intersex and predisposition to Wilms tumor. DDS is associated with WT1 mutations, the majority being missense mutations in the zinc-finger region.
Case description:
We present a child who presented with nephrotic syndrome and ambiguous genitalia (hypospadias, nonpalpable gonads) with XY karyotype at 8 months of age with negative family history. At 28 months of age he underwent nephrectomy (Wilms tumor) followed by chemotherapy. Hemodialysis treatment was started.
We found a novel heterozygous frameshift mutation in exon 8 [p.H245Tfs*2(c.1393delC)] in our patients. This frameshift mutation generates a premature stop codon after two amino acids from changed amino acid at 245 position of WT1 protein
Conclusions:
In conclusion, frameshift WT1 gene mutations may be related to a more severe phenotype than previously thought. Our case provides important clinical evidence for early removal of native kidneys in patients with nephrotic syndrome caused by WT1 mutation due to increased risk of Wilms tumor development even in the absence of tumor at the time of diagnosis of the DDS. Therefore, we recommend the immediate test to detect the de novo WT1 mutations in nephrotic syndrome and intersex.

P - 355 NEPHROPATHIC CYSTINOSIS MIMICKING BARTTER SYNDROME: NOVEL MUTATION

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Introduction:
Cystinosis is a rare autosomal recessive lysosomal storage disorder caused by mutations in the CTNS gene. The clinical manifestations include renal tubular Fanconi syndrome with hypophosphatemic rickets, hypokalemia, polyuria, dehydration and acidosis, Uncommonly findings with hypokalemic and hypochloremic metabolic alkalosis can mimic Bartter syndrome leading delays in treatment.
Case description:
A six years old girl diagnosed as Bartter syndrome previously was reevaluated and found to have nephropathic cystinosis. The patient's genetic analysis showed homozygous c.853-1G>A mutation in CTNS gene.
There have been few cases of cystinosis presenting like Bartter syndrome, with metabolic alkalosis reported in literature. Cystinosis is a disease that the progression can be avoided with appropriate treatment. Bartter like presentation may lead to delay in diagnosis and treatment. It should always be kept in mind that patients with cystinosis may present with Bartter like clinical findings.
Conclusions:
Our patients mutation is new reported in literature

P - 356 CASE SERIES HNF1BETA MUTATION – 6 YEAR TERTIARY CENTRE EXPERIENCE

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Introduction:
Hepatocyte Nuclear Factor-1 Beta (HNF1B)-associated disease is considered a multi-system disorder. Patients with mutations and deletions of HNF1B gene can have a variety of clinical features including abnormal renal development. Renal cysts are the most frequently detected renal anomaly however single kidneys and renal hypoplasia can occur. Extra-renal phenotypes include early-onset diabetes mellitus, pancreatic hypoplasia, genital tract malformations, abnormal liver function and early-onset gout.
We report our experience of patients with HNF1B mutation from 2009 – 2015
Material and methods:
Retrospective review of case notes from 2009-2015. We reviewed all the cases diagnosed over the last 6 years
Results:
There were 12 patients diagnosed during this period. Male female ratio was 2:1.

Family history of diabetes was present in 5/12 (42%) patients and renal disease in 6/12 (50%) patients. There was no family history of gout in any of the patients

Investigations – Renal ultrasound showed cystic kidneys in 10/12 (83%) and dysplastic kidneys in 1/12 (1%). In 1 patient ultrasound result was not available. HbA1c was done in 6/12 patients (50%), plasma glucose in 8/12 (75%) patients, urine glucose in 9/12 (75%) (all negative) and oral glucose tolerance test (OGTT) in 3/12 patients (25%) (following abnormal HbA1c after GH).

2/12(17%) patients were on growth hormone (GH)

Conclusions:

Following this audit, a series of recommendations were made.

1) Annual HbA1c, (if raised for OGTT) and urine glucose at clinic visits- if positive for glycosuria then the patient should have HbA1c and OGTT. Patients on GH therapy should have annual OGTT and HbA1c test
2) Re-audit our practice in 1 year
3) Cystic kidneys is not the only presentation for HNF1B mutation. Screening for HNF1B in all patients with dysplastic kidneys of unknown etiology

P - 357 WHAT ARE THE EARLY RISK FACTORS OF FREQUENTLY RELAPSING STEROID-SENSITIVE NEPHROTIC SYNDROME IN CHILDREN?

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Introduction:

Early identification of children at high risk of frequently relapsing nephrotic syndrome (FRNS) may be useful for the decision of the therapeutic strategy to reduce the incidence of steroid side-effects. We conducted the study to identify risk factors of FRNS in children.

Material and methods:

We performed retrospective analysis of medical records of 66 children (43M/23F) with steroid sensitive nephrotic syndrome (SSNS).All patients were divided into two groups according to frequency of relapses of nephrotic syndrome: 1) FRNS (n=43), 2) rare relapses of SSNS (n=23).

Results:

The median disease duration was similar between children with FRNS and rare relapses of SSNS: 36.0 (17.0-75.0) vs. 20.5 (0.5-78.0) months, respectively ($p>0.05$). There were no significant differences in proportion of boys between both of groups: 65.1% vs. 65.2% ($p>0.05$). Patients with FRNS compared with rare relapsing SSNS had significantly more often rate of age at onset <2 years: 23.3% vs. 0% (OR14.7; 95%CI: 0.8-264.1; $p=0.02$), duration of initial daily steroids <4 weeks: 87.5% vs. 52.4% (OR = 6.4; 95%CI: 1.6-24.6; $p = 0.007$), total duration of initial prednisone treatment <3 months: 20.9% vs. 0% (OR 12.9; 95%CI: 0.7-233.4, $p=0.02$), prolonged time to obtain of initial complete remission ≥10 days: 86% vs. 26.1% (OR =17.5; 95%Cl: 4.9-62.2; $p<0.0001$), fist relapse within 5 months after manifestation of the disease: 69.8% vs. 39.1% (OR=24.2; 95%Cl: 4.9-118.8; $p<0.0001$).

Conclusions:

In children with SSNS age at onset <2 years, initial short duration of daily steroid therapy <4 weeks and total course of steroids <3 months, prolonged time to obtain initial complete remission ≥10 days, and fist relapse within 5 months after onset of the disease might be considered as an risk factors for the developing of FRNS. Our findings may be useful for steroid-sparing agent treatment at an earlier date to prevent steroid side effects.

P - 358 QUALITY OF LIFE IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME ON RITUXIMAB AND ORAL IMMUNOSUPPRESSIVE TREATMENT

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Introduction:

Pediatric steroid dependent idiopathic nephrotic syndrome treated with oral immunosuppressive drugs or rituximab jeopardizes the patients' quality of life. We investigated general quality of life in these two patient groups and evaluated treatment appreciation in those who experienced both treatment modalities.

Material and methods:

We investigated all patients from two centers with high degree steroid dependent idiopathic nephrotic syndrome who were between 6 and 18 years old. Patients were divided in two groups, one on RTX and one on oral immunosuppressive treatment.

All patients completed a quality of life questionnaire (QOLQ) during their outpatient visits. Each questionnaire had 26 questions with a minimum score of -52 and a maximum of +52 which were divided into 4 groups (functional, relational, self-esteem, hobbies). Those patients who were on RTX after having received oral immunosuppression also completed a second questionnaire investigating their treatment appreciation.

Results:

Seventy-two patients (26 girls) completed the QOLQ. Thirty-six were on RTX and thirty-four on oral immunosuppression. Mean patient age of the whole cohort was 12.3±4.1 years, and 13.8 ± 3.7 years for patients on RTX.

Boys had a higher overall QOL score than girls (27.0±9.6 vs. 21.7±10.4; $p=0.03$). The score of RTX patients was +24.9±10.9 vs. +25.3±9.4 (n.s.) for patients on oral drugs. Evaluation of the 4 subgroups of QOL did not reveal significant differences among patients on RTX vs. oral drugs.

Among patients who experienced both treatment modalities 25/36 preferred RTX and 4 preferred oral drugs, whereas 7 were indifferent.

Conclusions:

The overall QOL in patients on RTX and oral immunosuppression was good and slightly higher in boys compared to girls. RTX was the preferred treatment option in the vast majority of patients and in particular in adolescents.

P - 359 CLINICAL CHARACTERISTICS OF STEROID DEPENDENCY IN CHILDHOOD STEROID-SENSITIVE NEPHROTIC SYNDROME

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Introduction:

Steroid-sensitive nephrotic syndrome (SSNS) is characterized by preservation of renal function and recurrent disease. The clinical course depends on the number of relapses which is highly variable. A subset of patients presents with relapses during or shortly after steroid therapy (steroid-dependent NS, SDNS). Mostly, childhood SSNS is of idiopathic origin with minimal change glomerulopathy (MCN) in renal histology. Aim of our study was the characterization of SSNS patients with regard to differences between SDNS and non-SDNS.

Material and methods:

We retrospectively analyzed 100 SSNS patients treated at the University Children`s Hospital Essen. Data collection comprised age at onset,

number/trigger of relapses, dose/duration of steroid therapy, time to response, further immunosuppressants, renal function, renal histology, and family history.

Results:

89% of patients experienced relapses (mean 9 (range 0-34)), 55% developed SDNS (after 15 (2-45) months from onset). In 80% of cases trivial infections triggered SSNS relapse. 60% of patients received further immunosuppressants (95% cyclophosphamide, 58% ciclosporin A; sustained disease remission in 24/51%, respectively). Renal biopsy was performed in 70% (93% MCN, SDNS and non-SDNS). SDNS patients were significantly younger at disease onset (4.16 ys (SDNS) vs. 5.34 ys (non-SDNS), P=0.035; all patients 4.7 ys). Mean time to first relapse was significantly shorter in SDNS (6.3 months vs. 16.3 months non-SDNS; P<0.001; all patients 9.8 months). Response to steroids at disease onset was faster in non-SDNS (6.8 days vs. 11.7 days SDNS; P<0.001). SDNS patients developed secondary steroid resistance in 20% (2% non-SDNS; P<0.01; all patients 12%).

Conclusions:

55% of patients developed SDNS and differed from non-SDNS patients by a younger age at disease onset, a shorter time until first relapse and a slower therapy response.

P - 360 A RANDOMISED CONTROLLED TRIAL TO ASSESS THE EFFECT OF VITAMIN D SUPPLEMENTATION IN STEROID SENSITIVE NEPHROTIC SYNDROME.

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Introduction:

Nephrotic Syndrome (NS) is associated with immune dysregulation and osteoporosis. Vitamin D has modulating effects on both immune and skeletal systems. Our aim is to assess the effect of Vitamin D supplementation on bone biochemistry, bone mineral density (BMD) and on relapse rate and steroid requirement in children with steroid sensitive NS over a period of 6 months.

Material and methods:

A randomised, controlled, open label trial, was designed to have 30 patients (ages: 2 - 10 years) in each arm, to yield > 90% power. The test group is prescribed Vitamin D and calcium supplements. Treatment of NS is continued according to standard protocol. Serum creatinine, albumin, calcium, phosphate, alkaline phosphatase and 25-hydroxy-cholecalciferol (25(OH)D); urine protein/ creatinine and calcium/ creatinine ratios are documented at study entry, 1 month and 6 months. Renal ultrasound and lumbar BMD are performed at study entry and 6 months. The number of relapses and cumulative steroid dosage during study period are documented.

Results:

This is an ongoing study and till date, 40 patients have undergone randomisation while 26 have completed the study (test group: 12, controls: 14). Interim analysis indicates that between groups, at study entry, there was no difference in NS type, mean age, 25(OH)D levels or lumbar BMD. The mean initial 25(OH)D level was 6.4 ng/ml which correlated significantly with serum albumin (r=0,39, p=0.013), but not with NS type or BMD.

The mean difference over 6 months in 25(OH)D levels was +20.1 ng/ml in the test group and +0.9 ng/ml in the control group (p=0.002), while the mean difference in BMD was +8.7% and +3.3% (p=0.27) respectively. Four (33%) patients in the test group had relapses compared to 10 (71%) in the control group (p=0.1). None of the children in either group had hypercalciuria or nephrocalcinosis.

Conclusions:

On study completion we expect to understand whether optimisation of serum 25(OH)D levels reduces relapse rate and steroid requirement or maintains BMD in children with steroid sensitive NS in the short term. This will help in formulating guidelines for the requirement of such supplements in this chronically relapsing disease.

P - 361 DOES RENAL BIOPSY INFORM MANAGEMENT OF CHILDREN WITH NEPHROTIC SYNDROME WHEN USING CALCINEURIN INHIBITORS?

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Introduction:

Few data describe renal biopsy findings prior to commencing calcineurin inhibitor (CNI) therapy and on continued treatment with CNI's in children with steroid sensitive (SS) and steroid resistant (SR) nephrotic syndrome (NS).

Aim:

Our objective was to evaluate findings of renal biopsy (i) pre-commencement and (ii) on subsequent biopsies whilst continuing on CNI therapy.

Material and methods:

Retrospective single centre case-notes review of all children with NS who were commenced on tacrolimus between 2004 and 2014.

Results:

63 children with NS (39 SS and 24 SR), including 36 boys had renal biopsy performed at various stages of the disease. Their average age at diagnosis was 5.16 years (SD 3.62). Overall, 12 patients were excluded, as they did not have a pre-CNI biopsy.

SS Group: The most common histological finding was MCD (45%), with FSGS (38%), MCD IgM (10%), and C1qN nephropathy (7%) in others. *SR Group*: The most common histological finding was FSGS (59%), with IgM MCD (18%), MCD (14%), C1qN and Membranous nephropathy 4.5% each, in others. Overall, 5 patients showed any evidence of acute CNI toxicity.

Conclusions:

Baseline biopsy provides accurate histological diagnosis and estimates of established damage. Sequential biopsies add to this baseline information, often displaying worsening in extent of established damage. This is likely to be useful in the clinical management of children with NS.

P - 362 THE RELATIONSHIP BETWEEN SERUM HEAT SHOCK PROTEIN LEVELS AND CLINICAL COURSE IN IGA NEPHROPATHY AND IDIOPATHIC NEPHROTIC SYNDROME

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Introduction:

Heat shock proteins (HSPs) family contains several members which regulate the cell response to any hazardous factors to prevent protein structure. The aim of the study is to determine whether serum levels of HSPs increase in children with glomerular diseases and indicate renal injury.

Material and methods:

Seventy two patients and 24 healthy controls were enrolled in the study. Thirty one of the patients had IgA nephropathy/Henoch-Schönlein Purpura

nephritis (IgAN/HSPN) and 41 patients had idiopathic nephrotic syndrome (INS). Renal function was normal in all patients. Serum levels of HSP27, HSP40, HSP60, HSP70 and HSP90 were measured by ELISA.

Results:

Mean age of the patients was 10.9±4.8 years. Age and gender distributions of patient and control groups were not significantly different ($p>0.05$).

Serum levels of HSP27, HSP40, HSP60, HSP70 and HSP90 were significantly higher in the patient group than in controls ($p<0.05$). Additionally, all these HSPs were found to be significantly higher in the patients with IgAN/HSPN than in INS group and in controls ($p<0.05$). Serum HSP40, HSP60, HSP70 levels were significantly higher in the patients with INS than in controls ($p<0.05$) whereas HSP27 and HSP90 were not different. There was no difference between the patients with IgAN and HSPN regarding serum levels of HSP27, HSP40, HSP60, HSP70 and HSP90 ($p>0.05$). None of these HSPs was related to presence of crescent and severity of proteinuria in IgAN/HSPN group.

Conclusions:

Serum HSPs increase in the patients with IgAN/HSPN rather than in INS and in controls suggesting that HSPs may have a role in the pathogenesis of IgAN/HSPN.

P - 363 HISTOLOGICAL CALCINEURIN-INHIBITOR NEPHROTOXICITY IN PATIENTS WITH STEROID DEPENDENT NEPHROTIC SYNDROME – REALITY OR DOGMA?

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Introduction:

To evaluate histological lesions compatible with calcineurin inhibitor (CNI) nephrotoxicity in children with CNI dependent idiopathic nephrotic syndrome (INS) on either cyclosporine (CyA) or tacrolimus (Tac).

Material and methods:

We retrospectively included all children on Cya or Tac for steroid dependent (INS) with a duration of CNI treatment of at least 1 year. Only patients in whom CNI could not be replaced by mycophenoloc acid were included. All included patients underwent a transcutaneous kidney biopsy using a 16 gauge needle. Arteriolar hyalinosis was considered as chronic CNI nephrotoxicity and vacuoles in tubular epithelium were considered as acute CNI toxicity.

Results:

Sixteen children (4 girls) were included. Age at disease onset was 47.5 (8-147 months, treatment duration on CNI was 33 (12-90) months. Age at kidney biopsy was 143 (22-195) months. Number of relapses was 8 (1-12) since disease onset. Serum creatinine level was transiently and moderately increased in two patients. Kidney biopsy revealed minimal change disease in 13/16 patients and focal segmental glomerulosclerosis in 3/16. Evidence for chronic CNI nephrotoxicity was found in one patient revealed by arteriolar hyalinosis and non-specific glomerular fibrosis in 50% of glomeruli. This patient required particularly high doses of CyA in the first two years to achieve disease control (CyA: 10 mg/kg/day; trough levels 150 – 175 ng/ml). On the other hand high dose CyA with comparable pharmacocinetic data and treatment duration was used in one other patient without any signs of CNI nephrotoxicity.

Conclusions:

CNI induced chronic nephrotoxicity is very rare in paediatric patients with CNI dependent INS. Renal function is not a good predictor for histologic lesions because of potential functional toxicity. In patients who require long-term and/or high-dose CNI treatment kidney biopsies might be useful to exclude chronic CNI induced lesions.

P - 364 CONGENITAL AND INFANTILE NEPHROTIC SYNDROME, A SINGLE CENTER EXPERIENCE

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Introduction:

Congenital and infantile nephrotic syndrome is a rare kidney disorder characterized by heavy proteinuria starting rapidly after birth. The majority of cases are caused primarily by a defect mutation in gene that encodes structural and regulatory protein of the glomerular filtration barrier. Management of these patients depends largely on the magnitude of the proteinuria and the outcome can be poor. We propose a retrospective review of our congenital (CNS) and infantile nephrotic syndrome (INS) aiming to characterize genotype/phenotype correlations and to analyze their evolution.

Material and methods:

All cases diagnosed between 1989 and 2015, in our department, were reviewed. Demographic data, clinical features genetic mutations, treatment and outcome were extracted from clinical records from diagnosis to their first kidney graft.

Results:

26 patients were included (13 girls; 13 boys). We detected a disease causing mutations in 69% of patients (represented respectively as : NPHS1 38.5%, WT1 11.5%, NPHS2 7.5%, PLCE1 7.5%, LAMB2 4% and no mutation 30.5%). As many as 72% of patients with congenital onset (0-3 months) and 50% with infantile onset (4-12 months) of NS were explained by mutations. 46% of these families were consanguineous. 12 patients were transplanted and got no disease recurrence. 7 patients died at the mean age 1.3 year old (3 therapeutic withdrawal and 4 whilst on dialysis). We realized single nephrectomy for 30% and double nephrectomy for 23% of our patients at the mean age of respectively 2,6 and 2,1 years old. Interestingly, in this cohort 2 patients with an initial aggressive NS got a favorable evolution without need for renal replacement therapy. One of them has NPHS1 mutation, no mutation was found for the other one.

Conclusions:

We herein report our experience in the management of CNS and highlight heterogeneity in their evolution.

P - 365 IMMUNOHISTOCHEMICAL AND ULTRASTRUCTURAL FEATURES OF HUMAN PODOCYTES DURING NORMAL DEVELOPMENT AND IN CONGENITAL NEPHRITIC SYNDROME OF THE FINNISH TYPE (CNF)

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Introduction:

During development, human podocytes acquire characteristics of terminally differentiated cells with typical cytoskeleton

organization and lose of proliferation ability. The structure and function of podocytes are changed in nephrotic syndrome of the Finnish type (CNF). Spatiotemporal pattern of podocyte differentiation shows interspecies differences, while data on human development are inconsistent. Here we investigate features of human podocytes during normal glomerulogenesis and in CNF.

Material and methods:

Histological section of tissue samples of normal developing kidneys (7-38-weeks-old) and CNF kidneys were stained by double immunofluorescent method using antibodies against nestin, nephrin, Ki-67 and alpha-smooth-actin (α-SMA). Different stages of glomerular development were analyzed in electron microscope (EM).

Results:

EM discloses that podocyte precursors in S-shaped nephrons appear as aggregated polyhedral cells with abundant cytoplasmic organelles. In fetal glomeruli, podocytes develop cell processes and accumulate microfilaments. During the investigated period, nestin expression characterizes the metanephric cup, podocyte precursors and blood vessels in C-or S-shaped nephrons, and then spreads to all glomerular cell populations. Nephrin initially appears in ampullae and weakly in metanephric cap, and then increases in podocytes of maturing glomerules. Proliferation (Ki-67) significantly decreases during glomerulogenesis. α-SMA expression first appears in peripheral metanephric cap cells, later in walls of blood vessels and podocytes, and then predominantly in surface glomerular cells (podocytes). CNF kidneys are characterized by reduction in nephrin and α-SMA expression, nestin expression and presence of proliferating cells.

Conclusions:

In early nephrogenesis, metanephric cap mesenchyme is characterized by partially overlapping nestin, weak nephrin and α-SMA expression. Later on, nestin, nephrin and α-SMA co-expression becomes restricted to podocyte population, in association with development of podocyte foot processes and contractility. In maturing glomeruli, proliferation is not confined to podocytes. In CNF, reduction in nephrin and α-SMA expression accord with loss of podocyte foot processes and function.

P - 366 DEVELOPMENT OF A REPRODUCIBLE BIOMARKER TO DETECT CIRCULATING FACTOR DISEASE IN NEPHROTIC SYNDROME

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Introduction:

Idiopathic (primary) and genetic (secondary) forms of focal and segmental glomerular sclerosis (FSGS) exist. Both are characterized by significant loss of podocytes from the glomerular filtration barrier (GFB) leading to massive protein loss (proteinuria). In the idiopathic form, relapse of the disease in the transplanted kidney sustains the circulating-factor hypothesis in the pathogenesis of the disease.

We have previously published work showing that adding diseased plasma from patients with post-transplant relapse, directly to conditionally immortalised podocytes in culture causes activation/phosphorylation of vasodilator stimulated protein (VASP) in podocytes. The reproducibility is highly significant and the corresponding remission plasma from the same patient, or control plasma, shows significantly lower phosphorylation by comparison. VASP is ubiquitiously expressed and intricately involved in defining cell shape and motility through regulation of actin cytoskeleton dynamics and remodelling which is essential in maintaining a healthy GFB anchored podocyte.

Material and methods:

Use of conditionally immortalised podocytes; immuno-fluorescence, western blotting and ELISA technique

Results:

To date we have assayed discarded plasma from approximately 19 patients including 15 paired (relapse and remission) and 6 control plasma samples. Nine of these paired samples, excluding a further 7 which are currently unpaired, originated from the UK RADAR programme. To demonstrate the robustness of VASP as a biomarker for FSGS we have expanded the cohort to include 5 international patient plasma samples from Japan.

Importantly we show that patient peripheral blood samples can also be tested with consistent outcomes with blood tested in up to 12 of these patients. Clinical protein/creatinine ratios collected from three patients have shown very good consistency with the corresponding assayed VASP signal.

Conclusions:

One of our goals is to achieve high throughput testing of VASP presence in FSGS patient samples using ELISA technique in an effort to develop a podocyte stimulation test; which could represent a clinically applicable biomarker of circulating factor disease, thus aiding in early decision making for therapy.

P - 367 USE OF LEVAMISOLE IN STEROID SENSITIVE NEPHROTIC SYNDROME: A SINGLE CENTRE EXPERIENCE

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Introduction:

Steroid sparing agents (SSAs) such as Levamisole have been used for a number of years to obviate the steroid side effects of patients with frequently relapsing (FR) steroid sensitive nephrotic syndrome (SSNS). Levamisole has the particular advantage of having a low side-effect profile but its efficacy has been queried and in a number of centres is not used at all. The study therefore sought to examine our use of this drug in our centre in terms of its success rate.

Material and methods:

We reviewed our database of children with FR SSNS. The need to introduce alternative SSA was used to determine treatment failure. Data on children who had been on Levamisole for at least a minimal follow-up period of 6 months were analysed. Children who did not require alternative SSAs after Levamisole therapy were deemed to have had successful therapy.

Results:

Of the 129 children identified with FR SSNS, Levamisole treatment (2.5 mg/kg body weight on alternate days) was introduced in 81. In 5 children Levamisole was instituted after another SSA had been used and therefore were excluded from analysis. In 3 children, less than 6 months follow-up data was available. In the remaining 73 (28 girls), the mean age of the children at the start of Levamisole was 6.1 (range, 2 – 14.1) years.

In 40 (60%) children, no alternative SSA was required after a mean follow up period of 3.2 (range, 0.6 – 8.2) years. In two children, the Levamisole had to be stopped early as they developed some renal impairment concurrent with the start of Levamisole for unclear reasons. There was no difference in age of the children who responded to to Levamisole. Asian children were more likely to respond to Levamisole (22/40 of the responders *vs.* 10/33 of the non-responders), p=0.034.

Conclusions:

Levamisole remains a useful first line agent for children with FR SSNS especially if relapses are occurring when off steroids. Children of Asian ethnicity in these circumstances are more likely to respond.

P - 368 SURVELLIENCE BIOPSIES OF TACROLIMUS EFFECT IN CHILDHOOD NEPHROTIC SYNDROME

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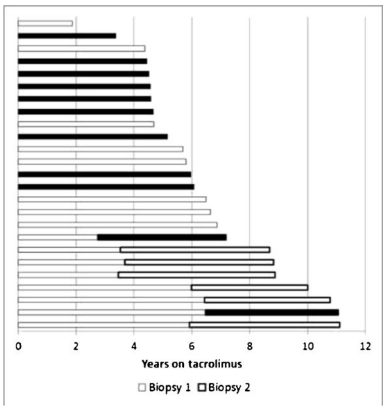
Introduction:
Tacrolimus is increasingly advocated as a steroid sparing agent in the management of nephrotic syndrome. As concerns exist about long term nephrotoxicity, interval renal biopsies have been advocated to detect early changes.
Material and methods:
Single centre review of surveillance renal histology of children who received tacrolimus to treat nephrotic syndrome between 2002 - 2015.
Results:
25 children (16 male, 1 non-caucasian, 21 minimal change, 4 FSGS) commenced tacrolimus at median age 4.0 years (range 1.4 - 8.9). 9/25 (35%) of first biopsy taken after median duration 4.7 years (range 1.9 to 6.9) demonstrated features of calcineurin inhibitor (CNI) nephrotoxicity. Toxicity was associated with higher mean 12-hour trough serum tacrolimus levels: 0/11 showed toxicity with levels of 4.4 to 5.5 μg/L vs. 9/15 (60%) with levels 5.7 to 7.4 μg/L ($p < 0.0001$). No association was found with number of relapses, gender or duration of time on tacrolimus. Eight patients without initial CNI toxicity underwent second biopsy at a median time of 4.9 (range, 4.0 – 5.4) years later. Two developed toxicity. Estimated glomerular filtration rate in those who developed toxicity was normal. We attempted weaning in 20 patients: 11 patients relapsed, 4 within 2 months, further 5 within 1 year after dose reduction.



Graph. Each row represents one patient. Black filled bars denotes toxicity on biopsy
Conclusions:
Significant number of children on tacrolimus showed histological nephrotoxicity after a short duration of therapy. In this small single centre experience, toxicity correlated with tacrolimus level rather than duration. A high number relapsed shortly following dose reduction. We suggest maintaining tacrolimus levels ≤5.5 μg/L to minimise nephrotoxicity.

P - 369 LOW ZINC LEVELS IS A COMMON FINDING IN PATIENTS WITH NEPHROTIC SYNDROME

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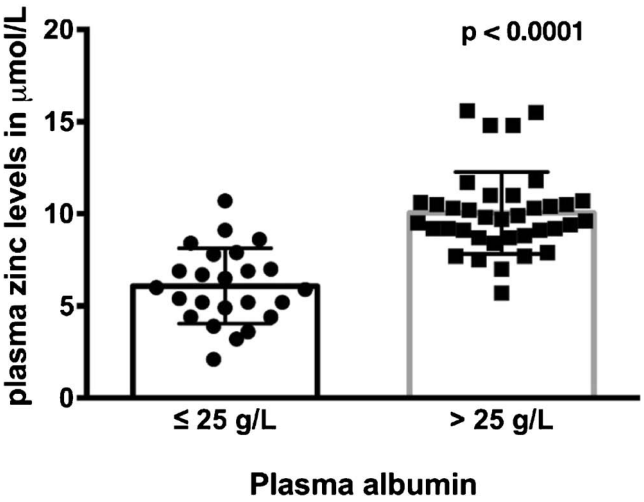
Introduction:
Nephrotic syndrome leads to loss of albumin in the urine along with many albumin-bound substances such as calcium, and trace elements such as zinc[1]. Zinc is highly albumin-bound and in cases of frequent relapses, patients can become significantly deficient and require zinc replacement. Low zinc levels can be associated with poor growth, impaired immune function, hypogonadism, skin disorders and cognitive dysfunction.
Material and methods:
We investigated the zinc levels of patients with a diagnosis of nephrotic syndrome and looked to see if this correlated with their albumin levels. Zinc levels were measured both in patients in remission and those in relapse from their nephrotic syndrome.
Results:
We measured zinc levels in a total of 62 children (22 girls) with nephrotic syndrome aged from 0.1 – 16.5 (median, 6.9) years old. Low zinc levels (<11 μmol/L) were detected in 53 (85%) of the children. As expected, zinc levels were significantly lower in patients with plasma albumin levels ≤25 g/L (5.9 μmol/L (n=24) when compared with patients with a plasma albumin of > 25g/L (9.7 μmol/L (n=37)), ($p < 0.0001$). See Figure below.



Conclusions:
Low zinc levels are in important part of nephrotic syndrome needing close attention and replacement in cases where there are frequent relapses or remission is difficult to achieve to prevent long-term zinc deficiency in this patient group.
Reference:

1. Lu, J., Stewart, A.J., Sadler, P.J., Pinheiro, T.J. & Blindauer, C.A. Albumin as a zinc carrier: properties of its high-affinity zinc-binding site. *Biochem. Soc. Trans.* **36**, 1317-1321 (2008).

P - 370 ROLE OF CTLA4 POLYMORPHISM IN IDIOPATHIC NEPHROTIC SYNDROME AND TREG LEVELS

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Introduction:
Imbalance in peripheral blood regulatory and effector T cells (Teff) are linked to cell mediated immune response and may be associated with steroid response in nephrotic syndrome (NS). The decreased Tregs may result in Teff cells activation and secretion of proinflammatory cytokines causing persistent proteinuria. Circulating factors also contribute to podocyte injury and enhance CD80 expression. CTLA-4 is a CD80 inhibitor may involve in regulation at local level by inadequate podocyte CD80 expression censoring, impairing production of CTLA-4. Many single nucleotide polymorphisms (SNPs) have been identified for CTLA-4 gene, affecting expression of either membrane-bound or soluble CTLA4. The G allele of CTLA-4 leads to reduced CTLA4 expression and down regulation of T-cell response. Aim was to explain does CTLA4 cause Treg decrease in SRNS and how does SNPs of CTLA4 affect patients' outcome?
Material and methods:
We investigated Treg levels and CTLA4 SNPs relationship to treatment response in 20 (16 boy) NS patients between 3-10 years old. All were negative for NPHS1, NPHS2, WT1 mutations. Treg levels were determinated at beginning and the end of treatment.
Results:
Renal biopsy showed FSGS (14), IGM nephropathy (4), MLH (2). AA SNPs was the most frequently encountered (11). Tregs levels were low at all stages. There was no relationship with treg levels and CTLA4 SNPs. The most severe diseases occur in GG SNPs. Two patients with GG SNPs were unresponsive to treatments, even rituximab. Six of ten patients in remission revealed CTLA4 AA SNPs. In contrast to patients with idiopathic FSGS, one patient with AA SNPs of CTLA4 presented with nephrotic syndrome at earlier age was nonresponsive to any immunosuppressive treatment and transplanted.
Conclusions:
G allele may lead to reduced CTLA4 expression on podocyte and results down regulation of the T-cell response. Anti-CD80 therapy using abatacept or belatacept could be considered as treatment option in SRNS especially in CTLA4 GG homozygous and studies should be conducted in effectiveness and safety of CD80 blockade in SRNS.

P - 371 DYSFUNCTION OF ECT2 GENE MAY CAUSE TUBULOINTERSTITIAL INJURY LEADING TO SECONDARY FOCAL SEGMENTAL GLOMERULOSCLEROSIS IN THE MOUSE MODEL OF KIDNEY INJURY WITH ARISTOLOCHIC ACID ADMINISTRATION

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Introduction:
Secondary focal segmental glomerulosclerosis (FSGS) follows congenital or acquired tubulointerstitial alterations. Failure of adequate regeneration after tubulointerstitial injury or abnormal tubulogenesis can disturb intrarenal blood circulation, causing excessive glomerular filtration. We previously reported two patients with severe tubulointerstitial disorders, followed by secondary FSGS. These patients have a nonfunctional genotype of epithelial cell transforming sequence 2 gene (ECT2). The product of ECT2 is a transforming protein related to Rho-specific exchange factors and cell cycle regulators. ECT2 protein is present at cell-to-cell contact sites and in the nucleus; it is involved in cell polarity, organogenesis, and structure and function of intercellular tight junctions. On the other hand, alistorochic acid (AA) is known as oncogenic material causing Balkan endemic nephropathy (BEN). One of the locations of DNA injured in BEN, which was located on 3q26.1～3q26.3, was consistent with ECT2 mutation which had been showed in our patients.
Material and methods:
Then, we made a mouse model of kidney injury with AA injection and investigated the relationship between ECT2 dysfunction and kidney injury. We investigated histological features and gene expression of ECT2 in both groups to evaluate the association between ECT2 mutation and FSGS.
Results:
Their histological features of kidney at 20 weeks of their age showed cloudy degeneration, vacuolation of uriniferous tubules, tubular epithelial cell detachment and glomerular swelling. These features were similar to the damages which were shown in ECT2 mutation. Then gene expression was screened by the comparative genomic hybridization. Down-regulation of ECT2 was observed in some mice injected AA. ECT2 is one of the cell adhension molecule of tubuler cell. Thus, dysfunction of this gene might cause the tubulointerstitial injury followed by glomerular injury as FSGS. On the other hand, ECT2 dysfunction, which is caused by administration of AA, could be the primary cause of BEN. Our results supposed that ECT2 mutation of our patients congenitally occurred structural and/or functional tubulointerstitial disorder and gradually contributed to the progression of secondary glomerular sclerosis.
Conclusions:
In conclusion, Congenital mutation of ECT2 might associate with the development of tubulointerstitial injury and focal segmental lesions in some of patients with FSGS.

P - 372 A RARE CAUSE OF HEAVY PROTEINURIA IN AN ASYMPTOMATIC CHILD

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Introduction:
Coenzyme Q10 (CoQ10) deficiency has been associated with a wide variety of clinical phenotypes but only rarely with steroid-resistant nephrotic syndrome (SRNS).
Material and methods:
We report the case of a 5-year-old boy with positive screening for proteinuria by routine urine analysis for school children.
Results:
Physical examination revealed no edema, normal male external genitalia, dysplastic ears with abnormal folded pinna, a short uvula, normal filtrum, and normal body weight and height for age. Albumin level was of 41 g/L, and urine contained 2g/24h of proteins from glomerular origin. All the other biochemical investigations were normal. Renal ultrasound showed enlarged kidneys, perimedullary hyperechogenicity and a left duplex kidney. A treatment by an ACE inhibitor was started. Renal biopsy showed signs of FSGS with 65% of severe glomerular lesions, tubular atrophy and interstitial fibrosis. Heavy proteinuria worsened to 4 g/24 h and he failed to respond to prednisone (60 mg/m²/day for 1 month) and other immunosuppressive agents (cyclosporine A and mycophenolate mofetil).Because of a clinical deterioration and the advent of end-stage renal failure, hemodialysis was started four years after his first presentation. Suspected gene loci implicated in BOR syndrome, CHARGE association and SRNS were tested. Our patient presented compound heterozygous mutations in the aarF domain containing kinase 4 (*ADCK4*) gene (NM_024876.3), (nucleotide alterations c.649G>A and c.748G>T). The genetic test of the parents confirmed the autosomic recessive transmission of the condition observed in our patient. *ADCK4* gene is one of the genes involved in CoQ10 biosynthesis located in chromosome 19q13.2. and is expressed in podocytes. CoQ10 supplementation has proved to be beneficial in some patients if started early in the disease process.
Conclusions:
Discovery of important proteinuria in a asymptomatic child should prompt early genetic investigations.

P - 373 INITIAL MANIFESTATION OF NEPHROTIC SYNDROME IN 310 POLISH CHILDREN - REPORT FROM NEPHROSIS ONLINE PLATFORM

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Introduction:
The annual incidence of idiopathic nephrotic syndrome (INS) in Europe ranges from 2 to 7 per 100000 children. A male predominance among young children and median age at onset (30 months) with rare onset in adolescence has been reported by the ISKDC Study for the cohort of European children and confirmed by further national reports. Almost 80% of children in the ISKDC study achieved remission following steroid treatment. The aim of the presented study was to compare the initial clinical manifestation of INS among children in Poland two generations later

Material and methods:
Nephrosis Online is a platform established in 2013 aimed at collecting prospective data on children with new onset nephrotic syndrome from 14 centers in Poland

Results:
Among 310 children registered online between January 2013 and January 2015, 302 subjects demonstrated primary nephrotic syndrome. The median age at onset of INS was 43,8 months. 222 (73%) children were younger than 6 years. 37 subjects (12%) were ≥ 10 yrs of age. A nearly equal distribution was observed for boys and girls in both the whole population [162/302 boys and 140/302 girls (53.6% v. 46.4%)] and in the preschool subset [125/222 boys and 97/222 girls (56.3% v. 43.7%)]. In 32 /274 children INS was preceded by an infection. In 30/274 allergy was reported and in 18/274 rampant dental caries was diagnosed. Haematuria was present in 78/247 and hypertension in 45/201 at presentation. 280/310 (90.3%) responded to initial steroid therapy and 30/310 were steroid-resistant (9.7%) from onset.

Conclusions:
A lack of male predominance , higher proportion of initial onset in adolescence and association with dental caries was noted in a contemporary cohort of children with INS in comparison to previous reports on clinical manifestation in European children

P - 374 PATHOPHYSIOLOGY OF NEPHROTIC OEDEMA IN CHILDREN

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Introduction:
The pathophysiology of nephrotic edema in children is complex: two archetypes are classically accepted, the underfilled (with avid sodium retention related to stimulated renin aldosteron-levels, and overfilled type with primary renal sodium retention and low renin-aldosteron levels) but limited physiologic studies have been performed in children. This study aimed to further elaborate the pathophysiological mechanism involved.

Material and methods:
Eighty children with nephrotic syndrome (NS) in remission (n= 35) and nephrotic state (n=45) received a hypotonic fluid charge to increase circulating blood volume. NS patients were further subdivided into children with normal renin (LoRe) (n= 16) or high renin (HiRen=29). Water loading test was performed to induce hypervolemic state using a standardized protocol. Blood tests were performed at 0,1,2 hours and sent for renin, aldosterone, and vasoactive hormones.

Results:
The significant increase in blood volume, resulted in appropriate suppression of all vaso-active hormones in the LoRe-group (renin, aldosteron catecholamines) (mean±SD at 0 hour: 29.3±13.9, 31.0 ±26.6; 2 hours: 20.2±12.0, 16.0±20.2, respectively) as in the remission-group (0 hour: 30.0±15.3, 49.2±26.6; 2 hour: 20.7 ±15.7, 24.3±30.8, respectively) ($p<0.01$), but inappropriate high ANP levels (0 hour: 89.2±47.6; 2 hour: 182.3±217.9), suggestive for functional hypervolemia.
In the HiRe group,the induced increase in blood volume resulted in a decrease of several vaso-active hormones(renin, aldosterone) (0 hour: 352.9±249.6, 769.2±810.9; 2 hours: 232.8±199.8, 323.5 ±327.5, respectively) , in line with the expected hypervolemia theory, but not reaching normal values, suggestive for inappropriate suppression of renin/aldosteron by hypervolemia. That ANP was rather high normal was unexpected (0 hour: 62.1±26.4; 2 hour: 119.9±118.6, respectively).

Conclusions:
The pathogenesis of nephrotic oedema is more complex than hypo-versus hypervolemia, as is demonstrated by the inappropriate response of several vaso-active hormones after increasing the circulating blood volume.

P - 375 ARE THE DIFFERENCES IN IDIOPATHIC STEROID-RESISTANT NEPHROTIC SYNDROME BETWEEN ADOLESCENTS AND CHILDREN?

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Introduction:
The data on the clinical-pathological spectrum and outcome of adolescent-onset steroid-resistant nephrotic syndrome (SRNS) are limited. The aim of the study was to identify clinical or histopathological features or differences in outcome of idiopathic SRNS in adolescents comparing with children.

Material and methods:
We conducted a retrospective single-center study of 106 patients (48M/58F) with idiopathic non-familial SRNS. Histological findings were FSGS in 45.3%, mesangial proliferative glomerulonephritis (GN) in 20.8%,

membranoproliferative GN in 17.8%, minimal change disease (MCD) in 10.4%, membranous nephropathy (MN) in 5.7% patients. All SRNS patients were divided into 2 groups according to their age of onset: 1) childhood-onset (1-9.9 years; n=51); 2) adolescent-onset (10-18 years; n=55).

Results:

At the onset of SRNS median age of adolescents was significantly higher compared with children: 13.0 (11.0-14.5) vs. 5.0 (3.2-8.0) years ($p<0.0001$) with similar frequency of increased serum creatinine: 38% vs. 28.6% ($p=0.3$) and hematuria: 87.3% vs. 72.5% ($p=0.16$). Median duration of follow-up was significantly lower in adolescent-onset than in childhood-onset group of patients: 34.8 (19.2; 46.8) vs.42.0 (24.0; 60.0) months ($p=0.04$). Median proteinuria at the time of kidney biopsy was not different significantly between adolescents and children: 2.9 (1.3; 7.4) vs. 3.0 (1.6; 5.7) g/1.73m^2/d ($p=0.73$).Adolescents compared with children had significantly higher frequency of MN: 10.9% vs. 0% ($p=0.03$) and significantly lower of MCD: 3.6% vs. 17.6% ($p=0.03$) with equal proportion of FSGS: 47.3% vs. 43.1% ($p=0.7$), interstitial fibrosis: 73% vs. 55% ($p=0.07$) and arteriolosclerosis: 18% vs. 14% ($p=0.6$). The combined rate of complete and partial remission achieved on calcineurin inhibitors (CNIs) (cyclosporine, tacrolimus) in adolescent-onset FSGS was not different significantly compared with childhood-onset group: 39% vs. 55% ($p=0.37$). The rates of chronic renal failure with eGFR <60 mL/min/1.73m^2 at the last follow-up and median annual slope of eGFR decline were similar between adolescents and children: 10.9% vs. 23.5% ($p=0.12$) and -1.3 (-7.7; 2.7) vs. -2.8 (-8.9; 0.3) mL/min/1.73m^2 per year, respectively ($p=0.19$).

Conclusions:

Adolescent-onset of idiopathic SRNS differs from the childhood-onset in having only higher proportion of MN and lower rate of MCD without other clinical-pathological features with equal response to CNIs in FSGS and similar outcome of the disease.

P - 376 THE NEGATIVE INFLUENCE OF ALLERGY ON IDIOPATHIC NEPHROTIC SYNDROME IN CHILDREN

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Introduction:

The aim of the study was to assess the influence of allergy on the course of idiopathic nephrotic syndrome (INS) in children.

Material and methods:

The study was performed in 19 children (9 girls and 10 boys) aged 4.8±2.6 years with the first bount of nephrotic syndrome. Before starting of glucocorticosteroids (GCS) treatment in all patients medical history of allergy was evaluated and serum level of IgE (IgE) and specific IgE (sIgE) for 20 food and 20 inhalled allergens were measured. During 12 months observation, time of maintain proteinuria, number of relapses and days without GCS were analyzed.

Results:

Positive allergic history was found in 9 children (47.4%): allergic dermatitis in 3, recurrent obstructive bronchitis in 3, skin rash in 2, asthma in 1 child. Serum level of IgE was elevated in 8 children (from 17 to 493 KU/L, median 53.9 KU/L;). Elevated serum level of sIgE was observed in 10 (53%) children. Time of maintain proteinuria was 9±3.14 days, number of relapses 2.04 ±1.67/patient/year. In children with elevated serum level of IgE in compare to children with normal serum level of IgE the higher number of relapses was observed (2.62±1.18 vs 1.36±1.56, $p=0.073$). Number the days without GCS was from 0 to 212 median 45. Possitive correlation between elevated serum level of IgE and number of INS relapses during one year observation was found ($R= 0.42$ $p=0.013$) and negative between positive allergic history and number of the days without GCS ($R= -0.37$, $p=0.026$).

Conclusions:

Allergy predisposes to recurrences of proteinuria in patients with INS.

P - 377 WATER HANDLING IN CHILDREN WITH NEPHROTIC SYNDROME

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Introduction:

Water retention in nephrotic edema is attributed to primary water-and sodium retention, although many reports demonstrated hyponatraemia, suggestive for a water retention predominant over sodium retention. Decreased free water clearance can be related to inappropriate vasopressin suppression, and or hypersensitivity to vasopressin. Research in children has mainly concentrated on primary versus secondary sodium retention (overfilled versus underfilled theory). This study aimed to further elaborate on the pathophysiologic mechanism involved in water handling.

Material and methods:

Eighty children with nephrotic syndrome (NS) in remission (n= 35) and nephrotic state (n=45) received a waterload , followed by hypotonic fluid perfusion to suppress endogeneous vasopressin levels. Nephrotic patients were subdivided into hypovolemic and hypervolemic patients, depending on circulating plasma renin activity. Water loading test was performed to induce hypervolemic state using a standardised protocol. Blood tests were done at 0,1,2 hours for vasopressin levels.

Results:

Plasma vasopressin levels were significantly decreasing after the water loading in both NS (hypo and hypervolemic group) and remission group (mean ±SD at 0 hour: 4.1±2.6, 7.4±5.4, 4.1±2.7; at 2 hours: 1.4±0.9, 1.9±1.1, 1.7 ±2.6, respectively)but should not result in appropriate diluting capacity in the hypovolemic NS patients. This mechanism is not vasopressin-related since vasopressin level was appropriately depressed after water load.

Conclusions:

Pathogenesis of waterhandling in nephrotic oedema is more complex than just the overfilled versus underfilled theory. Patients with hypovolemia have inappropriate free water clearance than cannot be explained by the inappropriate decrease in vasopressin.

P - 378 COMPARING CYCLOPHOSPHAMIDE AND RITUXIMAB IN STEROID DEPENDENT NEPHROTIC SYNDROME

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Introduction:

Compare time to first relapse after treatment of steroid dependent/frequently relapsing nephrotic syndrome with either a course of oral cyclophosphamide or IV rituximab

Material and methods:

Retrospective analysis of all patients between 01.01.2006 and 31.03.2015 with steroid dependent/frequently relapsing Nephrotic syndrome who received either 3mg/kg for 8 weeks or 2mg/kg for 12 weeks cyclophosphamide, or 1 to 2 infusions of 750mg/m2 rituximab. The time to relapse was compared.

Results:

84 patients (male=55) with a mean age of 6 (range 1 to 15 years) received a course of cyclophosphamide and 42 patients (male=34) with a mean age of 10 (range 5 to 16 years) received rituximab.

At 6 months 49% of patients in the cyclophosphamide group had relapsed once, For rituximab, 15% of patients had relapsed.

By 12 months 64% of patients in the cyclophosphamide group and 45% in the rituximab group had relapsed once. Median time to relapse for cyclophosphamide group was 7 months (range 0 to 85 months) compared to 19 months (range 1 to 83 months) in the rituximab group.

All patients who received cyclophosphamide were on prednisolone only, 82% of them were weaned off.
Patients who received rituximab were on prednisolone (n=13) Prednisolone and CNI (n= 18), prednisolone and MMF (n=9) or prednisolone + CNI + MMF (n=2). 88% of patients weaned off prednisolone, 85% of patients weaned off CNI and MMF.
Conclusions:
Despite the cohort receiving rituximab being biased to more difficult patients, relapsing despite 2 or more medications, remission rate with rituximab compared favourably to cyclophosphamide with less apparent side effects. Further trials are needed to prospectively compare rituximab with cyclophosphamide.

P - 379 COMPARATIVE EFFICACY AND SAFETY OF TACROLIMUS AND CYCLOSPORINE IN STEROID-RESISTANT NEPHROTIC SYNDROME DUE TO FOCAL SEGMENTAL GLOMERULOSCLEROSIS IN CHILDREN

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Introduction:
The data on comparative efficacy of tacrolimus (TAC) and cyclosporine (CsA) therapy in children with steroid-resistant nephrotic syndrome (SRNS) due to focal segmental glomerulosclerosis (FSGS) are very limited. The study was conducted to compare efficacy and safety of TAC and CsA in children with SRNS and FSGS.
Material and methods:
A retrospective study included 24 children (16F/8M) aged 11.0 (6.5; 13.0) years with SRNS due to FSGS. All patients were divided into 2 groups according to the medications: 1) TAC (n=10); 2) CsA (n=14). The initial TAC dose was 0.1 mg/kg/24h to achieve a target trough level of 5-10 ng/ml and CsA - 5 mg/kg/24h to keep a target level of 80-150 ng/ml.
Results:
Prior to the initiation of therapy children on TAC in comparison with patients on CsA had no significant differences in median age: 12.5 (7.5; 16.0) vs. 10.5 (5.5; 11.3) years (p=0.32), frequency of hypoalbuminemia <25 g/l: 30% vs. 42.9% (p=0.68), median eGFR: 117.0 (106.0; 141.3) vs. 124.0 (105.5; 153.0) ml/min/1.73m^2 (p=0.48), rate of sclerosis ≥40% glomeruli: 33.3% vs. 15.4% (p=0.61).The time from diagnosis to initiation of TAC treatment was significantly longer in comparison with CsA: 7.0 (2.5; 33.8) vs. 1.0 (0.5; 9.0) months (p=0.03). TAC was used as the 3rd line immunosuppressive agent significantly more often compared with CsA: 40% vs. 0% (p=0.02). The proportion of using TAC as the 1st and 2nd line of treatment was comparable with CsA: 30% vs. 57.1% (p=0.24) and 30% vs. 42.9% (p=0.68). The combined rate of complete and partial remission of disease achieved on TAC was similar to CsA at 6 and 12 months of treatment: 60% vs. 71.4% (p=0.68) and 75% vs. 83.3% patients (p=1.0). The rate of nephrotoxicity was similar in children on TAC and CsA: 33.3% vs. 35.7% (p=1.0).
Conclusions:
Our findings suggest that TAC may be alternative to CsA for the treatment of SRNS due to FSGS in children with comparable efficacy and rate of nephrotoxicity.

P - 380 EFFICACY OF CYCLOSPORINE TREATMENT IN CHILD WITH NEPHROTIC SYNDROME DUE TO NAIL-PATELLA SYNDROME

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Introduction:
Nail–patella syndrome (OMIM #161200) is a rare autosomal-dominant disorder due to mutations in the gene *LMX1B*, a transcription factor important for the development of podocytes. The disease characterized by the association of nail dysplasia, bone abnormalities and renal involvement (proteinuria with occasional nephrotic syndrome, hematuria) with progression to ESRD in 30% of cases by the 3rddecade of life.
Material and methods:
We report an efficacy of cyclosporine (CsA) treatment in an 11-year-old girl with nephrotic syndrome due to nail-patella syndrome.
Results:
A girl, first child of healthy unrelated parents, had bilateral elbow contractures, hypoplastic patella of both knees, dystrophic fingers and toenails, and managed with clinical diagnosis of nail–patella syndrome. She had isolated proteinuria (0.48 g/d) since age of 2 years, which increased to nephrotic range by the age of 11 years. The child was treated with ACE inhibitors (0.2 mg/kg/d) at the local hospital without effect on proteinuria. On admission to our Renal Clinic at age of 11 years the girl had nephrotic syndrome with proteinuria 2 g/d, hypoalbuminemia 26 g/l without oedema. Blood pressure was 100/60 mmHg. Her renal function was normal with serum creatinine level 41μmol/l and eGFR 165 ml/min/1.73 m^2. Renal biopsy showed focal segmental glomerulosclerosis with 1/9 global and 2/9 segmental sclerosed glomeruli without tubular athrophy, interstitial fibrosis and vascular lesion. Immunofluorescence examination was negative. Electron microscopy showed presence of specific for nail-patella syndrome glomerular lesion - collagen fibers irregularly distributed within thick glomerular basement membrane, diffuse effacement of podocytes foot processes were described. Treatment with CsA was started at the initial dose of 3.5 mg/kg/d that was increased gradually to 6 mg/kg per day to achieve a target trough level of 80-150 ng/ml. Partial remission of nephrotic syndrome was obtained at the 4 week of CsA therapy (proteinuria 0.8 g/d, serum albumin level 33 g/l). At the 10 month of CsA treatment complete remission of nephrotic syndrome was achieved (proteinuria 0.2 g/d, serum albumin level 35 g/l). The girl had stable renal function with serum creatinine level 49μmol/l and eGFR 144 ml/min/1.73 m^2.
Conclusions:
Treatment with CsA might be a reasonable option for patients with nephrotic syndrome due to nail-patella syndrome who don't respond to ACE inhibitor therapy. We speculated that CsA efficacy in the index patient may be explained by its action on podocyte dysfunction due to *LMX1B* dysregulation.

P - 381 SUCCESSFUL TREATMENT OF DENSE DEPOSIT DISEASE USING RITUXIMAB: A PEDIATRIC CASE REPORT

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Introduction:
Dense-deposit-disease(DDD) is a destructive renal disease that leads to renal failure within 10 years of diagnosis in about half of affected patients. Rituximab is a chimeric monoclonal antibody against the CD-20 antigen

on the surface of B-lymphocytes. It binds to CD-20 and causes cell death by antibody and complement mediated cytotoxicity.

Material and methods:

We present a patient with DDD who was resistant to various treatments, but improved with rituximab.

Results:

A 10-year-old girl admitted with progressive generalized edema for three weeks. Her past medical and family histories were unremarkable. Physical examination findings were normal except facial swelling and pitting edema of lower limbs. Blood-pressure was normal. First laboratory tests revealed hypoalbuminemia(1.2g/dl), hyperlipidemia, low C3-complement level(C3c), normal C4-complement level. Urinary(u) sediment contained 78 erytrocytes with 8 leukocytes/hpf; culture was sterile. U-protein/creatinine was 14.5 mg/mg. Renal biopsy revealed prominent C3c staining along the glomerular basement membrane(GBM) and also within the mesangium, without immunoglobulin deposition on immunofluorescence. Electron microscopy revealed GBM thickening, subepithelial and intramembraneous electron-dense deposits. Initially, the patient received oral prednisolone at a dose of 60 mg/m^2/day. When renal biopsy resulted, pulse methylprednisolone(a dose of 1000mg) was given on six alternate days. At the 6th week of treatment, cyclophosphamide was added to alternate day prednisolone. Although the regression of the generalized edema, hypoalbuminemia, microhematuria, nephrotic-range proteinuria and hypocomplementemia persisted. A remission could not be obtained after the treatments with intravenous cyclophosphamide, oral cyclosporine and mycofenolat mofetil. In the fourth year of her admission, rituximab was given 375mg/m^2 weekly for 4 consecutive weeks. After six weeks of rituximab therapy, C3c elevated and u-protein/creatinine ratio decreased. Our patient is still in remission at 12 months after the treatment of rituximab. Serum-C3c level is normal and urinary protein/creatinine ratio is 0.46 mg/mg.

Conclusions:

Rituximab could be proposed as a treatment choice of DDD.

P - 382 SERUM LEVELS OF 25/OH/D IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME

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Introduction:

The patients with chronic renal diseases are at increased risk of vit D deficiency. In children Vit D deficiency contributes to the developing of osteomalacia and osteoporosis. The long- term treatment with glucocorticoids, poor dietary intake, urinary loss of vit D – binding protein may cause Vit D deficiency in children with idiopathic nephrotic syndrome/NS/. Our aim was to estimate the 25/OH/D levels in children with NS during episodes of relapse or remission.

Material and methods:

We studied 25 children(11 girls and 14 boys) aged 1-17(mean age 8,8 ±1, 9) with idiopathic NS and normal renal function. Serum levels of 25/OH/D, PTH, albumin, calcium, phosphate and alkaline phosphatase were assayed.

Results:

We found a severe Vit D deficiency(9,18±1,23nmol/l) in five children, who were in relapse and receiving steroid therapy. In five children in remission, but still receiving steroid therapy, Vit D insufficiency (level 36,90±12,80 nmol/l) was established. Nine of the children in remission and free of steroid therapy had normal 25/OH/D levels(59,56±11, 75nmol/l). The serum levels of 25/OH/D showed a positive and significant correlation with the levels of serum albumin and the dose of steroid therapy($r = 0,71$; $r = 0,77$; $p< 0,0001$).

Conclusions:

We found a severe Vit D deficiency in our patients during period of relapse. The level of 25/OH/D remains low even after achieving remission with ongoing corticosteroid therapy and normalizes after prolonged remission. The children with NS have a high risk of Vit D deficiency. Supplementation with Vit D is recommended in conditions of Vit D deficiency to prevent bone damage.

P - 383 THE GUT-KIDNEY CONNECTON IN PEDIATRIC IDIOPATHIC NEPHROTIC SYNDROME

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Introduction:

Pediatric idiopathic nephrotic syndrome (INS) is defined as an increase in glomerular permeability leading to massive proteinuria, hypoalbuminemia, dyslipidemia and generalized edema. Although its etiology remains unknown numerous reports have highlighted a strong association between INS and atopic diathesis. Among patients with INS almost 50% have clinical signs of an atopic disease, with or without elevated sIgE level. Starting from this finding some authors have tried a diet of exclusion, which resulted in decreased proteinuria, but does not significantly reduced the number of relapses. However, no study so far has examined the link between INS and food intolerances.

Material and methods:

Three patients at the onset of INS, aged 1, 7 and 12 years. Both allergy (sIgE) and food intolerance (sIgG4) tests were performed. In addition to prednisone the treatment protocol was focused on: reducing intestinal inflammation, restoration of the balance of systemic inflammatory response and gut microflora. All patients were placed on a diet of exclusion which removed dairy products, gluten and all allergenic foods.

Results:

In all three cases of INS the exclusion from the diet of gluten and dairy product and of foods for which there was an immune reaction (IgE or IgG4) led to rapid decrease of proteinuria, allowed the reduction of the total duration of corticotherapy and prevented the appearance of relapses over a period of one year. There was no significant correlation between IgE and IgG4 reaction to foods.

Conclusions:

There are strong evidence today about the association between food sensitivity, altered gut microbiota, intestinal inflammation and immune-related conditions in children (i.e. nephrotic syndrome, celiac disease). The presence of sIgE or sIgG4 reaction to foods may represent a marker of increased intestinal permeability due to intestinal inflammation and altered microbiota. Therefore, restoration of intestinal health may be the cornerstone of treatment of many immune-related diseases including INS.

P - 384 RITUXIMAB IN DIFFICULT PAEDIATRIC NEPHROTIC SYNDROME - KOLKATA EXPERIENCE

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Introduction:

To retrospectively analyze the utility of rituximab in a multi centre cohort of difficult nephrotic syndrome (NS).

Material and methods:

Data were collated from May 2011 to 2014. Children with either steroid resistant or steroid dependent / frequently relapsing NS treated with

rituximab were identified. Complete response (CR) for SRNS was defined as normalisation of serum albumin and urinary protein creatinine ratio (UPCR) whereas for partial response (PR); 50% improvements in these parameters with albumin ≥ 2gm/dl. In cases of SDNS/FRNS; CR was defined as stoppage of steroid and absence of relapses for at least a year and PR as discontinuation of steroid without any relapses for ≥ 6 months or reduction in steroid threshold by ≤ 50%.

Results:

24 children (45% male) were identified (SRNS =10, SDNS/FRNS =14). Majority were minimal change (MCNS) (59%) followed by focal segmental glomerulosclerosis (FSGS, 27%). Median age was 7.9 (Range 2.5 – 16.5) years with median follow up post rituximab 275 (Range 13 to 720) days. Among the SRNS, serum albumin rose from median 1.85 (Range 1 – 2.8) to 2.35 (Range 1.3 -4.5) g/dl, (p=0.06) and urinary PCR fell from median 12.9 (Range 7.8 – 38) to 10.2 (Range 0.3 -32) p= 0.15. Overall two SRNS achieved CR and another two PR. Steroid threshold among SDNS/FRNS fell from median 0.42 (Range 0.2 – 1) to 0.03 (Range 0 – 0.5) mg/kg, p =0.0007 and dose of steroid at last follow up fell median 0.6 (Range 0.2 – 2.3) to 0.18 (Range 0-1.1) mg/kg] p =0.02. 64% of SDNS/FRNS (n=9) did not have any relapse during the follow up period and median time to first relapse was 6 (Range 1.8 – 11) months. For the nine children who completed at least 6month follow up three were off steroid and three on steroids half their original threshold.

Conclusions:

Rituximab was demonstrated to be useful in difficult nephrotic syndrome with overall 72.7% (n=17) showing either CR or PR.

P - 385 RITUXIMAB EXPERIENCE OF A TERTIARY REFERRAL CENTER FOR DIFFICULT-TO-TREAT NEPHROTIC SYNDROME

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Introduction:

Rituximab (RTX) has been proposed as an alternative treatment modality for steroid dependent nephrotic syndrome (SDNS), frequently relapsing nephrotic syndrome (FRNS) and steroid resistant nephrotic syndrome (SRNS).

Material and methods:

We evaluated the data of SDNS, FRNS and SRNS patients under RTX treatment. Initial RTX course consisted of 2-4 weekly infusions at the dose of 375mg/m2.

Results:

Nineteen patients (12 girls, 7 boys) were included in the study. The mean age of the patients was 13±4.9 years (range; 2.5-20.1 years). The median age of NS diagnosis was 4 years (range, 1.4-14.6 years). Renal biopsy performed to all patients before RTX and revealed focal segmental glomerulosclerosis in 11, minimal change disease in 8 patients. A total of six patients were categorized as SRNS, two patients as FRNS and 11 patients as SDNS according to steroid response. All SRNS patients were also resistant to calcineurin inhibitors (CNI). Mean duration of all patients between nephrotic syndrome and initial RTX dose was 6.5±4.5 years. The mean age of RTX treatment was 12.01±4.51 years (range, 2.25-18.66 years). Transitory side effects were observed in two patients (throat soarness, erythematous rash; respectively). With the cessation of the infusion, symptoms resolved spontaneously. Median duration of follow-up after RTX treatment was 12 months (1-44 months). Seven patients received regular maintenance treatment every 6-9 months and the rest received irregular maintenance treatment. At last visit, four out of six SRNS patients, one out of two FRNS and 10 out of 11 SDNS patients were in remission for a median period of 12.5 months (6-38 months). In SDNS and FRNS group, steroids and CNIs could be stopped in five and three patients, respectively.

Conclusions:

Rituximab seems to be effective and safe treatment option for difficult-to treat nephrotic syndrome patient groups.

P - 386 STUDIES ON MUTATIONAL ANALYSIS OF 18 GENES IN CHINESE CHILDHOOD-ONSET STEROID-RESISTANT NEPHROTIC SYNDROME

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Introduction:

A few genes have been identified to be causative for congenital and infantile steroid-resistant nephrotic syndrome (SRNS),however, genetic screening for childhood-onset SRNS(aged 1-13years) has been taken only a little attention.Aim of the study was to assess the frequencies of mutations in 18 genes reported as possible causes of SRNS among a cohort of children with this disease with onset between the ages of 1 and 13 years.

Material and methods:

Mutational analysis was performed to sequence target 18 genes(*NPHS1*, *NPHS2*, *CD2AP*, *PLCE1*, *ACTN4*, *TRPC6*,*INF2*, *WT1*,*LMX1B*,*LAMB2*, *LAMB3*,*GLA*, *ITGB4*,*SCARB2*,*COQ2*,*PDSS2*,*MTTL1*, *SMARCAL1*)using a PCR-based MassArray technology in 38 patients.The cohort included 10 sporadic cases and 28 familial cases abtained from 7 families with SRNS aged 1-13years.

Results:

Analysisrevealed mutations in expected genes such as *NPHS1* and *NPHS2* in7 of 38 patients (18%).Of these,a pathogenic mutation of *NPHS1* was detected in 3 of 7 families and a patient without family history(42% familial cases,10% sporadic cases,13% overall), who all carried a heterozygous missense mutation(p.E447K).In addition,a missense *NPHS2* mutation(p.R291W)which was also disease-causing was identified In 2 patients from another family(14% familial cases,0% sporadic cases,5% overall). The mutations of remaining 16 genes were not found.

Conclusions:

Our results reveal a low prevalence of pathogenic mutations in NPHS1 and *NPHS2* genes in Chinese childhood-onset SRNS.These genetic mutations seem to be a rare cause of child-onset SRNS,however,it suggests genetic mutations remain playing a underlying role in the pathogenesis of children-onset SRNS.

P - 387 LONG-TERM OUTCOME OF STEROID-SENSITIVE/STEROID-DEPENDENT FREQUENTLY RELAPSE NEPHROTIC SYNDROME IN CHINESE CHILDREN: A SINGLE-CENTER STUDY

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Introduction:

To evaluate the outcome of children suffered steroid-sensitive/steroid-dependent frequently relapse nephrotic syndrome [FR(SS/SDNS)] in a single-center in China.

Material and methods:
He hospitalized children diagnosed with FR(SS/SDNS) in our center in China were enrolled in this study. Medical records of those patients were collected and outcome was evaluated after 6 months to 6 years follow-up.
Results:
A total of 243 patients diagnosed with FR(SS/SDNS) were involved in this study and the median follow-up period was 28.8 months. 88 cases used corticosteroid only, without immunosuppressant. 67 (76.1%) of them applied full dose of corticosteroid again and the ratio of proteinuria remission was 92.5%. 155 cases were treated with immunosuppressant. The most common choice was cyclosporine A (CsA) (42.0%), followed by tacrolimus (FK506) (48.0%) and cyclophosphamide (CTX) (33.0%). The patients treated by FK506 got the highest remission rate (88.9%), followed by CsA (88.2%) and CTX (80.5%), and there was no statistical significance ($P>0.05$). The relapse rate of the children treated by CsA (62.2%) was the highest, but there is no statistical significance among FK506、CsA and CTX ($P>0.05$). During treatment, the relapse rate of the children treated by CsA was remarkably higher than by CTX ($P<0.001$). At the end of the follow-up, 218 cases (89.7%) were involved. 78.0% of them could achieve complete remission and 14.7% children could reach partial remission.
Conclusions:
The remission rate of FR(SS/SDNS) treated by FK506 and CsA is 88.9% and 88.2% respectively. The relapse rate among the children treated by CsA (62.2%) is the highest. During treatment, the relapse rate of the children treated by CsA is remarkably higher than by CTX. 78.0% of cases with FR(SS/SDNS)could achieve complete remission after treated by corticosteroid and immunosuppressant.

P - 388 THE PREDICTOR FACTORS OF STEROID DEPENDENT AND FREQUENT RELAPSES IN SSNS

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Introduction:
The most common cause of pediatric idiopathic nephrotic syndrome (NS) is minimal change disease (MCD), which is generally responsive to steroid therapy. Empirical steroid therapy is given to patients with a high probability of having MCD without confirmation of the diagnosis by renal biopsy. The aim of this study was to identify characteristics of patients with steroid sensitive nephrotic syndrome (SSNS) and a high risk of frequent relapsing (FR) or steroid dependent (SD).
Material and methods:
We analyzed 42 children with idiopathic NS. The follow-up was 4.0 years. Two different steroid regimens were used: the long steroid course (pred-long) (prednisone 60 mg/m2/24h for 6 weeks followed by alternate-day prednisone 40 mg/m2 for 6 weeks with tapering by 15 to 20 mg/m^2) and the short steroid treatment course (pred-short) (prednisone 60 mg/m2/24h for 4 weeks followed by alternate-day prednisone 40 mg/m2 for 4 weeks with tapering by 15 to 20 mg/m^2).
Results:
In this study 20/42 of the patients were classified with FR/SD. FR/SD patients were younger at onset compared to non-FR/SD patients (4.4±3.1 years vs 8.4±4.1 years, $p<0.005$). Males were more numerous in the FR/SD group (69% vs. 38%, $p = 0.03$). No differences were found regarding hematuria, hypoalbuminemia or remission time.
Conclusions:
In our pediatric population the high risk of FR/SD was based on low age at onset and male gender, while there was not association with the length of steroid therapy.

P - 389 LONG-TERM OUTCOME OF STERIOD-SENSITIVE NEPHROTIC SYNDROME IN CHINESE CHILDREN: A SINGLE-CENTER STUDY

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Introduction:
To evaluate the outcome of children suffered steroid-sensitive nephrotic syndrome (SSNS) in a single-center in China and to identify risk factors for frequently relapse in those patients.
Material and methods:
The hospitalized children diagnosed with SSNS in our center in China were enrolled in this study. Medical records of those patients were collected and outcome was evaluated after 6 months to 6 years follow-up. Cox-regression was performed to analysis the risk factors of frequently relapse
Results:
365 childhood patients with the initial episode of primary NS were treated by corticosteroid. A total of 288 patients (78.9%) showed sensitive to steroid were included in this study. For the 288 cases with the initial episode ofSSNS, the median time of proteinuria remission was 9 days. The duration of using full dose of corticosteroid was 6 weeks and the median course of treatment was 12 months. At the end of study with a median 37.6 months follow-up, 228 cases (79.1%) were involved, 103 cases (45.2%) of which with no relapse and 77 cases (33.8%) with cessation of corticosteroid. There were 125 cases (54.8%) had relapses and 48 cases (21.1%) had frequent relapses. The COX regression identified IgG level lower than 1.5g/L and first remission time cost more than 9 days as the independent risk factors for frequently relapse.
Conclusions:
There are 78.9% children with primary NS responded to corticosteroid in the initial episode. With the treatment of full dose corticosteroid applied for 6 weeks and 12 months duration of treatment, 45.2% cases show no relapse, among which 33.8% cases with cessation of corticosteroid. This result points out the key to reduce the relapse in initial episode of NS is full dose and long-term of therapy. 21.1% cases suffer frequently relapse. IgG level lower than 1.5g/L and first remission time costs more than 9 days are independent risk factors for frequently relapse.

P - 390 TOXIC TUBULAR NECROSIS - RARE CAUSE OF NEPHROTIC SYNDROME IN CHILDREN

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Introduction:
Various treatments in children (cyclosporine, tacrolimus, ACE inhibitors, aminoglycosides, amphotericin B, cisplatin, contrast agent) may produce renal side effects. The most common are acute kidney injury (AKI) with disturbances of salt and water metabolism.
Material and methods:
CASE REPORT: We present two cases of nephrotic syndrome induced by nephrotoxic substances. First is an infant, 5 months old, who came with generalized edema. The child had been treated for a pneumonia with Gentamicin for 12 days in another hospital. In the admission presented clinically generalized edema, oliguria (0,23ml/kg/h), and biologically AKI pIIIRifle (GFR = 7,48 ml/min/1,73m²), dislipidemia, hipoalbuminemia, hematuria and nephrotic proteinuria (>50mg/kg/day). We suspected a congenital nephrotic syndrome, but kidney biopsy

showed acute tubular necrosis in regenerating phase. The infant remained symptom-free, full recovery of kidney function after 1 week of peritoneal dialysis and was discharged. The second case is a girl, 16 years old, diagnosed with Basedow disease 3 years ago. Received therapy with Carbimazole with good evolution of thyroid disease. From august 2014 develop generalized edema. Was admitted in our clinic and diagnosed with nephrotic syndrome. We tried coticotherapy, without remission. Moreover, renal function decline was recorded (GFR Schwartz - 52ml/min/1,73mp). We made kidney biopsy wich showed tubular necrosis and interstitial fibrosis, without glomerular lesions. The patient required interruption of toxic treatment and thyroidectomy for save the kidney.

Results:

The both cases illustrates toxic effect of some drugs on renal tubules. The particularity of this cases consists of clinical and biological expression of acute tubular necrosis as nephrotic syndrome.

Conclusions:

It known that aminoglycosides give acute tubular necrosis. Carbimazole, an anti-thyroid drug, is quoted only in few cases of tubular necrosis. The both may trigger a spectrum of kidney disease including tubular, or interstitial nephritis, but in rare situation are combined with nephrotic syndrome, followed by acute or chronic renal failure.

P - 391 ADRENOCORTICOTROPIC HORMONE THERAPY FOR THE TREATMENT OF IDIOPATHIC NEPHROTIC SYNDROME IN CHILDREN AND YOUNG ADULTS: A SYSTEMATIC REVIEW OF EARLY CLINICAL STUDIES WITH CONTEMPORARY RELEVANCE

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Introduction:

Adrenocorticotropic hormone (ACTH) treatment for nephrotic syndrome (NS) re-emerged over the last decade. Current data are chiefly limited to adults with treatment-resistant NS. Largely unknown today is the existence of early clinical studies, following ACTH's introduction in the 1940s, showing sustained proteinuria response in idiopathic NS in predominantly pediatric, treatment-naïve patients. Before ACTH, patients suffered severe edema and high mortality rates with no reliable or safe treatment. ACTH dramatically altered NS management, initially through recognition of diuresis effects and then through sustained proteinuria remission. The current analysis synthesizes this early clinical literature to inform current NS patient management.

Material and methods:

A MEDLINE search used the MeSH terms "adrenocorticotropic hormone" and "nephrotic syndrome," with limits 1945 to 1965 and English. The chief inclusion criterion for analysis was the use of defined outcome standards for proteinuria response and/or diuresis with edema resolution. Studies were divided into 2 groups: short-term (≤28 days; daily administration) and long-term (>5 weeks; short-term initial daily followed by long-term intermittent). ACTH therapy and results were aggregated.

Results:

A total of 60 papers with 1137 patients were found. Fourteen studies (9 short-term, 5 long-term, N=419 patients) met inclusion criteria. The patients were predominantly pediatric (88%; 341/388 with ages given) with age ≤20 years. An initial response, defined as diuresis, occurred in 74% (265/356) of patients/treatment courses across 9 short-term ACTH studies. Analyzed in 8 of the 9 short-term studies, proteinuria response occurred in 56% (156/279) of patients/treatment courses. Across 5 long-term ACTH studies, proteinuria response was shown in 71% (63/89) of patients and was sustained up to 4.7 years following treatment.

Conclusions:

This inventory and re-evaluation of early clinical data broadens the evidence base of clinical experience with ACTH, informing current treatment strategies for patients with NS and aiding in the design of future studies. Funding for editorial support by Mallinckrodt Pharmaceuticals.

P - 392 LEVAMISOLE AND MYCOPHENOLATE MOFETIL ASSOCIATION IS SAFE AND TOXIC-DRUGS SPARER IN IDIOPATHIC NEPHROTIC SYNDROME.

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Introduction:

Primary nephrotic syndrome (NS) is the most common glomerular disease in children. Therapeutic options for frequent relapser and steroid-dependent patients are not uniform but frequently include long lasting treatment with prednisone and calcineurin antagonists.

Material and methods:

We analyzed patients treated with an association of mycophenolate mofetil (MMF) and levamisole. Steroid-resistant patients were not included. Ten patients were analyzed (male=50%, median age at diagnostic=3.9 years (2; 5)). Three patients were frequent relapsers and 7 were steroid-dependent. The median time from diagnosis to initiation of MMF and levamisole was 65.5 months (27.2; 96.7). Previous treatment included cyclosporine (7 patients), Rituximab (5 patients) and cyclophosphamide (1 patient). All patients had a full B cell repletion at the onset of the association. Two patients received tacrolimus at the onset of the treatment. Results were expressed as median (interquartile 25; 75).

Results:

The median length of the treatment was 380 days (277; 405). Steroids were stopped for 8 patients, 5 of them (50%) experienced 1 relapse within one year. Tacrolimus was stopped for the 2 patients. Annual steroid burden fell from 3155mg/m^2 (1520; 5370) the year prior MMF/levamisole to 1450mg/m^2 (873; 2607) the year during treatment. Two patients are still in remission 10 and 15 months after the withdrawal of all treatment. None of the patient experienced any serious adverse effect. Leukocytes and more specifically polymorphonuclear leukocytes decreased slightly but remained well within normal limits.

Conclusions:

The association of MMF and levamisole, was given to optimize the withdrawal of steroids and calcineurin inhibitor in patients with idiopathic nephrotic syndrome. No side effects were observed. Interestingly 2 patients remained free of treatment after withdrawal of mycophenolate and levamisole but the efficiency of this association needs larger studies to be demonstrated

P - 393 LEVAMISOLE-INDUCED NECROTIZING VASCULITIS IN A GIRL WITH NEPHROTIC SYNDROME: IT SCARES, BUT IT HEALS.

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Introduction:

Levamisole is used as immunomodulator in steroid-dependent nephrotic syndrome (SDNS) or frequently relapsing nephrotic syndrome (FRNS).

Material and methods:
A 6 year old girl begins with painful, rapidly progressive erythematous-purpuric plaques with central necrotic areas on both cheeks and earlobes. Four years ago, she was diagnosed (at 26 months of age) of nephrotic syndrome; after 3 months became steroid-dependent and oral levamisole (2.5 mg/kg/48h) was introduced. Because of frequent relapses she also received oral Cyclophosphamide (cumulative dose of 170 mg/kg), that allowed tapering doses of steroids.
Results:
After 3 years without significant side effects (levamisole, prednisone), she developed urticarial lesions and palpable purpura on the legs. At this time, two skin biopsies 3 months apart showed neurtophilic dermatosis suggesting Sweet Syndrome and leukocytoclastic vasculitis without IgA deposits, respectively.
During her illness regular blood tests with full blood count, renal, hepatic function and immunologic studies were normal. At the time of appearance of facial skin lesion ANCA (anti-MPO, PR3), IgM anticardiolipin antibodies and lupus anticoagulant got positive, with low levels of C3 and CH50. Levamisole-induced necrotic vasculitis was suspected, Levamisole discontinued and prednisone augmented to 1mg/kg/day, with complete recovery in 5 weeks time. She is doing fine after 3 months only on prednisone, at the same maintenance dose (0.2mg/kg/48h). ANCA, IgM anticardiolipin and lupus anticoagulant are still positive but with declining titres, complement levels have normalized.
Conclusions:
Levamisole has been a cocaine adulterant worldwide since 2002, and numerous cutaneous side-effects of levamisole have been published in adult consumers of cocaine since then.
Vasculitis in children treated with Levamisole is exceptional, but may appear in longer treatments (mean 24 months). It is important to recognize this adverse effect because rapid diagnosis and early discontinuation of the drug allows complete resolution within 2-3 weeks, although autoantibodies can remain positive for up to 14 months.

P - 394 A SURPRISING ETIOLOGY OF GROSS HEMATURIA IN A CHILD WITH MINIMAL CHANGE NEPHROTIC SYNDROME: NUTCRACKER SYNDROME

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Introduction:
Gross hematuria in any child with idiopathic NS is exceedingly rare .Given the risk of thrombosis in INS, renal vein thrombosis is considered in patients with significant hematuria. Gross hematuria is accepted one of the major renal biopsy criteria in nephrotic syndrome because of frequency of chronic glomerulonephritis.
Case description:
We are reporting an 11 years old girl with MCNS who was admitted with gross hematuria secondary to nutcracker syndrome.
11 years old girl admitted with edema. She underwent viral upper respiratory tract infection, 2 weeks ago. Physical examination revealed edema and normal blood preassure. Massive proteinuria, hypoalbuminemia, hypercolesterolemia and normal renal functions is detected in laboratory examination. Urinalysis revealed microhematuria. Serum complement-3, ASO and IgA levels were normal ranges. Antinuclear antibody, hepatitis B Ab, hepatitis C Ab and anti-HIV tests were negative. Gross hematuria and left flank pain was occurred after 2 days of her admittion. She had also history of recurrent left flank pain aggravated by physical activity. Renal venous doppler USG and renal MR angiography revealed nutcracker syndrome. Renal biopsy revealed IgM nephropathy is a variant of the MCNS.
Conclusions:
Most common type of nephrotic syndrome is MCNS in childhood. Gross hematuria, renal insufficiency, steroid-resistance and severe hypertension is most common biopsy criteria for diagnosis of chronic glomerulonephritis in children with nephrotic syndrome. Children with nephrotic syndrome occasionally present with gross hematuria. The frequency of macrohematuria depends on the histological subtype of nephrotic syndrome. It is more common in patients with chronic glomerulonephritis, especially membranoproliferative glomerulonephritis (MPGN) and IgA nephropathy. Nutcracker syndrome is characterized by impeded outflow from the left renal vein into the inferior vena cava due to extrinsic LRV compression, often accompanied by demonstrable lateral dilatation and medial narrowing. Symptoms are often aggravated by physical activity and commonly include hematuria, pain and orthostatic proteinuria.
We need to keep in mind that gross hematuria may be due to a reason other than glomerulonephritis in children with nephrotic syndrome. Nutcracker syndrome is one of the non-glomerolonephritic reasons for gross hematuria in MCNS.

P - 395 GROUP EDUCATION AND PEER SUPPORT IN NEPHROTIC SYDROME

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Introduction:
Nephrotic syndrome and associated treatments can place significant burden on caregivers and educating about disease prognosis, treatment options and side effects can be time and resource consuming for clinicians. We aimed to implement a carer information program to enhance knowledge about nephrotic syndrome and to analyse the effectiveness of this program with qualitative feedback forms before and after the education events.
Material and methods:
The care givers of all patients with a diagnosis of nephrotic syndrome seen by our unit in the last 7 years were invited to attend a 2 hour information evening. The structure of the event included an educational presentation by medical staff with question and answer session, a prolonged social break to allow informal peer discussions and networking, and a presentation by our departmental social worker on psychological impacts of chronic disease and support strategies.
All carers were invited to provide feedback prior to the event to help target education and following the event to assess its effectiveness.
Results:
Carers of approximately 20% of our prevalent nephrotic population attended the educational event.
The pre-event surveys highlighted multiple common areas in which carers sought further information including: definitions, medication side effects, and long term prognosis.
The post-event surveys indicated the event was highly successful. Responders on average rated the event 4.6/5 in meeting their expectations. Qualitative feedback was overwhelmingly positive with carers commenting that it was useful to have information repeated, a forum in which to address questions and the opportunity to share experiences and access peer support.
All carers who completed feedback forms indicated they would recommend the information night to other families.
Conclusions:
A targeted information event for carers of children with nephrotic syndrome is an effective way to provide additional education and facilitate peer support networks.

P - 396 EFFICACY OF RITUXIMAB IN CHILDREN WITH STEROID-DEPENDENT AND STEROID-RESISTANT NEPHROTIC SYNDROME

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Introduction:
Rituximab (anti-CD 20) has recently been introduced for the treatment of NS and was successfully used in both severe SRNS and SDNS. In this report we present a single-center experience with the RTX treatment in children with SD/SRNS.
Material and methods:
74 children with NS were followed (2011-2014). RTX was indicated in 8 patients. Those followed for at least 12 months after their last RTX infusion were enrolled in this retrospective study (6; 3 SDNS, 3 SRNS). RTX was indicated in case of failure and/or lack of response to immunosuppression. The cohort consisted of 2 patients with primary steroid resistance (FSGS), 3 with severe steroids/cyclosporine dependency (MCD), 1 with primary resistance to prednison (Hodgkin's lymphoma history, HL). The age of onset of NS was significantly lower in SDNS than SRNS (x=2.3y. vs. 11.6y., $p<0.01$), the median duration of SDNS pre-RTX was insignificantly longer compared to SRNS (x=10.3y. vs. 1.8y. p=0.30). RTX (375mg/m^2) was given every 1week-1month, 2-6 doses per patient in total.
Results:
No effect of RTX on proteinuria was observed in 2 children with SRNS despite complete CD19+ cell depletion (0%; 11.0g/day, 8.4 g/day respectively). In a 10y. old girl with FSGS progressive deterioration of renal function developed requiring dialysis within 2y. after RTX. On the other hand, in the patient with HL rapid resolution of proteinuria was observed (24.0g/day vs. 0.2g/day; $p<0.01$) after the first RTX infusion and sustained remission has been achieved for >2 years. RTX induced long-term remission for >1y. in 2 children with SDNS allowing immunosuppressives withdrawl. No relapse occurred despite CD19+ recovery. Finally, 1 patient with SDNS had a single relapse 6 months after RTX (CD19+ 12%).
Conclusions:
Our preliminary results confirm efficacy and good safety of RTX in SDNS in a small cohort of patients. However, RTX was ineffective in FSGS and failed to prevent progression of renal disease.

P - 397 A CASE OF DENSE DEPOSIT DISEASE WITH PSORIASIS IN A 2-YEAR OLD GIRL.

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Introduction:
Dense deposit disease (DDD) is a rare complement-mediated kidney disease, characterized by hematuria proteinuria and decrease of renal function in 50% of cases. Complement activation is involved in psoriatic pathogenesis too. We report a case of nephrotic syndrome due to DDD with psoriasis.
Material and methods:
The girl has a history of steroidresistant nephrotic syndrome and familial psoriasis (her father and grandmother also have a psoriasis vulgaris, and she has no relatives with renal disease). At age of 2 years she developed a hematuria and proteinuria 3 g/l, triggered by acute respiratory illness. Laboratory findings were moderate signs of nephrotic syndrome (proteinuria 1.5-3 g/day, hypoproteinemia 54 g/l, hypoalbuminemia 31 g/l, hypercholesterolemia 7,35 mmol/l) and hematuria with hypocomlpementemia (C3 0,17 g/l, C4 0,4 g/l) and normal renal function (serum creatinine 47 μmol/l, eGFR Schwartz 119 ml/min). Kidney biopsy showed double contours of glomerular basal membrane and positive immunohystochemichal staining for C3, electron microscopy showed intramembranous linear dense deposits. Steroid therapy and immunosuppressive therapy with mycophenolate and cyclosporine was not effective. We perform a next-generation sequencing with Roche 454 platform for analysis of selected regions of genes, involved in complement regulation system (CFH, CFI, CFB, MCP and THBD).
Results:
Next-generation sequencing of CFH, CFI, CFB, MCP and THBD genes did not discover any mutations. Level of anti-CFH antibodies was 103%. Despite the absence of mutation and antibodies, plasma CFH activity was undetectable. During 7 years we observe a permanent course of nephrotic syndrome, hypocomplementamia and psoriatic skin lesions. Steroids and immunosuppression stopped after 7 years of therapy because no influence on proteinuria and stable renal function.
Supported by Russian Science Fund, grant No14-15-00994.
Conclusions:
We suggest, that our case may demonstrate that clinical phenotype of extrarenal manifestations of complement disorder in DDD can include not only partial lipodystrophy, described before, but also psoriasis.

P - 398 THE EVALUATION OF HEARING IN PEDIATRIC PATIENTS WITH NEPHROTIC SYNDROME RECEIVING CYCLOSPORINE

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Introduction:
We aimed to evaluate the ototoxicity of cyclosporine A (CsA) in patients with nephrotic syndrome (NS).
Material and methods:
The data of pediatric patients with steroid dependent, frequently relapsing or steroid resistant nephrotic syndrome (SDNS, FRNS, SRNS), followed in pediatric nephrology department between 1995-2015 with a mean follow-up duration of 91.9±56.3 months were evaluated retrospectively. The patients receiving CsA and immunosuppressives other than CsA for at least 6 months formed two groups. Current age, age at first clinical presentation, gender, type of NS, duration and cumulative doses of immunosuppressives were noted. The hearing function of the patients were evaluated by pure tone audiometry and evoked otoacoustic emission tests(OET) in the remission period. Children with known previous hearing defect, inner ear trauma or surgery, recurrent otitis media and using hearing aid were excluded. The results were compared between the groups.
Results:
Twenty four patients(M/F:13/11) were enrolled into the study. Five of the patients were SRNS, 1 was FRNS and 18 were SDNS. There were 12 patients in both groups. Current age, age at first clinical presentation, gender, number of relapses, serum creatinine, sodium, potassium, calcium and albumin levels at the time of hearing tests were similar between the groups. Cumulative dose and duration of steroid use were significantly higher in CsA group (p:0.020,0.045, respectively). Patients in the CsA group were more frequently exposed to angiotensin converting enzyme inhibitor(0.014) and mycophenolate(p:0.038) and patients in non CSA group were more frequently exposed to cyclophosphamide. Ratio of exposure to other treatment options(angiotensin receptor blocker, corticosteroids, levamisole, tacrolimus, mycophenolate and rituximab) were

similar between the groups. Thresholds for hearing at frequencies of 250, 500, 1000, 2000, 4000 and 8000 Hz, and the results of OET were similar between the groups and compatible with normal hearing.

Conclusions:

CsA is not responsible for sensorineural hearing loss in children with NS.

P - 399 LEVAMISOLE-INDUCED CUTANEOUS VASCULITIS IN A 10-YEAR OLD BOY WITH STEROID-SENSITIVE NEPHROTIC SYNDROME AND CELIAC DISEASE.

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Introduction:

The golden standard to treat children with steroid-sensitive nephrotic syndrome (SSNS) is corticosteroids. Up to 90% of them have relapses of which almost 50% have frequent relapses, placing them at risk for the adverse effects of corticosteroids. Levamisole is an immunomodulator used to diminish steroid doses in steroid-dependent patients or to prolong periods of remission. Very few side effects have been described, most frequent haematological abnormalities and cutaneous reactions.

On the occasion of a case report, the literature was searched to see whether there is an association between levamisole induced cutaneuous vasculitis in children with nephrotic syndrome and other auto-immune diseases.

Material and methods:

We report about a 10-year old boy with a history of celiac disease and idiopathic nephrotic syndrome who developed the rarely seen cutaneous vasculitis on the ear lobes after 2.5 years treatment with levamisole. The PubMed database was consulted with keywords “steroid-sensitive nephrotic syndrome - children - levamisole - cutaneous vasculitis - auto-immune”.

Results:

Seven patients with nephrotic syndrome and levamisole induced cutaneous vasculitis were found in the literature and compared to one another. The mean age of the children is 10 years, with the remarkable note that all but one are boys. When therapy was discontinued, the side effects disappeared spontaneously. The cutaneous symptoms appear with a sudden onset; typically involved are the ear lobes. There is a long latency, ranging from 1 to 3 years, between the start of the levamisole treatment and the appearance of the cutaneous vasculitis. Serology often shows positive antibodies, most frequently lupusanticoagulant (LAC) and p-ANCA. The pathogenetic mechanism provoked by levamisole is not totally understood, however activation of an immunological cascade with loss of tolerance to self-antigen is probable.

Conclusions:

Cutaneous vasculitis due to therapy with levamisole is a rarely described adverse effect in the treatment of SSNS. Involvement of the ear lobes is typically seen in all cases and appears after a long latency period. Side effects dissolve spontaneously when therapy is discontinued. In the literature we could find no significant association between children with nephrotic syndrome and the chance to develop other auto-immune diseases, more specific celiac disease, as was the case in our patient. More research is necessary to accept or reject this.

P - 400 NEPHROTIC SYNDROME IN A PATİENT WITH KAWASAKI DISEASE

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Introduction:

Kawasaki disease (KD) is a self-limiting systemic inflammatory disease that occurs predominantly in children younger than 5 years. Renal involvement has occasionally been reported in KD, usually consisting of sterile pyuria and trace proteinuria. Nephrotic syndrome (NS) has been reported very rarely in KD.

Case description:

Here, we report a 9 year old previously healthy boy admitted to our hospital with fever for past 10 days and a poor general condition.

Physicial examination showed erythematous tonsillitis, strawberry tongue, diffuse maculopapular rash, bilateral nonpurulent conjunctivitis, cervical lymphadenopathies, systolic murmur and edema of the hands and feet. Labaratory tests revealed elevated C-reactive protein and erytrocyte sedimentation rate, thrombocytosis, normal albumin level and no proteinuria. Echocardiography was normal. The child was diagnosed as KD and intravenous immunoglobulin (IVIG) was given with a dose of 2 g/kg. Acetylsalicyclic acid and ibuprofen therapy was also started. Although patient received IVIG, patient’s fever continued and coronary artery dilatation (CAD) were detected in repeated echocardiography. In addition nephrotic range proteinuria (38 mg/m^2/hr) and hypoalbuminemia (1.5 g/dL) developed after the 8thday of the hospitalization. Despite patient being treated with IVIG, due to develeopment of CAD (but not for the treatment of NS), pulse steroid treatment was given for 3 days and continued at a dosage of 2 mg/kg/day. The protein in urine was negative at the 7th day of steroid treatment. Then steroid therapy was tapered and stoped in 13th day of treatment. There was no relapse of NS in next 10 months.

Conclusions:

Although steroid therapy that was given for CAD improved NS also, due to respond to steroids in a short period and no recurrence of NS, we thought that NS in KD has a good prognosis and no need for steroid therapy, if there is no CAD resistant to treatment of IVIG as in our case.

P - 401 IMMUNOSUPPRESSIVE THERAPY IN PATIENTS WITH STEROID RESISTANT NEPHROTIC SYNDROME (SRNS) DUE TO NPHS2 AND SMARCAL 1 MUTATION

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Introduction:

Steroid Resistant Nephrotic Syndrome (SRNS) is most often associated with focal segmental glomerulosclerosis (FSGS) and a high risk of progressive chronic kidney disease (CKD). Most patients with hereditary SRNS are unresponsive to medication.

Material and methods:

We retrospectively evaluated data of 4 patients with hereditary SRNS associated with FSGS receiving immunosuppressive treatment, i.e. Cyclosporine A (CsA) or Tacrolimus (Tac), over a long treatment period in addition to ACE-inhibitors. Two patients had compound heterozygous mutations in the *NPHS2-gene*. Two siblings with Schimke syndrome had the same homozygous *SMARCAL1 mutation*.

Results:

Patient 1: PU at the age of 2 years (y), CsA-therapy at the age of 8 y, PU 6.5g/l. Reduction of PU below 1 g/l under treatment during the following three years, increase of s-Albumin (Alb) from 20 to 28-30 g/l. Five years later therapy was switched to mycophenolate mofetil (MMF) for 18 months.

Patient 2: Proteinuria during the first months of life; CsA at the age of 2y; PU 9.3 g/g crea decreased to 0.25 – 1.5 g/g crea during the following years. Ongoing immunosuppressive therapy until the age of 18.5 years; the s-Alb level increased from 24 to 32 – 37 g/l.

Patient 3: At the age of 6y, PU 8.9 g/l. CsA, later Tac resulted in reduction of PU to 0.5-1.5 g/l and an increase of s-Alb from 18 g/l to 35-43 g/l. During adenovirus infection one year later PU increased and immunosuppressive therapy was stopped.

Patient 4:PU at the age of 3 y. Tac-therapy at the age of 4y, reduction of PU from 10 to 2,8 g/l increase of s-Alb from 12 to 20-28 g/l; increase in PU one year later due to adenovirus infection.

Conclusions:

Add-on immunosuppressive therapy may be beneficial in selected cases of SRNS by reducing PU, edema formation and the frequency of hospitalization.

P - 402 PHENOTYPE-GENOTYPE HETEROGENEITY IN DENYS-DRASH SYNDROME AND FRASIER SYNDROME: EXPERIENCE IN BRUSSELS.

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Introduction:

Denys-Drash syndrome (DDS) and Frasier syndrome (FS) are characterized by male pseudohermaphrodism, progressive glomerulopathy, and development of genital or renal tumors.

Material and methods:

This study is a retrospective review of renal diseases related to *WT1* gene mutations in six patients (one boy and 5 girls) followed in our hospital.

Results:

Patient 1: A 8-year-old female child has steroid-resistant nephrotic syndrome (FSGS). Hemodialysis was started at age 10 years and she received a kidney transplant at age 11 years. At age 16 years, she was referred for primary amenorrhea. She had normal female external genitalia but abnormal internal genitalia. The caryotype was 46,XY. Mutational analysis of *WT1* showed the splice site mutation IVS9+5 G>A, (FS).

Patient 2: A 6-year-old female child was identified with heavy proteinuria. She had normal female phenotype and 46,XX karyotype. Renal biopsy demonstrated FSGS. Mutational analysis of*WT1* showed the splice site mutation IVS9+4 C>T (FS). She developed renal insufficiency at 15 years of age, and she was treated by PD. She is on a waiting list for a kidney transplant.

Patient 3: A 9-month-old female was admitted for nephrotic syndrome and renal insufficiency. She had a female phenotype and 46,XX karyotype. The exon 9 mutation nt1186G>A (DDS), was found. Biopsy showed Wilms'tumor and diffuse mesangial sclerosis. She was treated by binephrectomy and received a kidney transplant 2 years later.

Patient 4: A 4-year-old female was admitted for renal insufficiency and nephrotic syndrome. Karyotype was 46,XX. Biopsy demonstrated diffuse mesangial sclerosis. The exon 9 mutation nt1180C>T (DDS), was found. Hemodialysis was started at age 5 years and she received a kidney transplant 1 year later.

Patient 5: A 19-month-old male child was identified with unilateral Wilms'tumor fortuitously. He was treated by chemotherapy and right nephrectomy. He had a bilateral cryptorchidism and left streak gonad. At 6 years, he was identified for heavy proteinuria. The exon 9 mutation nt1372C>T (DDS) was found. He is followed closely.

Patient 6: A one-week-old female newborn was admitted for renal insufficiency, nephrotic syndrome and hypertension. The exon 9 mutation nt1284G>A (DDS), was found. She had normal female phenotype and 46,XX karyotype. She unfortunately died at age 3 months, after therapeutic discontinuation.

Conclusions:

There is a large phenotype and genotype heterogeneity in *WT1* gene mutations. *WT1* mutation analysis should be routinely done in children with steroid-resistant nephrotic syndrome, especially in cases with anomalies of genitalia. This is important for prophylactic and curative oncologic care. We suggest that all children with Wilms'tumor undergo urinalysis for proteinuria. If proteinuria is significant, *WT1*mutation analysis should be undertaken.

P - 403 OUTLINES OF CHILDHOOD NEPHROTIC SYNDROME IN ALBANIA

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Introduction:

Nephrotic syndrome (NS) is a frequent sort of kidney disease distinguished in children. To establish the models in children with nephrotic syndrome in our country, we retrospectively revised 27 nephrotic patients appraised and pursued-up in the pediatric hospital of Tirana in Albania. The proportion among males and females 2:1. The occurrence of idiopathic NS was 1 to five cases per 100,000 children/year, whilst the prevalence was 10 cases per 100,000 children.

Material and methods:

We studied children with NS detected and treated from 2006 to 2011 at the Nephro-Pediatric department of University Hospital Centre:"Mother Theresa", in Tirana. All children' parents gave the permission for the study. All medical evidence of patients were involved to complete data assortment, with a focus on principles needed to identify NS, counting edema, enormous proteinuria (>40 mg/m^2/hr or a urine protein/creatinine proportion >0,2 mg/mg) and hypo-albuminemia. Laboratory research comprised a test for proteinuria in urinalysis, 24-h urine and hematuria.

Results:

Six patients (22,2%) had presented respiratory tract infection, four (14.8%) tender abdomen, 1 (3.7%) profuse hematuria, three children (11,1%) were presented with hypertension, six (22,2%) were presented with periorbital oedema and the remaining 7 (26%) presented to the hospital with no complications. Twenty one (77,7%) children were susceptible to the initial steroid course and 6 (22,3%) patients were steroid resistant. Nine (33,3.5%) children remained in remission, whilst 12 (44, 4%) patients turned into steroid dependent from those who reacted.

Conclusions:

We concluded that the outlines of NS and the reaction to treatment detected in this survey did not diverge considerably from studies of other countries in the world.

P - 404 FOCAL AND SEGMENTAL GLOMERULOSCLEROSIS (FSGS) AND SUCCESSFUL LONG-TERM THERAPY WITH PLASMAPHERESIS

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Introduction:

The natural history of focal segmental glomerulosclerosis (FSGS) varies widely. E.g. the clinical course contains edema which are difficult to handle, proteinuria that is refractory to corticosteroids and other immunosuppressive agents and progressive loss of renal function. In steroid-resistent patients, the average time from onset of proteinuria to end-stage renal disease (ESRD) is 6-8 years, although wide variations occur.

Case description:

We wish to report on a patient with FSGS who developed ESRD despite various immunosuppressive agents and who impressively improved under weekly plasmapheresis over 2,5 years.

The 14 year old patient was diagnosed as having nephrotic syndrome in 2012. Treatment with prednisone was started, however, she did not react. After 2 months and exclusion of genetic causes of FSGS she received mycofenolate-mofetil and then cyclosporine, both without success. Additionally she received

antiproteinuric therapy. Under that regimen we experienced an increasing impairment of kidney function (eGFR = 15 ml/min/1.73 qm). As a last attempt to escape the impending need for dialysis, plasmapheresis was performed with 1.5 times her plasma volume. There was a rapid decrease of retention parameters, protkrea-ratio and an increase of S-albumin. Due to anew increasing proteinuria, the patient received rituximab twice additionally in January 2013 but with no significant improvement. Under continuing plasmapheresis renal function is unrestricted, the protein excretion varies from 1200 to 3500 mg/g Krea and the S-albumin is within the normal range. A few months ago plasmapheresis was changed from 10-day to 14-day-cycle, and an increasing proteinuria excretion with consecutive hypoalbuminemia was seen. This finding made us return to the more intensified therapeutic regimen.

Conclusions:

Ultimately, the underlying pathomechanism and efficacy of our therapy is not fully explained. Circulating factors like the soluble urokinase receptor (suPAR) as disease-causing agents are discussed, however, we found no such agent in our patient.

P - 405 END STAGE KIDNEY DISEASE IN CHILDHOOD AS FIRST CLINICAL PRESENTATION ASSOCIATED WITH A WT1 MUTATION – CASE REPORT

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Introduction:

We report a case of a 5 year old girl with a *WT1* mutation and atypical presentation in end stage kidney disease (ESKD) without evidence of preceding nephrotic syndrome.

Material and methods:

Retrospective chart review of a single case.

Case description:

The child presented at the age of 5 years with ESKD, oliguria, periorbital oedema, severe hypertension (150/114 mmHg) and soon became anuric. Biochemistries showed a creatinine of 914 umol/l, mild hypoalbuminaemia (26 g/l) and 4+proteinuria by dipstick. Renal ultrasound showed morphologically normal kidneys (length: 40th centile for age) with hyperechogenic cortex. Echo revealed dilatative cardiomyopathy. Her past medical history was unremarkable. She is the older of 2 children born to healthy parents who are first cousins.

She was treated with dialysis and subsequent kidney transplantation with an excellent allograft function to date.

The underlying cause for ESKD remained undefined initially. Renal ultrasound ruled out congenital abnormalities and renal scarring. No evidence of inflammatory or autoimmune processes was found. Histopathology only revealed advanced chronic renal changes. In order to assess genetic forms of glomerulopathies, a genetic analysis was performed for *NPHP1*, *NPHS2* and*WT1*. A heterozygous *de novo* missense mutation was identified in *WT1* Exon 8 c.1115G>A, p.Arg372Lys considered pathogenic. The child has normal female genitalia and female karyotype 46,XX. A subsequent ultraound 3 years later shows an atrophic right kidney with multiple small cysts and the left kidney could not be visualised any more.

Conclusions:

Presentation with ESKD without preceding nephrotic syndrome as late as 5 years of age is highly unusal associated with a *WT1* mutation. Genetic screening for hereditary glomerulopathies should be considered in patients with ESKD as first presentation in childhood with undefined cause.

P - 406 NEPHROTIC SYNDROME AND IDIOPATHIC THROMBOCYTOPENIC PURPURA.

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Case description:

A 7.5 year old Moroccan boy with steroid-dependent nephrotic syndrome minimal change lesions with more than 20 relapses developed relapsing idiopathic thrombocytopenic purpura (ITP).

At the age of 3 years old,nephrotic syndrome was diagnosed and treated with steroids (60 mg/m² QD for 6 weeks,40 mg/m² alternate day for 4 weeks, followed by steroid tapering) and went in complete remission. After steroid tapering, he developed several relapses. Treatment with cyclosporine (5 mg/kg) was introduced succesfully. At the age of 5 years during cyclosporine treatment the patient developed severe thrombocytopenia (33x10E9/L).Renal biopsy revealed minimal change lesions:40 glomeruli; IF: negative for IgA, IgG and C1Q. Trace IgM and C3. Bone marrow showed increased megakaryopoiesis with mild dysplastic changes of megakaryocytes, but was otherwise normal.

The diagnosis of ITP was made. Lack of compliance and analphabetism of the parents during the cyclosporine therapy, was the cause of several relapses with extreme proteinuria (4+), making reintroduction of steroids necessary. During steroid treatment the platelet count normalized, while during tapering ITP occured, making him became steroid dependent. At the age of 6 years, cyclosporine treatment was reintroduced and induced longterm remission for his nephrotic syndrome. Since several months he received frequently immunoglobulin infusions (1gr/kg) to restore the platelet count.

Conclusions:

To our knowledge, we present the first patient with minimal change nephrotic syndrome and ITP. The next step will be treatment with rituximab in order to improve both ITP and steroid-dependent nephrotic syndrome. A Pub Med search was conducted in the English-language literature using the keywords " nephrotic syndrome" and "ITP". A 15 year old patient with focal segmental glomerulonephritis, developed after 13 years ITP and was succesfully treated with rituximab. Additionally, a few cases with idiopathic membranous glomerulonephritis associated with chronic ITP were reported.

P - 407 RITUXIMAB IN CHILDREN WITH STEROID-DEPENDENT NEPHROTIC SYNDROME: EXPERIENCE OF ONE TERTIARY CENTER AND REVIEW OF LITERATURE

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Introduction:

Rituximab (RTX) is a promising new treatment option in children with difficult-to-treat steroid-dependent nephrotic syndrome (SDNS). We aimed to evaluate the experience of one tertiary center and to give an overview of the current literature on this subject.

Material and methods:

We retrospectively evaluated the efficacy and safety of RTX in children with difficult-totreat SDNS followed in our center. Age at diagnosis, type and duration of immunosuppression, age at administration,

dose of RTX, possible adverse events, number of relapses, duration of remission and number of B-cells after administration of RTX were analyzed.

Results:

Seven children with a mean age at diagnosis of NS of 4.7 (range 2.08 - 11.33) years and a mean age at administration of RTX of 15.05 (range 3.33 - 18.92) years were included. Before administration of RTX they had a mean number of relapses per year of 2.28 (range 0.82 - 4.80). At last follow-up (mean 2.05 years), we report a reduction of mean number of relapses per year to 0.94 (range 0 - 2.62), despite stop or lowering the dose of immunosuppressive therapy. In two patients there were no more relapses after administration of RTX; in four out of five patients who relapsed after administration of RTX, this happened after reappearance of B-cells. No severe adverse events were noted.

Conclusions:

Our observation indicates that RTX is an effective and safe therapeutic option in children with difficult-to-treat SDNS, by showing a strong reduction of yearly relapses in the absence of severe adverse effects.

P - 408 FIBROGENIC CYTOKINES LINK TO URINARY ANGIOTENSINOGEN IN OBESE CHILDREN

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Introduction:

Fibrogenic cytokines are recognized as markers and putative drivers of disease activity and histopathological deterioration in various kidney diseases. Their local release occurs in close association with the intrarenal renin-angiotensin-aldosterone system (RAAS) overactivation and it might also be increased in the setting of obesity related-kidney injury. We aimed to compare the levels of urinary TGF-β1 (U-TGF-β1) and ET-1 (U-ET-1) in normal weight, overweight and obese children and to test their association with urinary angiotensinogen (U-AGT), a biomarker of intrarenal RAAS.

Material and methods:

Cross-sectional evaluation of 302 children aged 8-9 years, within the population-based birth cohort Generation XXI (Portugal). Anthropometric measurements and 24-hour ambulatory blood pressure (BP) monitoring were performed. The levels of U-ET-1, U-TGF-β1 and U-AGT were determined by immunoenzymatic methods using commercial ELISA kits.

Results:

Obese children presented the lowest levels of U-ET-1 and U-TGF-β1, only significant for U-ET-1: 27.1 (19.1-27.1), 33.5 (22.0-52.6), 24.4 (18.3-36.7) fmol/g creatinine, in normal weight, overweight and obesity groups, respectively, p=0.032),. Significant positive correlations were found between log U-ET-1 and log U-TGF-β1, HOMA-IR, eGFR and a negative correlation with serum aldosterone. Log U-TGF-β1 was negatively correlated with cystatin C and positively with urinary albumin and U-AGT. In multivariate models, in the normal weight group, U-ET-1 was independently associated with 24-hour systolic BP and HOMA-IR in the obese group and with HOMA-IR, aldosterone and U-AGT in the obese group. U-TGF-β1 model was only associated with U-AGT in the obese group.

Conclusions:

Whereas the initial hypothesis of finding higher levels of fibrogenic urinary cytokines in obese children was not supported by our results, both U-ET-1 and U-TGF-β1 are significantly associated with the U-AGT. These findings are likely to reflect an interplay between the RAAS and the process of tissue remodelling that occurs in the kidneys of obese young subjects.

P - 409 APOLIPOPROTEIN A-IV AND RENAL L-TYPE FATTY ACID BINDING PROTEIN: NOVEL BIOMARKERS OF TUBULAR INJURY IN PEDIATRIC NEPHROLITHIASIS

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Introduction:

In vitro and animal studies have shown crystal-induced oxidative stress and tubular injury, but there is little evidence of tubular damage in pediatric nephrolithiasis. Using a proteomic approach, we assessed the differences in the urinary proteins between children with renal stones (RS), and healthy controls (HC), with particular attention to the proteins involved in oxidative stress and tubular injury.

Material and methods:

Quantitative proteomic comparison of pooled urine from RS (N=30, 24 females, mean age 12.95±4.03 years) versus age- and gender-matched HC (N=30), using liquid chromatography-mass spectrometry (LC-MS/MS). Proteins of interest were selected using the following criteria: 1) ≥5 spectral counts; 2) ≥2-fold difference in spectral counts; and 3) ≤0.05 *p*-value for the Fisher's Exact Test. These findings were further investigated using ELISA testing.

Results:

Of the 1813 proteins identified, 230 met the above criteria, with 163 proteins up-regulated in RS group. Function analysis revealed 23 inflammatory proteins, 8 proteins involved in oxidative stress, and 6 involved in tubular injury (apolipoprotein A-IV APO A4, liver-type fatty acid binding protein L-FABP, beta 2-microglobulin, retinol-binding protein 4, cystatin C, and lysozyme C). ELISA analysis revealed significantly increased urinary levels of APO A4 only in children with hypercalciuria (N=10) compared to controls (median 341.23 ng/mg creatinine, IQR 116.777-635.15 vs median 89.62 ng/mg creatinine, IQR 57.74-198.81)(p=0.01). Additionally, hypercalciuric children showed significantly higher urinary levels of L-FABP compared to controls (median 30.64 ng/mg creatinine, IQR 30.64-73.59 vs median 5.73 ng/mg creatinine, IQR 1.68-16.20)(p=0.05).

Conclusions:

We provide proteomic evidence of oxidative stress, inflammation, and tubular injury in children with renal stones. We speculate that inflammation and changes in the oxidant-antioxidant balance may cause tubular damage in these patients. Urinary Apo A4 and L-FABP represent novel biomarkers for tubular injury in children with hypercalciuria and kidney stones.

P - 410 ABPM, BLOOD PRESSURE AND HEART RATE VARIABILITY IN OFICIALLY HYPERTENSIVE OBESE CHILDREN AND ADOLESCENTS

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Introduction:
We aimed to asses the impact of different degrees of obesity on ambulatory blood pressure monitoring (ABPM) measurements, blood pressure and heart rate variability (BPV and HRV, respectively) values.
Material and methods:
Obese children and adolescents with BP measurements >95p on three different occasions and referrred to ABPM between January 2010 and December 2014 were included into the study. Obesity was defined as BMI SDS ≥2 and severe obesity was defined as BMI SDS≥3. Age, gender, prematurity, height SDS, urea, serum creatinine, uric acid , left ventricular mass index (LVMI), hypertensive retinopathy (HTRP) findings, proteinuria levels, APBM measurements, BPV and HRV evaluated with regard to 24-hour, daytime and nighttime systolic, diastolic BP (SBP,DBP) and mean arterial BP (MAP) standard deviation(SD), coefficient of variancy(CV), delta(Δ) minimum(min) and maximum(max) BP levels, SDS levels of min and max BP measurements and Δ levels of the latter two were compared between the two groups.
Results:
There were 209 (M/F:108/101) patients included and 82(41%) of them were severely obese(SO). Age, height SDS, LVMI and HTRP rate were significantly higher in the SO group. 24-hour, daytime and nighttime SBP, SBPSDS, DBP, DBPSDS, MAP and MAPSDS levels; daytime and nighttime BP loads and systolic dipping values were significantly higher in SO group, except nighttime diastolic BPSDS (p:0.268), nighttime diastolic load (0.114) and diastolic dip (0.787). None of the BPV/HRV parameters other than nighttime SBPSD (p:0.07), nighttime minimum (p:0.008) and maximum (p:0.006) SBPSDS differed between the groups ($p<0.05$). On regression analysis, only weight for height levels, BMI and BMISDS were found to be significantly associated with LVMI (p: 0.001, 0.017 and 0.008 respectively).
Conclusions:
SO patients are at a greater risk for higher LVMI measurements, HTRP and worse ABPM outcomes. However, degree of obesity has no distinctive effect on BPV or HRV.

P - 411 ABPM IN OBESE CHILDREN AND ADOLESCENTS

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Introduction:
We aimed to identify the frequency of masked hypertension (MHT) in obese youth; to compare the demographic, laboratory and ABPM parameters of patients with MHT to others; to define factors predicting MHT; to determine the ABPM parameters effecting LVMI.
Material and methods:
Data of obese patients between March 2013 December 2014 were evaluated retrospectively. Patients with ambulatory hypertension(AHT), white-coat hypertension(WCHT), MHT or normotension(NT) were determined. Demographic and laboratory findings, office and ABPM measurements, blood pressure variability(BPV) and heart rate variability(HRV) parameters were compared between the groups. The factors predicting MHT and the association between LVMI and ABPM, BPV/HRV parameters were interpreted.
Results:
In 118 patients (M/F:52/66) included, none had WCHT. Three groups were formed: AHT(n:60,51%), MHT(n:46,39%) and NT(n:12,10%). Stria was significantly higher in AHT and MHT groups(p:0.003). Office BP indexes(BP/95p) significantly differed between the groups. Cut-off levels to predict MHT were 0.85 and 0.76 for systolic and diastolic BP(SBP,DBP) indexes, respectively. All ABPM parameters of MHT group except daytime DBP, DBPSDS, diastolic load, nighttime MAP and MAPSDS in addition to 24-hour minimum(min) SBPSDS, nighttime minSBPSDS, maximum(max) SBPSDS, minDBPSDS, maxDBPSDS, MAPSD, minMAPSDS, maxMAPSDS were as high as those of AHT group. All HRV values were similar between the groups. No demographic or laboratory factors predicted MHT. None of BPV/HRV values correlated with LVMI. On regression analysis, daytime MAP(β:0.340,$p<0.01$) and diastolic dip(β:-0.204,$p<0.01$) had significant association with LVMI.
Conclusions:
In our study, prevalence of MHT was higher than expected and cut-off levels for SBP/DBP indexes to predict MHT were defined. Stria may be a significant sign for MHT. As some ABPM and BPV parameters in MHT group were as high as those of AHT group, ABPM is mandatory in all obese patents. Our results failed to determine any association of BPV/HRV with LVMI. Only daytimeMAP and diastolic dip represented an independent association with LVMI.

P - 412 IS THERE A CORRELATION BETWEEN OBESITY, HYPERTENSION AND LEFT VENTRICULAR HYPERTROPHY?

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Introduction:
Obesity and hypertension are common in children. I studied whether there is significant correlation between both diseases as often decribed as well as between degree of hypertension and left ventricular hypertrophy (LVH).
Material and methods:
61 children evaluated for suspected hypertension between years 2009 and 2014 were included in the study. Ambulatory blood pressure monitoring was done in all of them. On the basis of this investigation hypertension, high-normal blood pressure or normal blood pressure was confirmed. In all of them body mass index (BMI) was calculated (above 95th percentile in obesity, between 85 and 95th in overweight and below 85th percentile in children with normal weight). Echocardiogram was performed in all children with confirmed hypertension and high-normal blood pressure. The statistical significance of correlation between BMI category / obesity and hypertension as well as between degree of hypertension and LVH was tested using the chi-squared and exact Fisher (if needed) test.

Results:
22 children (36,1 %) had normal blood pressure, 21 (34,4 %) high-normal blood pressure and 18 children (29,5 %) hypertension. Obesity was present in 9 patients with hypertension (50 %), in 13 patients with high-normal blood pressure (61,9 %) and in 10 patients with normal blood pressure (45,5 %). LVH was present in 12 patients with hypertension (66, 7 %) and in 8 patients with high-normal blood pressure (38,1 %). There was not a statistically significant correlation between obesity and hypertension (p = 0,82) nor between degree of hypertension and LVH (p = 0, 14).
Conclusions:
The study showed not a statistically significant correlation between obesity and hypertension nor between degree of hypertension and LVH. Other factors than obesity thus play more important role in the pathogenesis of hypertension. Evaluation for target organ damage (especially LVH) should be done also in patients with high-normal blood pressure.

P - 413 CHANGES IN EXPRESSION OF INTERMEDIATE FILAMENTS, FACTORS OF VASCULOGENESIS AND RECEPTOR OF ADVANCED GLYCATION END PRODUCTS ARE OBSERVED DURING NORMAL HUMAN NEPHRONOGENESIS AND PODOCYTE DIFFERENTIATION

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Introduction:
Normal course of nephrogenesis and podocyte differentiation are essential for normal morphology and kidney function. Information about human kidney development is scarce and contradictory. We analyzed the ultrastructural and immunohistochemical characteristics of developing nephrons, from metanephric cap stage through stages of renal vesicle, comma and S-shaped bodies, glomerular capillary and maturing glomeruli. Changes in morphology and intracellular protein content during maturation of podocytes are described.
Material and methods:
Human kidney tissues between the 7th and 38th developmental week were analyzed using double-immunofluorescence method and electron microscopy. Primary antibodies included intermediate filaments vimentin and cytokeratin-10 (CK10), factors of vasculogenesis CD31 and VEGF, and receptor of advanced glycation end products (RAGE).
Results:
Human nephronogenesis underwent transformation of metanephric cap into the maturing glomeruli. With progression of development, vimentin expression increased in gomerules, including podocytes and Bowman's capsule. CK10 was expressed in ampulla and metanephric cap, while during later nephronogensis it gradually decreased. CD31 was increasingly strong in developing glomerular vessels, while VEGF characterized population of differentiating podocytes and cells of Bowman's capsule. RAGE was strongly positive in some metanephric cup and ampullar cells, diffusely distributed in C- and S-shaped bodies, while restricted to podocytes in maturing glomeruli. Ultrastructurally, we detected filaments in podocyte cytoplasm and their accumulation at adherent junctions between neighboring podocytes.
Conclusions:
Transition of metanephric cap cells into renal vesicle were associated with early CK10 and RAGE expression that accorded with mesenchymal-to-epithelial transformation of metanephric mesenchyme. Reverse process of epithelial-to-mesenchymal transition, appearing during further nephronogenesis was associated with increase of vimentin expression, while CD31 and VEGF expression enhanced glomerular vasculogenesis. Later on, restriction of RAGE expression to podocyte population indicates importance of RAGE in normal metabolism and apoptosis of podocytes.

P - 414 VITAMINE D STATUS IN CHILDREN WITH A KIDNEY OF MONOFUNCTIONAL ORIGIN: THE KIMONO D STUDY

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Introduction:
The 25-hydroxyvitamin D (vitD) status in children with a kidney of monofunctional origin (KIMONO) is fully unknown. This study is designed to elucidate the vitD status of KIMONO-children. We hypothesized that a lower glomerular number can account for a lower vitD and subsequent lower 1.25-dihydroxy vitamin D level in KIMONO-children.
Material and methods:
A case-control study was performed at the VU University Medical Center in The Netherlands. 163 KIMONO-children (1-18 years of age) were included. Serum vitD levels, measured with high-performance liquid chromatography and tandem mass spectrometry were compared to cut-off levels based on age. VitD deficiency was defined as a vitD level <30 nmol/L and hypovitaminosis D as a level <50 nmol/L. VitD levels were also compared to vitD levels of children with two functioning kidneys (n=132) in the same age-group and living in the same geographic area.
Results:
The median vitD level in the KIMONO-group was 73 nmol/L [range: 18-216]. VitD deficiency was found in 10/163 KIMONO-children, and hypovitaminosis D in 33/163. Non-Western-immigrants more often demonstrated a vitD deficiency (odds ratio (OR) 7.58, 95% confidence interval (CI) 1.86-30.85; p=0.005) and hypovitaminosis (OR 3.04 CI 1.36-6.78; p=0.007) compared to native Dutch children. In KIMONO-children no differences in vitD deficiency were found for sex, age, BMI, vitamin D supplementation, calcium supplementation or season. Multivariate regression analysis showed less children with a vitD deficiency in the KIMONO-group (10/163) compared to the control group (39/132) (OR 0.24 CI 0.10-0.58; p= 0,001).
Conclusions:
KIMONO-children in general do not have a risk for vitD deficiency or hypovitaminosis D compared to children with two kidneys. KIMONO-non-Western-immigrants had lower levels of vitD compared to native Dutch KIMONO-children. Whether the lower glomerular number in combination with rather "normal" vitD levels also reflect the status of bone mineral density has to be investigated.

P - 415 CLINICAL OUTCOME OF CHILDREN WITH HORSESHOE KIDNEY AND RENAL ABNORMALITIES IN FAMILY MEMBERS

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Introduction:
Horseshoe kidney (HSK) is a well-known congenital anomaly characterized by a fusion of the lower poles of both kidneys by parenchymal tissue.

It occurs in 1 in 400–800 individuals and frequently found to be associated with other congenital anomalies.
The objectives of this study are to evaluate the additional abnormalities and renal outcome of children with HSK and to determine whether kidney or urinary tract abnormalities (AKUT) exist in affected families.
Material and methods:
The medical records of patients with HSK were retrospectively reviewed, renal and urinary tract abnormalities were recorded for all affected relatives.
Results:
We evaluated 59 patients (34 males, 25 females) with HSK. The mean age at diagnosis and follow-up time were 4.55±4.77 (median; 3.25) and 2.21±2.57 (median; 1.67) years, respectively. Four patients were diagnosed hydronephrosis prenatally. Consanguinity was present in 13 (22.03 %) family.
Seventeen (28.8 %) patients had associated urological anomalies: eight (47.1%) unilateral hydronephrosis, two (11.8%) unilateral grade 4-5 vesicoureteral reflux (VUR), one (5.9%) bilateral gr 1-3 VUR, three (17.6%) unilateral grade 1-3 VUR. All of the patients except one had normal renal functions.
Thirteen patients (22.03 %) had their relatives with AKUT. The most common abnormalities in relatives were chronic kidney disease in five (38.5 %), ureteropelvic junction stenosis in two (15.4 %), unilateral renal agenesis in one (7.7 %) and HSK in one (7.7 %) patients.
Conclusions:
Children with HSK should be examined for additional urological and nonurological abnormalities. Family members of HSK should be informed and followed carefully for the possible urinary tract abnormalities and renal functions.

P - 416 INTRAUTERINE DEVELOPMENT OF KIDNEYS UNDER THE INFLUENCE OF ELECTROMAGNETIC RADIATION

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Introduction:
The kidney refers to the key elements of the adaptational system, being extraordinary sensitive to different exogenic and endogenic modulators.
Material and methods:
The experimental study was carried out on the 3-months old Wistar rats (50 females and 50 males) and their offsprings in the newborn period. Adult females of the main group were exposed to the low-intensity electromagnetic radiation of the centimeter range (1-10 cm) with radiation flux density up to 3mW/cm² for 4 hours daily during 1 month before and 1 month during the pregnancy. Every day the animals of the control group spent 4 hours in the chamber of the same size as the chamber of the device. Morphological study of the renal tissue of the offspring rats was performed.
Results:
During the investigation it has been revealed that kidneys of the control group rats were coated with an evenly distributed layer of a connective tissue capsule. The cortical substance contained 5-7 rows of nephrons. The glomerular capillaries were located compactly, the capillary loops of the glomeruli were moderately plethoric. The kidneys of the main group rats were covered with the connective tissue capsule, in some places slightly wrinkled. It was observed that the number of the glomeruli in the kidneys of the main group rats was decreased in comparison with the control one. Separate glomeruli had web-footed segmental shape because of small amount of capillaries in a glomerule. There were less embryonal glomeruli than in the control group.
Conclusions:
Reduced amount of nephrons with activated morphological condition was revealed in kidneys of the main group rats. That is probably associated with their formation under the influence of the electromagnetic radiation that is stressful for the pregnant species.

P - 417 CONGENITAL ANOMALIES OF KIDNEY AND UPPER URINARY TRACT IN CHILDREN WITH CONGENITAL HYPOTHYROIDISM: A CASE-CONTROL STUDY

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Introduction:
Congenital hypothyroidism (CH) may be significantly associated with congenital malformations. The aim of this study was to compare the renal and upper urinary tract anomalies in children with and without primary CH (PCH).
Material and methods:
This case-control study was conducted on 200 children aged 3 months to 1 year, referring to Amir-Kabir Hospital, Arak, Iran. One hundred children with PCH, as the case group, and 100 children without CH, as the control group, were selected. For all children, demographic data checklists were filled and ultrasonography and other diagnostic measures (if necessary) were performed to evaluate renal and upper urinary tract anomalies (ureter and bladder).
Results:
The frequency of renal and upper urinary tract anomalies among 43 children with primary CH, with 83 cases (72.8%), was significantly higher than the frequency of anomalies among the 19 children in the control group, with 31 cases (27.1%). (OR=3; CI 95%: 1.6-5.4; p = 0.001) Among the anomalies studied, only the differences in frequency of uretero-pelvic junction obstruction (UPJO) (OR =6; CI 95%:1.3-28; p = 0.018) and hydronephrosis (OR =22; CI 95%:5-95; p = 0.001) were significant between the two groups.
Conclusions:
Our study demonstrated that PCH is significantly associated with the prevalence of congenital anomalies of the kidneys and upper urinary tracts.

P - 418 STONE COMPOSITION IN PEDIATRIC NEPHROLITHIASIS: A PEDIATRIC STONE CONSORTIUM ANALYSIS

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Introduction:
Scant data exists regarding stone composition in pediatric nephrolithiasis. We studied (1) the variation of stone composition by age and gender, and (2) gender-related differences in urinary risk factors in relationship to stone composition.
Material and methods:
A retrospective multicenter review of 122 children with upper urinary tract calculi was performed, analyzing both stone composition and urinary metabolic data.
Results:
The mean age was 12.87± 3.93 years, and 48.3% were males. Most stones were either pure calcium oxalate (CaOx) (44%) or CaOx mixed (44%), without significant differences in age and gender for either stone type.

Calcium phosphate (CaP) was present in 85% of the CaOx mixed group. Among children with pure CaOx, there were significant differences in urinary risk factors between males and females (Table). No significant differences were seen in the CaOx mixed group. Abnormal urinary calcium excretion was found in 26% of children with pure CaOx and in 31% of CaOx mixed.

Urine Component	Males (n=27)	Females (n=27)	p-value
Oxalate (mg/1.73 m²/day)	37.81 ± 10.57	31.74 ± 11.90	0.05
Sodium (mmol/kg/day)	3.41 ± 1.48	2.63 ± 1.00	0.02
Magnesium (mg/kg/day)	2.09 ± 0.86	1.67 ± 0.79	0.06
Citrate (mg/gm creatinine)	398.44 ± 286.24	547.46 ± 292.48	0.06

Conclusions:
CaOx, alone or in combination with CaP, was the predominant component of pediatric stones across all ages, and both genders. Approximately one third had hypercalciuria. In males with pure CaOx stones, higher urinary oxalate and sodium and hypocitraturia indicate the need for dietary evaluation/modification.

P - 419 NEPHROCALCINOSIS AND NEPHROLITHIASIS IN PRETERM NEONATES UNDER 1500 GRAMS BIRTH BODY WEIGHT

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Introduction:
Renal calcifications (nephrocalcinosis and nephrolithiasis) are common in both term and preterm infants who have had complicated neonatal period. Multiple factors and medications may cause hypercalciuria and nephrocalcinosis in neonates. The aim of this research was to determine the rate of renal calcification and its relation with some neonatal clinical complications and medications in preterm neonates less than 1500 grams birth body weight.
Material and methods:
In a cross sectional and analytic study, 250 premature neonates with birth body weight less than 1500 grams who hospitalized in the neonatal intensive care unit of Alzahra Hospital of Tabriz/Iran from 2012-2013 were studied. Data including gender, gestational age, birth body weight, APGAR score in first and fifth minute of birth, type of delivery and receiving mechanical ventilation or CPAP and medications were recorded. Renal ultrasound examination was done in all neonates at one month of age and was repeated at 40 weeks corrected gestational age.
Results:
The mean body weight and gestational age of neonates were 1233.45 ±634.45 gram and 29.34±3.7 weeks respectively. One hundred and four neonates (41.6%) were male and 146 cases (58.4%) were female. Renal calcification was reported in the first ultrasound exam in 11 neonates (4.4%) and in the second one in 74 cases (29.6%). There was not significant association between renal calcification and sex, gestational age, receiving surfactant, aminoglycosides and calcium ($P>0.05$). Mean body weight of neonates with calcification was significantly lower than those without calcification. Frequency of renal calcification was significantly higher in those who received mechanical ventilation or CPAP and those who received diuretics, methyl xanthines, vancomaycin and corticosteroids ($p<0.05$).
Conclusions:
We found renal calcification in less than one third of studied neonates. Nephrocalcinosis and nephrolithiasis are common finding in premature infants. All premature or low birth weight infants should be followed for renal calcifications.

P - 420 MICROVASCULAR DYSFUNCTION OF THE SKIN AS AN EARLY MARKER OF PRIMARY HYPEROXALURIA TYPE I LESIONS

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Introduction:
Primary Hyperoxaluria type I (PH1) induces excessive oxalate production and accumulation, leading to systemic oxalosis that appears when renal function is impaired and plasma oxalate (Pox) levels increased. Early non-invasive markers of oxalosis still need to be defined.
Material and methods:
Skin microvascular function was assessed by a non-invasive laser Doppler flowmetry before and after stimulation by pressure (PIV), thermic or pharmacological stimuli (nitroprussiate SNP or acetylcholine Ach). Thirteen PH1 patients (14.2±6.8 years, 8 girls, 6 past of combined liver-kidney transplantation CLKT) were included. Three groups were identified: PH1 patients under conservative therapy and normal Pox (PH1-CT, N=5), PH1 patients with a past of CKLT and normal Pox (PH1-Tx, N=5), PH1 patients with increased Pox (dialysis or renal impairment after CLKT, N=3). Results were compared to healthy volunteers (VITADOS cohort, N=68), using non parametric Mann Whitney and Kruskall Wallis tests.
Results:
When comparing PH1-CT to controls, age, height, BMI were not different. Nerve tactile sensitivity was decreased in PH1 children but the smooth muscle capacity to vasodilate was not different. Ach response was increased in PH1 ($p=0.04$) as well as the thermal response (initial peak, $p=0.03$; delayed plateau, $p=0.04$).
When comparing PH1-Tx to controls, age, height, BMI were not different. The CIV peak was significantly decreased in PH1-Tx ($p=0.03$), reflecting a likely inflammatory state in these patients. A hyperreactivity to Ach was also observed in PH1-Tx (peak Ach, $p=0.04$), as well as a decreased vasodilation in response to SNP ($p=0.017$).
Conclusions:
PH1-CT patients have an exacerbated endothelial dependent vasodilation and thermal-induced vasodilation, thus suggesting an early dysfunction of the microcirculation. However, PH1-Tx patients display a different profile with vascular hyperreactivity and decreased vasodilation capacities. It remains debatable whether this later observation is secondary to PH1 itself or to the vascular abnormalities and chronic micro-inflammation induced by immunosuppressive regimens.

P - 421 ETIOLOGIC RISK FACTORS AND VITAMIN D RECEPTOR GENE POLYMORPHISMS UNDER ONE YEAR OLD INFANTS WITH UROLITHIASIS

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Introduction:
The incidence of urinary tract stones in infancy has been increasing in Turkey.
Material and methods:
In total, 40 healthy infants and 20 infants with urinary tract stones aged <1 year were enrolled in both the summer and winter. Detailed surveys were

taken of all infants, and metabolic parameters, serum 25-hydroxyvitamin D (25(OH)D) levels, and *ApaI* and *FokI VDR* gene polymorphisms were investigated.

Results:

There were no differences in serum 25(OH)D levels among the four groups ($p>0.05$). However, infants with stones tended to more commonly be given formula ($p<0.05$) and multivitamins (vitamins A, C, D) ($p<0.05$). In addition, infants whose mothers wore headscarves during pregnancy had lowerserum 25(OH)D and calcium levels ($p<0.05$). There were no significant differences in *ApaI* and *FokI VDR* gene polymorphisms between the groups with stones and the control groups. However, hypercalciuria emerged as an underlying metabolic abnormality in the aetiology of stones, and was observed at a rate of 38%.

Conclusions:

Infants that are given formula and multivitamins for vitamin D supplementation are at increased risk for the formation of urinary tract stones.

P - 422 BONE METABOLISM IN CHILDREN WITH IDIOPATHIC HYPERCALCIURIA

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Introduction:

Aim of the study was to assess bone mineral density and serum concentration of selected bone metabolism markers in children with idiopathic hypercalciuria (IH).

Material and methods:

We studied 50 children with IH aged 5.0-17.7 years and 20 healthy children (control group) aged 5.0-16.8 years. The following parameters were evaluated: bone mineral density of total body (TB-BMD) and lumbar spine (L1–L4 BMD) by dual energy X-ray absorptiometry (DXA) expressed as Z-score, serum calcium (Ca), phosphorus (P), parathormone (iPTH), alkaline phosphatase (ALP), $25(OH)D_3$, 24hour urine collection of calcium, phosphorus, sodium and urine calcium/creatinine, phosphorus/creatinine ratio.

Results:

In the study group TB- BMD Z- score <-1 were found in 14%, between (-1) and 1 in 48%, >1 in 38% children; L1–L4 BMD Z- score < -1 were noted in 24% 12/50, between (-1) and 1 in 60% 30/50, >1 in 16 %. Mean value of L1-L4 BMD in the study group was lower than in the control group (-0,07 ± 1,17 vs 0,51 ± 1,26; p=0.09).

In both groups Ca, P, PTH, ALP were within the normal ranges. In the study group 34/50 (68%) children had serum concentration of $25OHD_3$ < 20 ng/mL. In the control group 8/20 (40%) had

serum concentration of $25OHD_3$ < 20 ng/mL. Number of children with decreased $25OHD_3$ < 20 ng/mL was significantly higher in the study group in comparison to the control group ($p=0.03$ chi^2).

Only in the study group positive correlations were found between TB-BMD Z-score and 24hour phosphorus collection and phosphorus / creatinine ratio (r=0.29, p =0.04; r=0,41, p=0.004) and between L1-L4 BMD Z-score and $25OHD_3$ serum level (r=0.31, p =0.03).

Conclusions:

Decreased bone mineral density of lumbar spine in patients with IH can depend on vitamin D deficiency.

P - 423 VITAMIN D RECEPTOR GENE POLYMORPHISMS IN CHILDREN WITH KIDNEY STONE DISEASE

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Introduction:

Kidney stone disease has a multifactorial pathology involving the interaction of genetic and environmental factors. There is increased risk of stone formation in the relatives of idiopathic stone patients, which can be explained up to 60% by genetic factors. This study was conducted to explore the association of vitamin D receptor (VDR) gene polymorphisms with the risk of nephrolithiasis.

Material and methods:

We investigated the VDR gene polymorphisms, *ApaI*, *BsmI*, *TagI*, *Cdx2*, *FokI*, in 52 children (26 boys, 26 girls) with nephrolithiasis and in 51 healthy children (22 boys, 29 girls) without nephrolithiasis. *Apa I*, *BsmI*, *TagI*, *Cdx2*, *FokI* genotypes were analyzed by *Apa I*, *BsmI*, *TagI*, *Cdx2*, *FokI* restriction enzyme digestion, respectively. The resulting alleles are designated as ABTCF (*ApaI*, *BsmI*, *TagI*, *Cdx2*, and *FokI* restriction site is absent), or abtcf (*ApaI*, *BsmI*, *TagI*, *Cdx2*, *FokI* restriction site is present), respectively. VDR expression is lower for aa, BB, tt, cc, and ff genotypes. Genotype and allele frequencies were calculated, and the association with nephrolithiasis was investigated.

Results:

Our data provide no statistically significant evidence for an association between nephrolithiasis and VDR *ApaI*, *BsmI*, *TagI*, *Cdx2*, and *FokI genotype* and allele frequencies. On the other hand, although it is not statistically significant we found higher genotypic (tt genotype: 44.2% and 35.3% for patients and controls respectively, p:0.2) and allelic frequencies (t allele: 68.3% and 58.8% for patients and controls respectively, p:0.19) for *TaqI* and lower genotypic (BB genotype: 9.6% and 15.7% for patients and controls respectively, p:0.29) and allelic frequencies (B allele: 27.9% and 38.2 for patients and controls respectively, p:0.13) for *BsmI* in children with nephrolithiasis compared to controls.

Conclusions:

Our data suggest that the VDR *ApaI*, *BsmI*, *TagI*, *Cdx2*, and *FokI* polymorphisms do not indicate a significant risk for nephrolithiasis.

P - 424 BONE IMPAIRMENT IN PRIMARY HYPEROXALURIA (PH): AN ULTRASTRUCTURAL BONE ANALYSIS

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Introduction:

Renal and bone deposition of calcium oxalate crystals is a hallmark of systemic oxalosis observed in patients with PH1 (less frequently PH2). Since the bone compartment stores massive amounts of oxalate, patients present with recurrent low-trauma fractures, bone deformations, severe bone pains and specific oxalate osteopathy on plain X-ray. The threshold of glomerular filtration rate at which this occurs is debatable and might be as high as 30 to 45 mL/min per 1.73m². The objective of the study is to present a single-centre experience of bone biopsy and bone ultrastructural analysis in oxalosis.

Material and methods:

We present data obtained in 10 samples from 8 patients with oxalosis (16-68 years) who underwent iliac crest bone biopsy and bone quality analysis using modern methods (microradiography, microindentation, Fourier

Transform InfraRed Microspectroscopy, transmission electron microscopy) in addition to histomorphometry.

Results:

Disseminated calcium oxalate deposits (whewellite) were found in the bone marrow space (with a granulomatous reaction) but not in the bone matrix. Calcium oxalate deposits were totally surrounded by macrophages and multinucleated giant cells, and a phagocytosis activity was sometimes observed. Very few calcium oxalate crystals were directly in close contact with the mineral substance of bone. Bone mineralization was not modified by the presence of calcium oxalate even in close vicinity. Bone quality analysis also revealed a harder bone than normal, perhaps in relationship with decreased carbonate content in the mineral.

Conclusions:

This study reports the specific location of calcium oxalate deposits (whewellite) in the bone marrow space (with a granulomatous reaction) and not in the bone matrix in patients with oxalosis. Bone hardness is increased, that could explain a more "brittle" bone. The formation and growth of calcium oxalate crystals in bone is independent of apatite. Despite these novel observations, the exact mechanisms leading to nucleation and growth of oxalate deposits are still unclear.

P - 425 PROLONG OUTCOME OF RENAL FUNCTION AND BODY GROWTH INDEX IN CHILDREN WITH NEPHROCALCINOSIS: A RETROSPECTIVE SINGLE CENTER STUDY

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Introduction:

Nephrocalcinosis (NC), defined as renal calcification , can be tubular or interstitial. Prevalence of NC in preterm neonates with birth weight less than 1500 gram is 27-64% and this risk increased by incidence of low birth weight and prematurity. NC is not a single concept and occurs due to various renal , metabolic disorders and medications. Etiology and clinical significance of nephrocalcinosis is not yet known, and the prognosis is not fully understood. This study is aimed at analysese retrospectively the etiology of NC and to evaluate the results of follow-up on growth index and renal function of patients with NC

Material and methods: :

This was a cross-sectional study performed on 30 patients who were refered to Loghman Hakim Hospital with diagnosis of NC between 2006 and 2013 . The records of patients were evaluated for age, sex, etiology of NC, GFR, hSDS and wSDS presentation, and follow-up period.

Results: :

Mean age presentation was 2.2±2.5 (range: 0.1-9.7) year. 14 patients (47%) were male. Mean follow-up time was 7.1±5.2 (range: 1.0-20.9) year. The most symptoms were urinary tract infection (25%) and growth retardation in 18% of patients. The etiology of NC included distal renal tubular acidosis (dRTA) in 34.5%, idiopathic hypercalciuria in 17.2%, Bartter syndrome in 10.3% and 6.9% unknown. Mean GFR was 75.6±29.1 in presentation and 105.7±21.9 ml/min/1.73m2 in follow-up time (P<0.001). Four of 30 (14.3%) patients had hSDS<-2 at presentation, remained at the last examination

Conclusions: :

Mean age presentation was 2.2±2.5 (range: 0.1-9.7) year. 14 patients (47%) were male. Mean follow-up time was 7.1±5.2 (range: 1.0-20.9) year. The most symptoms were urinary tract infection (25%) and growth retardation in 18% of patients. The etiology of NC included distal renal tubular acidosis (dRTA) in 34.5%, idiopathic hypercalciuria in 17.2%, Bartter syndrome in 10.3% and 6.9% unknown. Mean GFR was 75.6±29.1 in presentation and 105.7±21.9 ml/min/1.73m2 in follow-up time (P<0.001). Four of 30 (14.3%) patients had hSDS<-2 at presentation, remained at the last examination

P - 426 URINARY CYSTINE LITHIASIS IN CHILDREN

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Introduction:

In this study, we reviewed clinical findings, treatment and prognosis of patients with urinary cystine lithiasis.

Material and methods:

We evaluated the clinical, radiological and metabolic features of 18 children with urinary cystine lithiasis.The medical histories of these children(10 boys, 8 girls), from 28 months to 233 months, were reviewed retrospectively.

Results:

Of 18 patients, 11 (61%) were younger than 2 years of age at presentation. The mean age of the patients at presentation was 32.61+/-33.3 months. They were followed for a mean duration of 61.16+/-43.81 months.The most common presenting symptoms were pain or restlessness(38.8%) and urinary tract infection(16.6%), followed by acute kidney disease(11.1%), whereas 16.6% of the cases were detected incidentally during evaluation for other medical conditions.Urine analysis revealed abnormality other than cystinuria in 72.2% of the cases. There is high rate of parental consanguinity and positive family history for urolithiasis (61% and 67% respectively). In 89% of the patients, 2 or more stones were detected. The calculi were detected in the kidneys, the kidneys and the ureters, and the ureters in 10(55.5%), 6(33.3%) and 2(11.1%) patients, respectively.Twelve(66.6%) patients had bilateral and 4(22.2%) had unilateral kidney stone. In 12(66.6%) patients, the stone diameter was equal or larger than 10 mm and only in 2(11.1%) patients the stone diameter was less than 5 mm. Tiopronin was started for 5 patients. Extracorporeal shockwave lithotripsy(ESWL), surgical interventions and both of them were performed for 6(33%), 13(72.2%), and 5(27.7%) patients respectively. Nine(50%) patients had renal parenchymal disease.

Conclusions:

The early presentation of cystine stone was one of the most striking findings in our patients. They tend to occur multiple and bilateral, resisting fragmentation by ESWL and require surgical interventions mostly. There is a high risk of damage to the kidney due to its recurring nature.

P - 427 NAG, KIM-1 AND NGAL LEVELS FOR DETERMINING OF RENAL TUBULAR INJURY IN CHILDREN WITH UROLITHIASIS

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Introduction:
Although urolithiasis is known an adult disease, children suffer from this problem. It has been demonstrated that calculi formation is associated with crystal–cell interactions and may result in tubular damage. The aim of this study was to investigate renal tubular injury in children suffering from urolithiasis.
Material and methods:
We evaluated 71 children (37 girls) with urolithiasis or microlithiasis who had been referred our center and age-matched 45 healthy controls (18 girls) between July 2013 and September 2014. Anthropometric data, presenting symptoms, family history, physical, laboratory and radiological findings were recorded. Urine samples were analyzed for metabolic evaluation (urinary calcium, uric acid, oxalate, citrate, cystine, magnesium excretion) and urinary enzymes [N-acetyl-B-glucosaminidase (uNAG), kidney injury molecule-1 (uKIM-1) and neutrophil gelatinase-associated lipocalin (uNGAL)].
Results:
The mean age was 7.5±5.1 year (range: 0.5-18.2) in the patient group and 8.9±4.0 (0.9-16.7) in the control group. The most common presenting symptoms were restlessness and/or pain (70.4%) and hematuria (21.1%). Urine analyses revealed metabolic abnormalities in 23 (32.4%) of the patients. The most common metabolic risk factors were hypocitraturia (14.1%), hypercalciuria (4.2%) and hyperoxaluria (2.8%). Hydronephrosis (8.5%) was the most common radiological finding. Calculi were located in the kidneys (84%), ureters (11.6%) and bladder (4.3%). Urinary NGAL/creatinine ratio level was significantly higher in the patient group (P=0.049). Univariate analyses showed that significant relations between uNGAL/creatinine ratio and urinary calcium/creatinine (r=0.371, P=0.003), uric acid/creatinine (r=0.291, P=0.021), oxalate/creatinine (r=0.339, P=0.006) and cystine/creatinine (r=0.376, P=0.004) ratios. The urinary enzymes levels were compared between the patients who have hydronephrosis and the patients who don't, and there were no significant difference noticed.
Conclusions:
Urinary metabolic abnormalities are very common in children with urolithiasis and significantly associated with increased uNGAL/creatinine ratio levels, which might show renal tubular injury.

P - 428 REVERSIBLE NEONATAL NEPHROCALCINOSIS

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Introduction:
Temporary neonatal medullary hyperechogecinity disappears during the first 10 days. Apparently, this is not related to a renal pathology and is associated to renal immaturity. Nevertheless, when it does not disappear, one should consider conditions of a renal origin which do have a negative prognosis. There have been recently described rare cases of nephrocalcinosis when there has been a severe dehydration. These have been overcome when the latter has been treated.
Material and methods:
2 cases are presented.
Results:
Case1:Term infant (gestational overweigh) of 3 days of life is admitted to Neonatal Unit with hypernatremic dehydration (weighed loss:13%) despite a suplemented feeding. Presents oliguric renal insufficiency (ARI) with hyperuricemia (urea:95mg/dl, creatinine:2.28mg/dl, cystatine:2.95mg/l, uric acid 16.3mg/dl, Na153mEq/L, 335mOsm/kg, EFNa0.1). The sonogram shows medullary nephrocalcinosis. ARI and hyperuricemia (rasburicase) treatment is given and a positive evolution is observed. Biochemical data is not registered that may suggest a related renal pathology. Eleven days later, the newborn is released with the right weighed gain, and normal renal function. Nephrocalcinosis is dissolved (probably due to dehydration) and also uric nephropathy. Case2:Term infant is admitted to hospital 7 days after birth. The newborn shows hypernatremic dehydration (weighed loss:20%, Na161mEq/l), with a normal renal function. A treatment to control dehydration is started and the patient shows a positive evolution. Medical observation proved isosthenuria with polyuria (after hydration levels had been restored) being the rest of the biochemical data within the right levels. A sonogram shows medullary nephrocalcinosis. He is released with increasing weighed curve. Nephrocalcinosis is dissolved months after admittance with a subsequent normal urinary osmolarity (710mOsm/kg) and a normal diuretic rhythm.
Conclusions:
Neonatal nephrocalcinosis involves a differential diagnosis with conditions of a renal origin. Nevertheless, it might suggest crystal deposits if a hypernatremic dehydration is diagnosed. These deposits will dissolve after dehydration is treated and diuretic rhythm will be stabilized.

P - 429 SPORT HEMATURIA IN A HEALTHY CHILD : A CASE REPORT

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Introduction:
Hematuria is a common presenting complaint in children.
Case description:
We report a five year-old boy with the painless macroscopic hematuria after soccer matches. He was admitted to our department with the occurrence of the reddish-colored urine after one hour of soccer matches.
There was no history of fever, colic pain and recent injury to the flanks, abdomen, or perineum in our patients. Physical examination was unremarkable. The blood cell count, coagulation tests and serum biochemistry were normal. Serum complement C3 and C4, ANCA, ANA, and immunoglobulin A levels were normal. The anti-GBM antibody assay was negative. Urine analysis showed hematuria without crystal formation. Our patient had normal urinary excretion of calcium, uric acid, oxalate and citrate. Urine culture was negative. Renal ultrasonography and color Doppler examinations were normal. The day after, urine was clean and urine analysis was normal. We did not found any pathologic findings on uretherocystoscopic examination. The provocative test that consisted of climbing and going downstairs 3 times was performed for detection hematuria. The test was performed in morning after voiding, with collection and analysis of the urine specimens at each micturition just before the exercise and during the following 24 hours. Urine analysis showed hematuria after provocative test. Normal urine analysis was detected the following morning.
Conclusions:
Sport hematuria has been reported in adult runners. But this condition is very rare in children. To the best of our knowledge, only two children have been reported about the sport hematuria to date. The mechanism of the sport hematuria is unclear. Some reason for this may be foot-strike hemolysis, renal ischemia, the release of a hemolyzing factor and the peroxidation of erythrocytes. In conclusion, sport hematuria might be considered for evaluation of hematuria in children. The provocative exercise test may helpful for confirming the diagnosis.

P - 430 ISOLATED HAEMATURIA AND THE RISK OF UROLITHIASIS IN HEALTHY CHILDREN

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Introduction:
Children with urolithiasis show metabolic abnormalities. This is also followed by considerable changes in their urine.
Aim of the study was the investigation of healthy children with idiopathic haematuria and lithogenic risk present in their urine.
Material and methods:
Urine samples were gathered in 827 (370 Female and 457 Male) children 6-14 years old; one hundred twenty seven (127) of them were selected based on problems they had in urine parameters: persistent microhematuria, low urine pH, low 24 hours urinary volume. They didnt have any positive history in kidney disease or endocrine abnormalities. The children were asked on their dietary habits, any presence of urolithiasis in their family members and the presence of flank pain. Based in the 24 hours urinary volume, pH, Calciuria Ca/Cr ratio we selected lithogenic urine.
Results:
Twenty-four (24) children had persistent microhematuria (six months in consequence), others had intermittente microhematuria. Thirty-eight (38) children (20 male) had supersaturated urine, so they present a high lithogenic risk. Hypercalciuria is over than 4 mg/kg/24 hours in twelve (12) children. The average Ca/Cr ratio was 0.5 mg/mg. The prevalence of lithogenic risk in the studied children was 4.5% and 54 children (or 71%) had positive family history of urolithiasis. Seventy-eight (78) children presented low urine volume.
Conclusions:
Isolated heamaturia associated with hypercalciuria and low urine volume is a risk for urolithiasis in the coming years.

P - 431 SINGLE CENTRE EXPERIENCE OF ISOLATED KIDNEY TRANSPLANTATION IN METHYLMALONIC ACIDURIA

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Introduction:
Children with methylmalonic aciduria (MMA) are known to develop progressive chronic kidney disease. Isolated renal transplant (iRT) has been suggested as a better option than isolated liver or combined liver kidney transplant in the management of this condition.
Material and methods:
Single centre experience of iRT in 5 males with MMA and CKD stage IV-V.
Results:
Median age at iRT was 10.8 years (range 5.8 – 17.8). Two children were on dialysis and the remaining three had GFR <18ml/min/1.73m^2. Two were living related donor iRT. There were no episodes of metabolic decompensation in the immediate peri-operative period. One developed severe haemorrhagic pancreatitis on day 3 following iRT and died with a functioning graft on day 48. Another child developed bacterial endocarditis two months following iRT and then progressive deterioration in graft function. Following an episode of pancreatitis and neurological deterioration, care was withdrawn 13 months after iRT. The remaining three children remain well with good graft function and better quality of life in terms of reduced hospital admissions and reduced need for supplements 3 - 6 years following iRT.
Conclusions:
While iRT can be a treatment option in some patients with MMA, there is increased risk of pancreatitis and mortality.

P - 432 ARE WE PERFORMING ENOUGH PRE-EMPTIVE PAEDIATRIC RENAL TRANSPLANTS: A NATIONAL AND SINGLE-CENTRE COMPARATIVE STUDY.

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Introduction:
Pre-emptive renal transplantation (PRT) from living-related donors (LRD) is the gold standard therapy for children with ESKD, dramatically improving allograft survival and quality of life. We aimed to analyse the local and national pre-emptive renal transplantation rates of children in the United Kingdom.
Material and methods:
Retrospective local and national database review of living donor and/or pre-emptive renal transplantation rates, including UK Transplant data from 1 January 2003 to 31 December 2014. Local database case analysis of those not pre-emptively transplanted.
Results:
1,262 paediatric renal transplants were performed nationally over 12 years, of which 326 (26%) were from our single centre (local). There were 32% national and 40% local pre-emptive renal transplantation rates with nationally 47% (21%) and locally 57% (27%) living donor (and pre-emptive living donor) rates. Of the total pre-emptive transplants, there were 60% nationally versus 68% locally living donor rates. Out of the 60% local non-pre-emptive renal transplants performed, 13% could have been pre-emptively transplanted when independently reviewed (excluding those patients who presented in ESKD or were on dialysis within 3 months of presentation, anephric pre-transplantation (native nephrectomies for FSGS, Wilms' tumour etc.), non-adherence or social reasons).
Conclusions:
Paediatric nephrologists and members of the multi-disciplinary team need to ensure that renal transplant work-up is always performed promptly in appropriate children with chronic kidney disease to ensure that the goal of pre-emptive renal transplantation is achieved nationally and locally, where possible. National analyses indicated significant correlation between number of candidates for pre-emptive transplantation who were not transplanted pre-emptively and mean waiting times on UK deceased donor transplant waiting list. By increasing pre-emptive transplantation from living donors, patients whose only option is deceased donor listing, will face lower waiting times, improving overall patient care and outcomes.

P - 433 INDOLEAMINE 2,3-DIOXYGENASE (IDO) UPREGULATION IS AN INDEPENDENT PREDICTOR OF SUSCEPTIBILITY TO INFECTIONS IN KIDNEY TRANSPLANT PATIENTS

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Introduction:
Indoleamine 2,3 dioxygenase (IDO) is involved in systemic immune tolerance and control of infection.
Aim of the study was to detect IDO activity and immunological related markers in the first year after kidney transplantation.
Material and methods:
IDO-activity and IDO-mRNA were investigated in 26 patients receiving cadaveric kidney transplant (Tx) in parallel with Foxp3, IL17, Ror-C, TGFbeta, IL6 mRNA.
Sampling was 0, 15, 30, 60, 180, 360 days after Tx. IDO-activity was assessed in sera as Kyn/Trp ratio (Kyn/Trp), determined by isocratic RP-HPLC method with UV detection. mRNAs was assessed by real time PCR (Taqman) normalized on Abelson gene mRNA.
Results:
IDO activity decreases from T0 (19.1;IQR 16.3-20.8) to T30 (7.4;IQR 6.3-8.6) then increases at T60 (8.8; IQR 7.2-11) then stabilizes. A significant correlation between IDO-activity and IDO-mRNA was observed at T60 (p=0.05) and T180 (p=0.02). At T60 a significant increase of IDO-activity vs T15 (p0.001) and T30 (p=0.01)and IDO-mRNA expression was observed (p=0.02).
9/26 patients developed viral infections during follow-up (5 CMV after a median of 2 months, 3 BKV after 5 months, 1 HZV after 1 month). Patients with infections (INF) had induction (basiliximab and steroids) and tacrolimus through levels superimposable to those without infections (NONINF). At time of infection 6/9 pts were under MMF. 1/26 had CNI toxicity and BKV infection. At T60 IDO activity was significantly different among INF versus NONINF (INF Kyn/Trp median 11,40;IQR 8,75-17.5, vs NONINF 7.85;QR 7-9.8 p<0.05). IL-17 was significantly reduced in INF (IL-17 INF 0,3;IQR 0.04-1,27 vs NONINF 4.89;IQR 1.2-7.7 p=0.006) while Ror-C was significantly increased (Ror-C INF 1.23;IQR 0.7-1.7 vs NONINF 0.44;IQR 0.15-0.9, p=0.03). Foxp3, TGF beta and IL6 mRNA expression did not differ at T60 between the two groups.
Conclusions:
IDO activity 60 days after Tx was significantly higher in patients later developing viral infections, not correlated to other parameters of infection or overimmunesuppression. Increased IDO activity and decreased IL-17 can be expression of infections permissive environment and could represent a useful biomarker.

P - 434 ARTERIAL HYPERTENSION AND ANTIHYPERTENSIVE MEDICATION IN PEDIATRIC RENAL TRANSPLANT PATIENTS: AN ANALYSIS O THE CERTAIN REGISTRY

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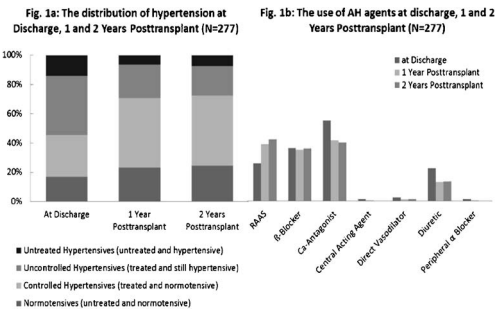
Introduction:
Our study aimed to describe the prevalence of hypertension, blood pressure (BP) control and the use of antihypertensive (AH) medication in pediatric renal transplant patients.
Material and methods:
The distribution of casual BP were analyzed in 427 pediatric renal transplant patients from the CERTAIN Registry, for which data entries were available at discharge and 1 year and/or 2 year follow up visit. The AH medication, immunosuppression, BMI and GFR and its relation to casual BP were analyzed in 277 patients with complete visits. Patients were classified as "normotensive" (if untreated and normotensive), "controlled hypertensive (HT)" (if treated and normotensive), "uncontrolled HT" (if treated and still HT) and "untreated HT" (if untreated and HT). As the patient age at transplantation ranged from 6 months to 25 years (median age 10.96 years), we calculated SDS values for casual systolic, diastolic BP and BMI, respectively.
Results:
At discharge 17% were normotensive, 29% controlled HT, 40% uncontrolled HT and 14% untreated HT. At 1(2) years posttransplant 24(25)% were normotensive, 47(48)% controlled HT, 23(20)% uncontrolled HT and 7(8)% untreated HT (Figure 1a).
At 2 years posttransplant, 26 to% of the patients were treated with single medication, 23% with a combination of two, and 19% with three to five AH agents. The pattern of drugs used changed over time: At discharge calcium antagonists (56%) and ß-blocker (37%) were most commonly used, whereas at 1 and 2 years posttransplant RAAS Blockers (39% and 43%, respectively) were the more commonly after calcium antagonists (Figure 1b).
A significant positive correlation were identified between systolic BP and tacrolimus trough level at 1 year posttransplant (R=0.2). Patients with higher cyclosporine trough level (≥102 μg/L) showed higher casual BP. SBP was significantly associated with BMI at 1 year posttransplant. GFR levels were decreasing over time, but there was no significant correlation with SBP.



Conclusions:
About 70% of the patients in this cohort were under AH treatment and this proportion is consistent over time. At discharge 51% of the patients had elevated BP levels, this proportion decreased at 1 year to 28%, and remained stable thereafter. As only less than 20% of patients received three or more AH agents, there is potential for further improvement in BP control in this population.

P - 435 RE-TRANSPLANTATION IN THOSE FIRST TRANSPLANTED IN CHILDHOOD AND ADOLESCENCE

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Introduction:
Children and adolescents are likely to require more than one kidney transplant. Outcomes following a failed transplant in this young Australian population have not been described to date. We aimed to describe the population first transplanted under 18 years of age, with a

failed graft, and to analyse factors associated with non-re-transplantation, time to retransplant and 2nd graft loss.

Material and methods:

A retrospective analysis was undertaken from Australian and New Zealand Dialysis and Transplant Registry (ANZDATA) for those transplanted between 1963 and 2012 at < 18 years of age, with 1st graft failure during this time. Multinomial logistic regression was used to examine factors associated with non-re-transplantation. Cox regression was used to explore determinants of time to re-transplant, and survival of a 2nd graft. All models were adjusted for transplant era and donor type.

Results:

There were 529 failed transplants in this time, with 68% of these patients re-transplanted. Non-re-transplantation was more common for those with a 1st deceased donor transplant, older donor, and for those with 2 HLA-DR mismatches. In the multivariate regression model, time to re-transplant was significantly longer for those who had a 1st deceased donor transplant, increased HLA-DR mismatches, and 1st graft loss due to non-compliance or chronic allograft nephropathy. Of the 360 re-transplanted patients, there were no1st transplant factors significant in the multivariate model for 2nd transplant survival. Factors associated with increased hazard for 2nd graft loss were 2nd graft donor more than 60 years of age and deceased second donor. Neither 1st nor 2nd graft HLA mismatches were significant in determining survival of the second graft.

Conclusions:

Factors associated with first kidney transplantation are significant in determining relative likelihood and timing of re-transplant. Both 1st and 2nd graft HLA mismatching and other 1st transplant factors are not significant in the survival of the second graft in this population.

P - 436 POPULATION PHARMACOKINETICS OF TACROLIMUS IN STABLE PAEDIATRIC RENAL TRANSPLANT RECIPIENTS TRANSLATED INTO CLINICAL PRACTICE

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Introduction:

The aim of this study was to develop a population pharmacokinetic model of tacrolimus in paediatric patients at least one year after renal transplantation. We aimed to identify factors contributing to the variability of tacrolimus pharmacokinetics and determine individualised dosage regimens.

Material and methods:

We included 45 children with 120 2- or 4-hour profiles. The median age at baseline was 11.1 years (range: 3.8 - 18.4) and the median time since transplantation 16.2 months (range: 11.4 – 124). The pharmacokinetic analysis was performed using the non-linear mixed-effects modelling software (NONMEM). The impact of covariates including concomitant medications, age, *CYP3A5*3* and *ABCB1 C3435T* gene polymorphism on tacrolimus pharmacokinetics was analysed.

Results:

A two-compartment model adequately described tacrolimus pharmacokinetics. The apparent oral clearance (CL/F) was associated with weight (allometric scaling), but not age. Children with lower weight required higher tacrolimus doses. CL/F was inversely associated with hematocrit ($P < 0.05$) and gamma glutamyl transpeptidase (γGT) levels ($P < 0.001$) and was increased by 45% in carriers of the *CYP3A5*1* allele ($P < 0.001$). Tacrolimus pharmacokinetics was not associated with concomitant medications. The median area-under the-concentration-time curve (AUC) was 97 h x ng/ml (range: 39-209).

Conclusions:

Children with lower weight and carriers of the *CYP3A5*1* allele have a higher tacrolimus CL/F and therefore higher dose requirements.

P - 437 ANTI-EBNA SEROCONVERSION AND RISK OF EBV-RELATED PTLD IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS

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Introduction:

EBV-related post-transplant lymphoproliferative disorder (PTLD) is one of the most serious complications associated with kidney transplantation (KTx). Anti-Epstein Barr Nuclear Antigens (EBNA) seroconversion after EBV infection is a marker of resolution of active infection, while the lack of EBNA-IgG is related with chronic EBV infection. Our aim is to evaluate the correlation between anti-EBNA seroconversion and EBV-related PTLD onset in a renal transplanted pediatric cohort.

Material and methods:

We retrospectively reviewed 144 children undergoing KTx at our department between 2005 and 2012. We included 108/144 patients with at least 2 years follow-up and with regular monitoring of EBV-DNA viral load and EBV serology.

Results:

At the time of transplant, 62/108 (57,4%) were anti-EBNA seropositive. During follow-up 12/62 (19%) had a positive EBV viremia (median viral load of 4.426 copies/mL [interquartile range 2.286-10.468], but nobody developed PTLD. Of the 46/108 (42.6%) EBNA-IgG negative patients, 20 (43%) had a positive EBV viremia (median viral load of 40.475 copies/mL [IQR 19.188-364.405]). At a median time of 6 months after viremia positivization (IQR 0.75-25), 8/20 (40%) had anti-EBNA seroconversion: only one of these (12.5%) developed PTLD. The 12 remaining cases (60%) persisted anti-EBNA seronegative and, among these, 7/12 (58.3%) had PTLD. A survival analysis (Kaplan-Meyer method) applied to pre-transplant EBNA-IgG negative recipients showed a slightly significant difference in PTLD occurrence between patients with and without anti-EBNA seroconversion after viremia positivization ($p=0.07$, log-rank test). In Cox-regression analysis, anti-EBNA seronegative status was associated with a higher risk of PTLD (HR 5.59 95% CI 0.99-45.5; $p=0.062$).

Conclusions:

Our preliminary results suggest that pre-transplant EBNA-IgG positive recipients had lower risk of EBV-DNA positivization and PTLD onset after KTx. Pre-transplant anti-EBNA seronegative children are at higher risk of having positive EBV viremia and patients who remain EBNA-IgG negative after viremia positivization have higher risk of PTLD onset.

P - 438 THE WEST MIDLANDS RENAL TRANSPLANT TRANSITION SERVICE: EFFECT ON GRAFT FUNCTION

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Introduction:
Transition of paediatric renal transplant recipients to adult care is a critical period associated with high rates of graft loss. The West Midlands transition service between multidisciplinary Paediatric Renal Centre & Birmingham Adult Nephrology Hospital started in 2006, including investment in joint clinics, transition tours, workshops and social events. The aim was to review changes in eGFR & graft loss before & after introduction of service.
Material and methods:
Data was collected for 2 groups of patients: non-transition group (pre 2006) & transitioned group (post 2006). Age, height, creatinine & number of rejection episodes were retrospectively collected at 6-monthly intervals. GFR was estimated using modified Schwartz formula & analysed using segmented linear regression analysis. These models contained 2 covariates: 1.to estimate overall GFR gradient 2.to assess the magnitude of change in gradient post-transfer. Follow up was truncated at 2 yrs pre- & 4 yrs post transfer to prevent patients with longer followup becoming influential outliers. Graft survival was assessed using Kaplan-Meier curves. All analyses were performed using IBM SPSS 19 ($p<0.05$ statistical significance).
Results:
There were 30 patients in transition &12 non-transitioned patients. The segmented regression analysis found a sig. difference in GFR gradients of groups in pre-transfer period ($p=0.007$), with transitioned patients having a faster initial decline of 7.1 ml/min/1.73m2/yr, compared to only 1.5/yr in non-transitioned patients. After transferring, decline in transitioned patients slowed by 4.1 ml/min/1.73m2/yr (i.e. to 3.0/yr), whilst rate of decline increased in non-transitioned patients by an additional 1.9ml/min/1.73m2/yr (i.e. to 3.4/yr). These changes in gradients differed significantly between transferred and non-transferred groups ($p=0.028$).
A subgroup analysis was performed for transitioned patients, comparing those with GFR of <30 (N=8) & ≥30 (N=22) at transfer. This found that patients in the lower GFR group had a sig. faster decline pre-transition (gradient=-11.9 vs.-4.9 ml/min/1.73m2/yr, $p<0.001$). Post-transfer improvement in GFR<30 group was sig greater than in ≥30 group ($p=0.003$), resulting in gradients in two groups being similar after transfer (-2.4 vs. -3.4 ml/min/1.73m2/yr).
There was no significant difference in graft survival between transition & non-transitioned groups at 5 yrs follow up with 83% & 75%, respectively ($p=0.875$).
Conclusions:
Although transitioned group had a significantly faster decline pre-transfer than non-transitioned patients, this decline was slowed at transition, whilst non-transitioned patients declined hastened. Within transitioned group, patients with GFR <30 at transfer showed the best improvement in GFR gradient post-transfer. Therefore, the transition service is associated with a beneficial effect on GFR gradients, especially for those with a low GFR at transfer.

P - 439 RENAL TRANSPLANT IN CHILDREN WITH PREVIOUS INFERIOR VENA CAVA THROMBOSIS

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Introduction:
The vascular approach to the kidney transplant recipient with complete occlusive thrombosis of inferior vena cava (IVC) is limited but not impossible. These patients are often considered as not candidates for transplantation
Material and methods:
Of the 410 kidney transplants at our institution, six of whom were performed in five recipients with ICV thrombosis. Two of them were first transplants and four were further transplants. All recipients were male with a mean age of 10.7 and range of 2-18 years. All received prior treatment with dialysis. A 60% of recipients received a kidney from a living related donor. IVC thrombosis was discovered in five during pretransplant evaluation but in one case was an unexpected surgical finding. The pretransplant evaluation diagnosis of IVC thrombosis was confirmed by transjugular retrograde cavography
Results:
Venous anastomosis was different depending on the vascular status of recipient, thus hemiazygos, orthotopic renal, splenic or mesenteric veins were used during procedure. Arterial anastomosis was always in the abdominal aorta. Alterations in the study of thrombophilia were observed in 33%. All patients received some kind of anticoagulant treatment. Patient survival until transfer to pediatric or adult referral area was 100%. Only one patient had initial delayed graft function requiring dialysis for a month. Only one graft was lost at 11 years of follow up due to chronic rejection. At the first year of follow up the GFR was 76 ml / min / 1.73m2. Only one patient developed initial proteinuria.
Conclusions:
Kidney transplantation is possible in children with ICV thrombosis . Before establishing an absolute contraindication you must perform a complete vascular study in order to establish the surgical strategy

P - 440 LONGITUDINAL FOLLOW-UP OF CARDIOVASCULAR COMORBIDITY IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS - RESULTS FROM THE 4C-T STUDY

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Introduction:
Children with chronic kidney disease (CKD) carry an increased cardiovascular risk. Cardiovascular death is the second leading cause of death in children after renal transplantation. The 4C-T (Cardiovascular Comorbidity in Children with CKD and Transplantation) study evaluates cardiovascular target organ damage longitudinally in children prior to and after renal transplantation.
Material and methods:
The multicenter, prospective, observational 4C study enrolled 736 children aged 6 to 17 years with estimated GFR <40 ml/min/1.73 m^2 at 55 Pediatric Nephrology centres from 12 European countries. Of these, 226 have started renal replacement therapy (RRT) and entered the 4C-T sub-study. At annual study visits, the morphology and function of the heart and large arteries were monitored by noninvasive methods.
Results:
176 of the 226 patients on RRT had at least one visit after RRT start and were included in this analysis. 70 patients had started dialysis and 106 received a transplant. 62% of the patients were transplanted preemptively. Overall patients carried a higher cardiovascular risk compared to the agematched general population as documented by elevated age-adjusted aortic pulse wave velocity (PWV) and carotid intima-media thickness (IMT). Factors determining PWV, IMT and left ventricular

mass index (LVMI) were analysed using mixed longitudinal modelling (table).

	PWV		IMT		LVMI	
Effect	Estimate	p	Estimate	P	Estimate	p
Dialysis	0.4648	0.0024	0.2793	0.0448	4.1835	0.0068
Tx after dialysis	0.3980	0.0264	-0.00253	0.9876	3.9145	0.0283
Preemptive Tx	Reference		Reference		Reference	
BP	0.04065	<0.0001	0.01427	0.0212	0.1167	0.0054
PTH	0.009556	<0.0001	0.003614	0.074	0.07823	0.0003
Male gender	-0.4157	0.0019	-0.3076	0.0135	3.5783	0.0089

Conclusions:
Our data is consistent with the hypothesis that transplantation lowers cardiovascular risk. Mixed modeling allowed to decipher the positive effect of transplantation from interfering cardiovascular risk factors such as hypertension, hypercholesterolemia and PTH.

P - 441 PREPARING FOR THE FUTURE – A QUALITATIVE ANALYSIS OF THE TRANSITION PROCESS OF PAEDIATRIC RENAL TRANSPLANT PATIENTS

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Introduction:
As part of the TRANSNephro project on the transition of paediatric renal patients we analysed the existing structures in Germany and Austria. Here, we describe the staff's perspective of 22 paediatric renal outpatient clinics.
Material and methods:
We visited all units responsible for the outpatient care of paediatric renal transplant recipients in Germany and Austria. In each centre we conducted semi-structured interviews with members of staff covering the medical, nursing, and psychosocial professions. Interviews were transcribed ad-verbatim and analysed by content.
Results:
There was a wide variety of shaping transition both between the different centres as well as between the professions. Though most centres had oral agreements on their procedures, there was a lack of written guidelines and check-lists to navigate the process.
While most participants said that fostering patient autonomy was their main goal in preparing the young patients, many reckoned that their rather mothering behaviour and a lack of structures impeded their professional aims.
Furthermore, there was general dissatisfaction regarding a lack of cooperation with the adult nephrologists.
A major issue appeared to be external regulations, most notably a fixed date for transferring the patient. Most commonly the young adults are requested to leave paediatric care with their 18th birthday regardless their individual needs and competences at that time.
Conclusions:
Transition in Germany and Austria is suffering from both a lack of structures as well as overregulation.
On the one hand, existing rules - such as fixed dates for transfer - impede a transition process which is adapted to the patients' life-events and relevant needs.
On the other hand, a lack of guidelines within the departments increases the risk for neglecting a clearly defined, goal-oriented transition process and leads to acting on a day to day base.

P - 442 RATIONALE, DESIGN AND BASELINE CHARACTERISTICS OF PEDIATRIC RENAL TRANSPLANT RECIPIENTS IN CRADLE STUDY: A RANDOMISED STUDY TO EVALUATE THE EFFECT OF EARLY EVEROLIMUS INITIATION TO REDUCE CALCINEURIN INHIBITOR EXPOSURE AND TO WITHDRAW STEROID

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Introduction:
Immunosuppression with calcineurin inhibitors (CNI) and steroids in pediatric renal transplant recipients (pRTxRs) is associated with nephrotoxicity, growth impairment, glucose intolerance and bone diseases. CRADLE (NCT01544491) will evaluate efficacy and safety of early everolimus with reduced CNI and steroid withdrawal at Month (M) 6 in pRTxRs.
Material and methods:
CRADLE is a 12M, phase-III, open-label study with an additional 24M safety follow-up, pRTxRs (≥1-<18 years) receive initial immunosuppression with standard tacrolimus+mycophenolate mofetil+steroids. After a run-in-period of 4-6 weeks post-Tx, patients with eGFR >40mL/min/1.73m^2 are randomised (1:1) to either continue the same regimen or switch to everolimus+reduced tacrolimus+steroid withdrawal (M6). Primary objectives at M12 are to estimate: i) the rate of composite efficacy endpoint (biopsy-proven acute rejection, graft loss or death) and ii) renal function. Key secondary objectives include progression of interstitial fibrosis/tubular atrophy, post-transplant lymphoproliferative disorder, growth and sexual maturation.
Results:
The study is currently recruiting pRTxRs at 36 sites in 14 countries. In December 2014, the Data Monitoring Committee (DMC) reviewed data of 74 randomised pRTxRs and agreed to continue the study as planned. No safety/efficacy concerns were raised. Safety analysis included 69 patients; 35 (50.7%) female, 59 (85.5%) Caucasian; median (range) weight 29.2 kg (10.0-86.2), height 134.0 cm (76.0-181.5), BMI 16.9 kg/m^2 (10.2-29.2). The median age was 10.0 years (range 1.0-17.0): 18 (26.1%) patients, 1-<7 years; 19 (27.5%), 7-<12; and 32 (46.4%), 12-<18. Prior to RTx, 43 (62.3%) patients were on dialysis. The most common cause of RTx was renal hypoplasia/dysplasia (20.3%). Majority (94.2%) of patients received induction with basiliximab. At randomisation, median eGFR was 81.5mL/min/1.73m^2 (range 37-264). An update from the DMC is awaited in June 2015.
Conclusions:
CRADLE study will determine whether early everolimus introduction to reduce tacrolimus exposure and withdraw steroids is efficacious and safe in pRTxRs and will provide long-term data on growth and sexual maturation, and glucose intolerance.

P - 443 ROLE OF LUMINEX C1Q ASSAY IN FACILITATING TRANSPLANTATION OF HYPERIMMUNE PATIENTS

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Introduction:
We describe two hyperimmunized children successfully transplanted after organ allocation decided on the basis of cytotoxic antibodies's absence, studied with standard method (complement-dependent cytotoxicity: CDC) and C1q Luminex assay.
Material and methods:
Patient 1 is a 18 years-old boy with obstructive uropathy, who restarted hemodialysis at 13 years for chronic humoral rejection and developed hyperimmunization (PRA CDC 100% - Luminex 100%). Acceptable mismatches (MM) were 5. Since 2009 he was considered for a priority kidney allocation due to problems with vascular access.
Patient 2 is a 12 years-old girl, who lost the graft for recurrence of Atypical HUS and developed hyperimmunization (PRA CDC 50% - Luminex 100%). Acceptable MM were 12. Since 2010 she was on urgent waiting list due to complications of vascular access. Both patients underwent a protocol of desensitization which included apheresis, intravenous immunoglobulin, Rituximab and Bortezomib, but a mild reduction in HLA antibodies was observed only in the first patient. Therefore, we studied patients' antibodies with CDC, Standard and C1q Luminex assay and decided to consider unacceptable only MM identified by CDC and C1q.
Results:
Patient 1 received a renal transplant in January 2014 from a deceased donor with 5 acceptable MM, while patient 2 was transplanted in October 2014 with 3 MM. Patient 1 underwent three apheresis sessions and one Rituximab infusion. Maintenance immunosuppression protocol included calcineurin inhibitors, mycophenolate mofetil and prednisone. In addition, patient 2 received eculizumab. Both patients have a good renal function and no lymphocytotoxic antibodies detectable.
Conclusions:
A comprehensive study of immunological status with detection of lymphocytotoxic antibodies can give to hyperimmune patients a chance to receive a successful renal transplant.

P - 444 AMBULATORY BLOOD PRESSURE AND LEFT VENTRICULAR HYPERTROPHY IN RENAL TRANSPLANT RECIPIENTS

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Introduction:
Hypertension (HT) is a common complication after renal transplantation (RT) and is associated with increased cardiovascular risk. The aim of this study was to investigate the prevelance of post-transplant hypertension (HT) and left ventricular hypertrophy (LVH).
Material and methods:
A total of 31 stable RT patients (17 males) in whom 24-h ambulatory blood pressure measurement (ABPM) had been assesed were enrolled in this retrospective study. Echocardiography had been performed in a subgroup of 24 patients within 6 months. Hypertension is defined according to American Heart Association criteria. LVH is defined as left ventricular mass index (LVMI) greater than 95.p for age and sex of the patient.
Results:
The mean age was 16.0±3.5 years. Transplant age was 12.8±3.2 (4.3-17.7) years with a median follow-up of 34 (4-90) months. Mean GFR was 113±40 ml/dk/1.73m^2, mean BMI SDS was 0.74±1.2. ABPM revealed HT in 14 of 31 patients; 10 uncontrolled, 4 masked HT. Those who are normotensive on ABPM; nine had controlled HT, 4 had normal BP, 3 had white coat HT, 1 had prehypertension. The prevalence of day time HT, nocturnal HT and isolated nocturnal HT were 29%, 41%, 16% respectively. Twenty-one of the patients were systolic and/or diastolic non-dipper (%67). There was an inverse correlation between post-transplant duration and night-time SBP SDS (p=0.025, r=-0.401).
The mean of LVMI was 39.8±11,4 g/m$^{2.7}$ and the prevelance of LVH was 41% (n: 10/24) in our subgroup. In univariate analysis there was a positive correlation between LVM and 24-h MAP SDS (p=0.017, r=0.482), day-time SBP SDS and load (p=0.002, r=0.608; p=0.017, r=0.481), BMI SDS (p=0.028,r= 0.450). In multivariate analysis 24-h MAP SDS/day-time SBP SDS and BMI SDS were independent predictors of LVMI.
Conclusions:
Our findings reveal significant relationships between ambulatory BP and LVMI and underline the importance of ABPM to predict cardiovascular disease in renal transplant recipients.

P - 445 VALIDATION OF FORMULAE TO ESTIMATE GFR IN CHILDREN POST RENAL TRANSPLANT

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Introduction:
Estimating glomerular filtration rate (eGFR) has become popular very important method in clinical medicine for early diagnosis allograft nephropathy as an alternative to measured GFR (mGFR).The aim of our study is to determine the most accurate and closer to the "gold stand-ard method of estimating GFR in children after renal transplantation.
Material and methods:
Two creatinine-based (estimated GFR [eGFR]-Schwartz, urinary creatinine clearance), seven cystatin C–based (eGFR-Zappitelli1, Filler, Le Briconb (2000), Hoekb (2003) Larsson (2004), Grubb (2005) , Bokenkamp (1998)), and one cystatin C/creatinine–based (eGFR-CKiD III) estimates were compared with the gold standard GFR measured by Tc-99 single injection (GFR-Tc-99) in 11 children after renal transplantation. Evaluation of GFR was performed by in-travenous dose radioisotope Tc-99 children in accordance with their weight, height, age, and after taking the venous blood 1,2,3 hour after administration of the radiopharmaceutical. Measurement of the counting rate of Tc-99 was carried out in two ways: on gamma spectrometer with semicon-ductor purity germanium detector and by liquid-scintillation spectrometry method with device TRICarb 2700 TR, Canberra Packard Ind, USA. Included patients were 9–17 years of age.
Results:
Both methods of measurement the activity (gamma spectrometry and liquid scintillation spectrometry) showed the same result for the GFR estimation. Analysis of comparison of the GFR results obtained using different formulas of creatinine and cystatin C, in all cases showed a direct correlation with the results of GFR determined by using the "gold standard." However, the highest correlation was observed between the "gold standard" and the eGFR-CKiD III on the basis of creatinine and cystatin C (R-0,66, P <0,05).
Conclusions:
Based on these data we can conclude that the calculation formula eGFR-CKiD III can be used to determine the function of post renal transplant.

P - 446 COLLABORATIVE BRAZILIAN PEDIATRIC RENAL TRANSPLANT REGISTRY (COBRAZPED-RTX): A REPORT FROM 2004-2014

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Introduction:
The Collaborative Brazilian Pediatric Renal Transplant Registry started in 2004 as a multicentre initiative aiming to analyze, report and share the results of pediatric kidney transplantation in Brazil.
Material and methods:
Database from all pediatric kidney transplants performed between 2004 and 2014 were analyzed for demographic data, etiology of CKD, patient and graft survival.
Results:
From a total of 2792 pediatric kidney transplants performed in Brazil during the study period, we report data from 2128 pediatric renal transplants performed in 13 centers enrolled in the collaborative study. Median age at transplantation was 12.4 years old and most of recipients were male (55%). The most common underlying renal etiology were obstructive uropathy (31%) and glomerulopathy (26%). According to donor source, 1433 (67%) of transplants were performed with deceased donors (DD). Initial immunosuppression consisted mainly of tacrolimus, mycophenolate, steroids and induction therapy with anti- IL-2R antibodies. The graft survival at 1, 5, and 10 yr (death censored) was 94%, 84%, and 70% for living donor (LD) and 89%, 75%, and 59% for DD respectively (Log rank test $p<0.01$). There were 15% of graft losses, more frequently caused by vascular thrombosis, chronic allograft nephropathy, death with functioning kidney, acute rejection, and recurrent renal disease. Patient survival at 1, 5, and 10 years were 98, 95%, and 91% for LD and 97, 93%, and 83% for DD respectively. Mortality rate was 5.2%, mainly due to infection and cardiovascular disease. Recipients of deceased donors had 1.60 (1.29-1.97) times the hazard of graft loss compared with those of living donors.
Conclusions:
The results of this collaborative pediatric transplant study are comparable to international registries. Our effort has been able to maintain an exchange of information, both among the participating centers and with other international registries.

P - 447 THE NEPHROLOGISTS' PERSPECTIVES ON TRANSITIONING RENAL TRANSPLANT PATIENTS IN GERMANY – A TRANSNEPHRO SUBSTUDY

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Introduction:
As part of the TRANSNephro project on the transition of paediatric renal patients we analysed the existing structures in Germany and Austria. Among others, our aim was to describe the perspective of the German adult nephrologists who appear to play a decisive role in the setting.
Material and methods:
We invited all 1984 physicians who are registered with the German Society for Nephrology (DGfN) to participate in a short online survey. Data were analysed using SPSS statistical package for the social sciences. In addition, a selection of nephrologists participated in semi-standardised interviews to further explicate their thoughts and experiences. The interviews were transcribed ad verbatim and analysed by their content.
Results:
119 nephrologists (6%) completed the survey; 99 of whom said they were treating formerly paediatric patients. 59 physicians (60%) stated that caring for these patients appeared to be a challenge as compared to their other patients. They noted specific problems with regard to the young people's psychological, social and emotional development. Lack of adherence, insufficient autonomy and self-care were identified as critical factors which asked for increased alertness and extra time required for the appointments. In contrast, the participants described a lack of specialist staff and psychosocial support in their outpatient clinics. Also, they wished for further knowledge particularly in the field of social and psychological assistance.
Conclusions:
The poor response-rate suggests that the topic of transition is not yet consciously present but rather neglected in the German nephrologists every day work.
The participating nephrologists however are aware of particular challenges in treating young adult patients, namely aspects of autonomy, adherence and self-care. In parallel they name structural deficits such as lack of staff and information which impacts on the care of these patients.

P - 448 RECURRENCE OF NEPHROTIC PROTEINURIA IN CHILDREN WITH FOCAL SEGMENTAL GLOMERULOSCLEROSIS - EARLY TREATMENT WITH PLASMAPHERESIS AND IMMUNOADSORPTION SHOULD BE ASSOCIATED WITH BETTER PROGNOSIS

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Introduction:
FSGS is a glomerular disease, characterized by progressive renal function deterioration, nephrotic proteinuria, and risk of chronic renal failure.
Material and methods:
We present long-term results of 5 patients with primary FSGS and recurrence of nephrotic proteinuria after renal transplantation treated

with plasma exchange (PE) and immunoadsorption (IA). We retrospectively investigated the relationship between the delay in initiation of the therapy and treatment outcomes, particularly achievement of remission of proteinuria.

Results:

Remission occurred in all three patients who started PE/IA in interval 3-7 days after diagnosis of recurrence of FSGS. Remission was achieved after 3-4 weeks in two patients with 3 days of delay to the start of PE. The third patient (PE started with 7 days of delay) reached complete remission after 6 months of PE/IA treatment. All these patients had remission sustainable for a long time. The remaining two patients with 14 and 406 days of delay to PE treatment did not achieve remission sustainable for a long time. The two patients who did not achieve remission developed end-stage renal disease with graft loss (1 and 6.7 years after Tx). Patients who achieved remission of proteinuria during PE/IA treatment have still functioning grafts (2.8, 9.7 and 3.8 years after renal Tx). All these patients are still treated with PE/IA.

Conclusions:

The present 5 cases suggest that if recurrence of FSGS occurs, the probability of achieving remission is dependent on the early initiation of PE/IA therapy. Therefore, we suggest that PE/IA treatment might be started as soon as possible after recurrence of FSGS.

P - 449 TRANSITIONING RENAL TRANSPLANT PATIENTS IN GERMANY: CURRENT SITUATION OF PAEDIATRIC CARE, GRAFT FUNCTION AND MEDICATION ADHERENCE – A TRANSNEPHRO SUBSTUDY

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Introduction:

Transition from child to adult-oriented care is widely regarded a challenging period for young people with kidney transplants and is associated with a high risk of graft failure. Knowledge about the transition process of these patients in Germany is scarce.

Material and methods:

As part of the TRANSNephro project on the transition of paediatric renal patients we analysed the existing structures in Germany. A questionnaire and retrospective data on graft function and immunosuppressive levels 12 months before transfer were used to analyse current transitional care at 22 paediatric centres.

Results:

Most centres (68%) confirmed internal agreements on the transition procedure for adolescents.

Patients' age at transfer was subject to regulation in 70% of all centres. Most commonly the regional associations of SHI physicians required 18 year old patients to be transferred into adult care.

Median age at transition was 18.3 years (16.5 – 36.7). One year prior to transfer serum creatinine levels were 48 ±20 ml/min/1,73m² , and 47 ±20 ml/min/1,73m² at transfer, respectively.

21/110 patients had increased creatinine levels ≥20% (compared with baseline) just before transfer.

Biopsy proven rejection was found in 3/110 patients within the year before transfer. Additionally, 7 patients had a "borderline" finding (Banff classification) when biopsied. Three patients lost their graft within the year before transfer.

Mean coefficient of variation (CoV) of immunosuppression trough levels was 0.22 ±0.09 (n=98). 56/98 patients showed CoV consistent with good compliance (<0.20), and only 5/98 showed poor compliance (>0.43).

Conclusions:

The majority of German paediatric nephrology centres have internal agreements on transitional care.

Graft function within the year prior to transfer seems to be stable. More than half of the patients had CoV of immunosuppression trough levels consistent with good adherence. Though, about one fifth of the patients showed unexpected increase in serum creatinine close to transfer – a worrying finding.

P - 450 PREVALENCE OF HYPERTENSION AND RENAL DYSFUNCTION AFTER PEDIATRIC LIVER TRANSPLANTATION

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Introduction:

Liver transplant recipients are at increased risk of renal damage. The purpose of this study was to assess the prevalence of hypertension and glomerular and tubular dysfunction in children with liver transplantation

Material and methods:

Forty six patients, aged 7 to 18 years (mean: 12.2±3.3; 24 female) who were transplanted at least in the previous 6 months with GFR> 60, were enrolled in this cross sectional study. Patients' data, such as age, gender, date of transplantation were extracted from charts. Glomerular and tubular function were examined by cystatin C and creatinine based GFR, urinary Alb/Cr ratio, tubular reabsorption of phosphate (TRP), fraction excretion of Mg and uric acid(FEMg, FEUA), and urinary Ca/Cr. Blood pressure was taken by causal and ambulatory blood pressure (ABPM) methods.

Results:

The mean Cyctatin C –based GFR (66.4±14.4) was lower in comparison with creatinine-based GFR (149.5±36.2). The prevalence of CKD according to cystatin C based GFR was : stage 1 (4.3%), stage 2 (63%), stage 3a (28.4%), and stage 3b (4.3%). Creatinine based GFR showed CKD stage 1 in 97.8% and stage 3a in 2.2% of the patients. The ABPM showed hypertension in 20 patients (43.5%), systolic non-dipping in 37% and diastolic non-dipping in 36.6% of the patients. Office measurement showed 7 patients (15.2%) with high blood pressure. Hyperuricosuria was detected in 4.3% , micro-albuminuria in 26.1%, hypercalciuria in 6.5%, abnormal FEMg in 43.5%, and abnormal TRP in 4.3% of the patients.

Conclusions:

Glomerular and tubular function is impaired and the prevalence of hypertension is high in children with liver transplantation. Using Cyctatin C instead of creatinine for GFR estimation and blood pressure monitoring by ABPM is essential for detection of renal function disturbances in liver transplant recipients.

P - 451 MANAGEMENT OF ANTIBODY-MEDIATED REJECTION IN PAEDIATRIC RENAL TRANSPLANTATION: A RETROSPECTIVE STUDY

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Introduction:

The management of antibody-mediated rejection (AMR) in paediatric renal transplantation (R-Tx) remains to be defined; rituximab, plasma exchange and/or intravenous immunglobulins (IVIg) are commonly proposed.

Material and methods:

A retrospective study of paediatric patients receiving IVIg for AMR after R-Tx in our unit was performed. Between 01/01/2000 au 01/01/2012 a

total of 155 pediatric patients underwent R-Tx; among them 10 (6%) developed AMR. Results are expressed as median (min-max).

Results:

Primary kidney diseases were 8 CAKUT, 1 SRNS and 1 nephronophthisis. Age at R-Tx was 6(1-13) years, 9 patients undergoing a first R-Tx and 1 patient a second R-Tx. The number of HLA mismatches was 3(3-5). Concerning EBV and CMV, there were 6 and 0 mismatches, respectively. Four patients received blood transfusions before or during R-Tx. The median eGFR one year after R-Tx and one year before AMR was 79(51-133) and 61(12-112) mL/min/1.73m^2, respectively. AMR occurred 5(1-12) years post R-Tx, with an eGFR at that time of 61(15-85) mL/min/1.73m^2.First DSA were observed 47(7-149) months after R-Tx, from 19 months before to 1 month after AMR diagnosis (n=8 available data). 9/10 episodes were biopsy-proven (7 C4d-positive). Eight patients received rituximab, three plasma exchanges and all IVIg. The maximal MFI before and after IVIg therapy was 10847(2409-15215) and 0(0-12836), respectively. After IVIg therapy, eGFR was 39(17-92) mL/min/1.73m^2. Patients received 11(2-36) courses of IVIg with a total dose of 553(40-2300)g (mainly 4-week-intervals with 2g/kg given over 48h). Side effects were headaches (n=2) and hemolytic anemia (n=1). Three grafts were lost. At the last follow-up in functioning transplants, MFI was 54(0-12540) and eGFR 43(26-92) mL/min/1.73m^2, with an eGFR of 80(15-85) at the AMR onset.

Conclusions:

IgIV is a useful tool in paediatric AMR. Combined data from small cohorts should help us to improve management of these highly-specialized patients and long-term outcomes.

P - 452 TRANSPLANTATION OF ADULT LIVING DONOR KIDNEYS IN SMALL CHILDREN; A SINGLE CENTER EXPERIENCE

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Introduction:

Transplantation is the methode of choice to treat ESRD in children. Postmortal paediatric donor-kidneys are scarce, but fortunately most parents are willing to donate. However, RTx of adult kidneys in small children is a major challenge. In 2012 we set up a special program to make these adult living-related RTx in children under the age of 4 years possible. Eight children are included so far.

Material and methods:

Donor and recipient characteristics, surgical technique, ischaemia times and outcome measurements (serum creatinine, GFR, graft/patient survival) were analyzed. Mean age of 8 recipients (6 boys, 2 girls) was 2.6 (range: 1.5-4.1)yrs, length 87.1 (72.5-97)cm, and weight 13.5 (10.0-17.9)kg. All had congenital ESRD (PUV, polycystic kidney disease, reflux-nephropathy, nephronophtisis, renal dysplasia). Three were on haemodialysis, 5 had pre-emptive RTx. All donors were parents (3M, 5F), age 36.8 (24-45)yrs. Graft length was 11.2 (10-12.1)cm. All donornephrectomies were laparoscopic and without complications. All recipients underwent transverse laparotomy with vascular anastomoses on the abdominal aorta and inferior caval vein.

Results:

Warm (combined 1st and 2nd) and cold ischemic times were 37.8 (16.9-51)min and 3.5 (2.5-3.9)hrs, respectively. All children received immunosuppression according to theTWIST-protocol: Basiliximab/ Tacrolimus/ Mycophenolate. There were no cases of delayed graft-function. Patient and graft survival are both 100% (mean follow-up 12.5 mo). Early complications were druginduced delirium(2), septicaemia(1), and early postoperative haemorrhage, necessitating re-operation(1). In nephronophtisis patient (with pre-existent liver fibrosis) excessive postoperative lymphe-ascites was encountered. Mean PICU-stay was 10(5-17)days. Mean serum creatinine at 3 mo was 45.6 umol/l. Mean GFR was 6.7 (before RTx), 106 (at 1 mo), 84 (at 3 mo) and 81ml/min/1.73m2 at 6 mo after RTx.

Conclusions:

Transplantation of adult living-donor kidneys in children under the age of 4 years is challenging but feasible, with good graft function during mid-term follow-up. Therefore pre-emptive living donor transplantation is a valid option for the verg young recipient.

P - 453 AN ONLINE SURVEY ON PAEDIATRIC RENAL TRANSPLANTATION ACROSS INDIA

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Introduction:

To assess the current status of paediatric renal transplantation across India.

Material and methods:

An online questionnaire was emailed to the members of Indian Society of Pediatric Nephrology and Indian Society of Nephrology across India. The answers were analyzed to obtain an overview of the current state of paediatric renal transplantation.

Results:

We received total fifty responses from all over India, adult nephrologists (66%). On analyzing the responses most of the nephrologists (78%) reported to see on an average less than 1-5 new children with end stage renal disease (ESRD) per month. Congenital Anomaly of Kidney and Urinary Tract (CAKUT) was the most common cause of ESRD. Less than a quarter of children with ESRD progressed to renal transplant. Cost seemed to be the most important impediment. For centers which actively undertook paediatric renal transplantation the average was 1-5 paediatric transplantations per year and the usual age was above 10 years. Transplantation seemed to be more common in children above 15 Kg. Pre-emptive transplantation seemed to be uncommon in India. The standard immunosuppressant seemed to be the combination of steroid, mycophenolate mofetil and tacrolimus and induction was used in 40% cases.

Conclusions:

Our study showed that compared to our paediatric ESRD population, paediatric transplantation is still being done in low numbers. Most of the centers are comfortable at doing transplantation in older children with few reporting transplantation below 15 Kg or < 5 years.

P - 454 DOES THE REFLUX TO THE TRANSPLANTED KIDNEY SHORTEN ITS LIFESPAN? EVALUATION OF POST-TRANSPLANTATION VUR CASES

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Introduction:

Urinary tract infection (UTI) after renal transplantation is one of the most important cause leading graft dysfunction. Vesicoureteral reflux (VUR) to the transplanted kidney is common because of the surgical technique, predisposing to UTIs.

Material and methods:

All pediatric renal transplant recipients who were transplanted between January 2005 and December 2014, and had a follow-up period of at least

6 months were enrolled in the study. Patients were followed in terms of VUR after transplantation and necessary imaging tecniques were applied to investigate the occurence of UTI. The UTI incidence in the post-transplant first and second 6-month periods were investigated. Estimated glomeruler filtration rate (eGFR) was calculated at post-transplant 6th, 12th and 24th months using Schwartz formula.

Results:

Post-transplant VUR was detected in 23 out of 133 cases (17.2 %), 15 of whom had congenital anomalies of the urinary tract (6 posterior uretral valve, 5 VUR nephropathy, 4 neurogenic bladder). Primary cause of the kidney disease was not definitive for post-transplant VUR (p=0.53). Incidence of UTI in patients with post-transplant VUR was 54% and 68% within post-transplant 6 months and between 6-12 months, respectively, which was higher than patients without VUR (3.7%, 2.8%)(p<0.001). eGFR values of patients with and without post-transplant VUR were similar at post-transplant 6th, 12th and 24th months (67.3±22.2 vs 69.8±23.2, p=0.26; 45.6±16.6 vs 48.5±20.2, p=0.14 and 53.5±17.9 vs 56.3±18.2 ml/min/1,73m2, p=0.37, respectively). As therapy of VUR, all children received antibiotic prophylaxis; endoscopic treatment and open ureteroneocystostomy was applied to 15 and 5 children, respectively. Despite these therapies, one patient had graft loss due to recurrent UTIs.

Conclusions:

UTI is a common problem in patients with post-transplant VUR, which is not rare. Graft survival was not affected when these patients was closely followed up and treated appropriately.

P - 455 IMMUNOMONITORING BY VIRUS-SPECIFIC T CELLS AFTER PEDIATRIC KIDNEY TRANSPLANTATION (IVIST01-TRIAL): STUDY DESIGN AND STATUS

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Introduction:

After kidney transplantation (Tx) immunosuppressive therapy causes an impaired cellular immune defense with an increased risk of viral complications. Virus-specific T cells (Tvis) correlate with control of virus replication as well as with the intensity of immunosuppression. Serving as an indicator of overimmunosuppression, monitoring of Tvis may allow an assessment of individual susceptibility to infection and optimize dosing of immunosuppressants.The ongoing IVIST01-trial proves that steering of immunosuppressive therapy by Tvis levels leads to better graft function by avoidance of overimmunosuppression and drug toxicity.

Material and methods:

The IVIST01-trial is a prospective, multicenter, randomized study starting 4 weeks after Tx and ending 24 months after Tx. 64 pediatric kidney recipients are randomized either to an intervention group with additional Tvis monitoring or to a control group. In both groups the immunosuppressive drugs (cyclosporine A; everolimus) are adjusted within the same target range of trough levels. In the control group the immunosuppressants are only steered by classical trough level monitoring. In contrast, in the intervention group the dose of immunosuppressants is additionally adjusted according to Tvis levels. Tvis against different virus types (CMV, HSV, ADV) are measured by cytokine flow cytometry. Primary endpoint of the IVIST01-trial is the glomerular filtration rate 2 years after Tx; secondary endpoints are number and severity of viral infections and incidence of side effects of immunosuppressive drugs.

Results:

Until now 41 patients (64%) have been randomized (22 patients in intervention group; 19 patients in control group) and 24 patients have already completed the study period. Seven patients became drop-outs because of change of the immunosuppressive regimen.

Conclusions:

The IVIST01-trial provides a novel concept of personalization of immunosuppressive management after kidney Tx. The study design aims to improve graft function by steering the immunosuppressive therapy by Tvis monitoring (effect-related drug-monitoring). Until now study course and recruitment are favorable.

P - 456 GRAFT SURVIVAL IN LIVING RELATED DONOR TRANSPLANTATION FROM GRANDPARENTS

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Introduction:

Living related donor (LRD) transplantation (Tx) has been recommended as the first choice for pediatric kidney transplant recipients based on proven efficiency for improved clinical outcomes. However, a decline to pediatric LD and LRD Tx has been reported from large transplant registries including NAPRTCS and OPTX/SRTRThe aim of the present study was to investigate the short- and long-term graft survival after LRD Tx in pediatric patients.

Material and methods:

A single center retrospective study was conducted at a tertiary affiliated institution. We reviewed the medical charts of all pediatric kidney transplants performed at the division of transplantation, department of surgery between 1990 and 2012. Demographic, laboratory, clinical data, and immunosuppression protocols, as possible factors associated with outcome, were recorded.

Results:

In total 75 LRD Tx were performed from living related donors (LRD), 14 from recipients' fathers, 47 from their mothers, 12 from their grandmothers, and 2 from their grandfathers. Mean age at Tx was 11.72 ± 4.48 years. In 24 (34.3%) of the patients, LRD Tx was performed pre-emptively. There was a decreasing tendency in LRD Tx rates in decade 2 compared to decade 1 (47.1% vs. 62.7%, respectively, P=0.06). The 1-, 5-, 10-, 15- and 20-year graft survival in LRD Tx was 93.3%, 86.7%, 77.3%, 72%, 69.3%, respectively. Five- and 10-year survival in the two recipients of kidney graft from their grandfathers was 100% (Figure). There was no statistically significant difference in 1-, 5-, 10-, 15, and 20-year graft survival with regard to relation to living donor. Graft survival in kidney transplant recipients from parents was comparable to that of grandparents (93.4% vs. 92.9% at 1 year, 86.9% vs. 85.7% at 5 years, 71.4% vs. 78.7% at 10 years, 75.4% vs. 57.1% at 15 years, and 72.1% vs. 57.1% at 20 years after Tx, respectively, NS).

Conclusions:

Graft survival was favorable in all RLD groups irrespective of donor age. Of note graft survival from grandparents was comparable to that of grafts from parents. This finding suggests that older LRD are an excellent option for the 1st kidney Tx in children and adolescents, which could conquer for the observed decreasing trends of LRD worldwide.

P - 457 CHANGE IN ANTIBODY TITERS FOR MEASLES, RUBELLA, MUMPS, AND VARICELLA IN CHILDREN RECEIVING KIDNEY TRANSPLANTATION

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Introduction:
The symptoms of measles, rubella, mumps, and varicella are more aggravated in immunocompromised hosts. The purpose of this study was to investigate the change in antibody titers for measles, rubella, mumps, and varicella from before to after renal transplantation (KTx) in children.
Material and methods:
From February 2009 to February 2015, a total of 87 children 20 years old or younger (median age 9.0 years [range 2.0–20]) received KTx in our institution.Antibody titers for measles, rubella, mumps and varicella were measured in our institution before KTx and at 4 months and 1, 2, 3, and 5 years after KTx.Immunoglobulin G antibodies against measles, rubella, mumps, and varicella were measured using an enzyme-linked immunosorbent assay.
Results:
Significant decreases in median antibody titer were seen for measles from 21.8 (range 3.0 to 128) before KTx to 14.1 (2.1 to 105) at 1 year ($p = 0.012$), and for mumps from 8.4 (<2.0 to 128) before KTx to 4.4 (<2.0 to 112) at 2 years ($p = 0.043$). The median antibody titer for rubella decreased non-significantly from 17.8 (<2.0 to 165) before KTx to 9.7 (<2.0 to 309) at 1 year and significantly to 8.1 (<2.0 to 128) at 2 years, while that for varicella decreased non-significantly from 15.1 (<2.0 to 128) before KTx to 5.5 (<2.0 to 172). Only one patient developed herpes zoster.
Conclusions:
The antibody titers for measles, rubella, mumps, and varicella tend to decrease throughout the 5-year period following KTx, and that for measles decreases significantly in the first year after renal transplantation. Therefore precautions, such as vaccination, should be taken in children undergoing renal transplantation.

P - 458 REVIEW OF FACTORS ASSOCIATED WITH RENAL TRANSPLANT GRAFT OUTCOMES IN TRANSITION

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Introduction:
Transition of paediatric transplant recipients to adult care is a critical period associated with higher rates of graft loss. Our transition service was set up in 2006 comprising joint clinics, transition tours, workshops and social events to improve transition outcomes. The aim of this study is to review factors which influence graft function during transition.
Material and methods:
Data was collected on 30 patients in the transition service, including transplant details,, donor type, age at transplant and diagnosis of learning difficulties (LD). Data was retrospectively collected at 6-monthly intervals for age, height, creatinine, blood pressure, tacrolimus levels, non-attendances & rejection episodes. GFR was estimated using the modified Schwartz formula, and analysed using segmented linear regression analysis. These models contained two covariates, one to estimate the overall GFR gradient, and the other to assess the magnitude of change in the gradient, post-transfer. Follow up was truncated at 2 years pre-transfer, and at 4 years post transfer, to prevent patients with longer followup becoming influential outliers. All analyses were performed using IBM SPSS 19, with $p<0.05$ deemed to be indicative of statistical significance.
Results:
GFR of transitioned pts was declining by an average of 7.1 ml/min/1.73m2/yr pre-transfer, which reduced to by 3.0 ml/min/1.73m2/yr post-transfer. Relationships between several factors and GFR pre- and post-transfer were assessed and are reported in the table. The first column gives the pre-transition GFR gradients/yr & p-value comparing 2 groups. The second column shows how gradients changed after transition, and compares this between groups. GFR was found to decline significantly faster pre-transition in patients who received deceased donor organs ($p=0.004$), were transplanted at <13 yrs old ($p=0.016$), did not have LD ($p=0.002$), had a lower GFR at transfer ($p<0.001$), had more than 0.5 DNAs at adult unit/yr ($p<0.001$), did not attend the tour ($p=0.010$) or had DNAs at the tour ($p<0.001$).
After transition, patients with fewer than 0.5 DNAs at adult unit per year ($p <0.001$) and with no DNAs at tour ($p=0.022$) were found to do significantly better than those patients with more than 0.5 DNAs at UHB per year and with DNAs on tour, respectively.
Conclusions:
In our renal transition service, patients who attend clinics and tours at the adult centre, and who have a higher GFR at transfer have better graft outcomes. Patients with learning difficulties have better graft outcome compared to those without learning difficulties. This information has helped us to identify patients which are most at risk of graft loss.

P - 459 KIDNEY TRANSPLANTATION (KT) IN SMALL CHILDREN WEIGHTING ≤ 15 KG: A SINGLE CENTER EXPERIENCE IN BRUSSELS.

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Introduction:
Kidney transplantation (KT) in small children is perceived as a surgical and clinical challenge with high risks of complications. The aim of this study is to identify epidemiological data, underlying diseases, patient and graft survival, graft function and body growth in renal transplant recipients weighting ≤ 15 Kg transplanted at HUDERF-Brussels. Data concerning two transplantations periods, before and since 1996, are compared.
Material and methods:
A retrospective analysis is performed on 42 KTs in 38 children transplanted at weight ≤ 15 Kg between 1978 and 2014 at HUDERF-Brussels.
Results:
42 KTs have been performed, 20 (48%) before 1996 and 22 (52%) since 1996. The median age at transplantation was 3.2 years (range 1.3-6.9), and median weight 12.1 Kg (7.8-15). Living related-donor transplantations were performed in 24% of patients (15% before and 32% since 1996). In cadaveric-donor transplantations, cold ischemia decreased from a median value of 24 hours to 15 hours ($p<0.0001$) before and since 1996. 81% of cadaveric-donor KTs had post-surgery complications, 100% before and 60% since 1996 ($p<0.0001$). Dialysis for non-functional grafts was needed in 22% of cases (29% before and 13% since 1996 ($p=0.25$)). Organ rejection occurred in 40% of KTs (65% before and only 1% since 1996 ($p<0.02$)). Ten-year patient survival was 83% (78% before and 90% since 1996. Ten-year graft survival increased from 42% to 73% before and since 1996. Graft function deteriorated from a mean of 72 to 57 ml/

min/1.73m² within 10 years. There was a remarkable catch-up growth in post-transplant periods, from a median height of -3.1 SDS at transplantation to -1.3 SDS after 10 years (p<0.0001).

Conclusions:

Kidney transplantation in small children remains a challenging procedure. However, it has in recent years become safer, gives rise to fewer complications, offers a better long-term prognosis and improves catch-up growth significantly.

P - 460 SUCCESSFUL PAEDIATRIC HLA INCOMPATIBLE RENAL TRANSPLANTATION

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Introduction:

Sensitisation may occur due to previous blood transfusions, transplantation or pregnancies. Data from UK Renal Registry shows median waiting times for deceased donor for adults, highly sensitised children and unsensitised children are 1160, 1241 and 360 days, respecitvely.

Material and methods:

Prospective study of first two HLA incompatible living related renal transplants (positive B-cell flow crossmatch prior to desensitisation) in children in UK with 100% calculated reaction frequency after passing screening for feasibility of desensitisation with test plasma exchange.

Results:

100% patient and renal allograft survival with follow-up at 4 and 12 months

	Patient 1: 14yo F	Patient 2: 13yo M
Baseline B cell xmatch	107 MCS	131MCS
Desensitisation	PX + IVIg	DFPP + DFPP + IVIg
B cell xmatch pre-Tx	41MCS	58MCS
DSA specificities	B7, DQ8	A23, Cw7,DQB1*06:02,DP1
Induction	ATG	Alemtuzumab
Post-Tx Ab removal and DSA	Nil; fluctuating DSA	Nil; low DSA
Maintenance IS	CS + MMF + FK506	CS + MMF + FK506
For cause Bx	W2: No AMR	M4: No AMR
Protocol Bx	M3+M6: No AMR	M3+4: No AMR
Latest eGFR(mls/min/1.73m2)	49	50

Conclusions:

HLA incompatible renal transplantation from a living donor is a feasible option for a sensitised child but requires multi-disciplinary team from experienced centres.

P - 461 IMPACT OF 25 (OH) VITAMIN D ON GRAFT SURVIVAL IN RENAL TRANSPLANTED CHILDREN

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Introduction:

In children, vitamin D deficiency is common after renal transplantation, but the association between vitamin D status and allograft survival remains elusive.

Material and methods:

We studied a retrospective cohort of 61 children, who were transplanted at a single institution between September 2008 and July 2013.

Results:

Median 25-hydroxy-vitamin D concentration was close to reference values at the time of transplantation (29ng/ml, (IQR 19.0-39.5)), with 29.5% deficient patients (25(OH)D < 20 ng/ml), 21.3% insufficient patients (21-29 ng/ml) and 49.2% sufficient patients (>30ng/ml). Patients did not receive systematic vitamin D supplementation in the early post-transplantation period, to avoid risk of hypercalcemia and risk of calcium deposits in renal allografts. Subsequently, median 25(OH)D concentration rapidly decreased within the first 3 months to 20 ng/ml (IQR 12.0-26.0)(p<0.005). There was no correlation between 25(OH)D levels at 3 months and mGFR at 12 months. 58.3% patients with low 25(OH)D concentrations 3 months after transplantation (< 20 ng/ml) presented episodes of treated acute rejection during the first year following transplantation, whereas 26.9% patients with 25(OH)D levels above 20ng/ml did (p<0.05).

Conclusions:

Our data showed 1) a quick drop of 25(OH)D concentrations after transplantation, 2) an association between low serum 25(OH)D 3 months after transplantation and a higher incidence of acute rejection during the first post-operative year. Altogether, these results suggest that vitamin D is a modifiable risk factor for allograft outcome. We recommend systematic vitamin D supplementation early after kidney transplantation.

P - 462 RENAL TRANSPLANTATION IN CHILDREN BELOW 3 YEARS OF AGE IS A SAFE PROCEDURE

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Introduction:

RTx in children less than 3 years is regarded as challenging.

Material and methods:

We retrospectively reviewed the charts of all children having received RTx below 3 yrs of age at our center since 1987 (N=32, G1). They were matched for donor type and period of RTx with children aged 3-13 yrs (N=32, G2) and 13-18 yrs (N=32, G3). Cox survival model was performed after adjustment.

Results:

When comparing general characteristics among groups, there were no differences for sex, primary renal disease, number of patients on dialysis before RTx, and growth (SDS). In G1, peritoneal dialysis was more frequent (p<0.001), and there were more EBV mismatches (p=0.04); warm ischemia time was longer (32±2 *vs*. 28±1 *vs*. 23±1 min, p<0.001). There were no differences for cold ischemia time, HLA and CMV mismatches, immunosuppressive regimens and duration of follow-up (11±1 yrs in G1). In G1, 1 and 3 patients experienced early venous and arterial graft thrombosis, respectively (0 in G2 and G3). Graft survival rates were similar at 5 and 10 yrs in the 3 groups, i.e., 84% and 81% in G1, 81% and 71% in G2, 71% and 67% in G3 (p=NS). Graft survival free of acute rejection was also similar (p=NS). A total of 28 patients lost their graft (7 in G1, 11 in G2, 10 in G3), mainly due to chronic allograft nephropathy. 3 patients died in G1 and 1 in G2; 4 lymphomas were observed (3 in G1, 1 in G3) inducing 2 deaths (1 in G1, 1 in G3).

Conclusions:

RTx in young recipients yields similar results than in other pediatric age groups. As such, we should transplant these patients as soon as possible, provided a particular attention is paid to donors' selection and prevention/early diagnosis of complications.

P - 463 WHAT IS THE OPTIMAL PERIOPERATIVE BLOOD PRESSURE AND FLUID MANAGEMENT OF PAEDIATRIC RENAL TRANSPLANT RECIPIENTS?

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Introduction:
The roles of perioperative blood pressure and fluid status in paediatric renal transplant recipients (RTR) on outcomes such as glomerular filtration rate (GFR) and length of hospital stay are unknown.
Material and methods:
Retrospective study of RTR who received renal transplants over three years. Values for perioperative blood pressure and fluid status were obtained from anaesthetic records and clinic letters.
Results:
65 RTR, 34% pre-emptive (37% HD, 29% PD), 54% male, aged 1.4 to 17.3 (median 10.9) years and weighing 9.0 to 99.0 (median 29.5) kilograms at time of transplantation received grafts anastomosed to iliac vessels (68%) or aorta and inferior vena cava (32%).
There was a significant positive correlation between pre-transplant SBP *z* score and pre-transplant GFR ($p = 0.02$). Pre-transplant SBP *z* score had a significant positive correlation with intraoperative median SBP *z* score before graft perfusion ($p = 0.01$). A positive relationship was observed between intraoperative fluid volume and intraoperative median SBP *z* score after graft perfusion ($p = 0.08$). There were significant positive correlations between intraoperative fluid volume and both 1-week post-transplant GFR ($p = 0.01$) and post-transplant length of hospital stay ($p < 0.05$). There was a significant positive correlation between 1-week post-transplant fluid balance and 1-month post-transplant SBP *z* score ($p = 0.01$). However, 1-week post-transplant fluid balance and 1-month post transplant SBP *z* score had no effect on post-transplant GFR or length of hospital stay.
Conclusions:
Greater intraoperative fluid volumes and post-transplant fluid balance are associated with higher SBP *z* scores. Both higher pre-transplant SBP z scores and greater intraoperative fluid volumes are associated with improved GFR. Findings from this study can be used to inform patient management.

P - 464 DONOR SPECIFIC ANTIBODIES IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS

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Introduction:
Donor specific HLA antibodies (DSA) are associated with poor renal aloograft outcome. A renal biopsy is not routinely performed in children after kidney transplantation (tx). This study assessed whether there is a correlation between the clinical outcome (GFR and graft rejection) and the presence of Luminex DSA in pediatric renal transplant recipients.
Material and methods:
Between 2004 and 2014, 76 renal tx were performed in 68 children. The patient group was divided in two groups: a group in which renal biopsy was performed (B+) and a group in which there was no clinical indication for biopsy (B-). B+ consisted of 37 children (44 tx) and the B- of 31 children (32 tx). The complement-dependent-cytotoxicity (CDC) test and Luminex screen/Luminex Single Antigen test assays were performed to detect HLA class I and/or HLA class II DSA before and after tx. The prevalence of DSA were compared between B+ and B-. GFR was measured with Schwartz formula at 1,3,6, months and yearly after tx. Last GFR measurement was at the last visit, at the age of 18 yrs, or when graft failure occurred. Results are given in median (ranges).
Results:
The age at tx was 11.7 (3.2-17.8) in B+ and 8.0 (2.4-17) yrs in B- ($p<0.05$). Last measurement was at 17.1 (3.5-18.0) in B+ and 14.0 (2.4-18.0) yrs of age in B- (ns), with a median graft-age of 2.5 (0-11.9) and 3.9 (0-12.9) yrs resp ($p=0.069$). GFR at last measurement was lower in B+ (43, 6-74 ml/min/1.73 m^2) compared to B- (67, 8-115 ml/min/1.73 m^2) ($p< 0.05$). B+ had more graft failures than B- (15 (34%) versus 1 (3%)). In B+ 23 had biopsy-proven rejection. In both, B+ and B- there was no CDC DSA detectable prior to tx. In B+ Luminex class I and/or class II was positive in 60% , compared to 33% in the B- group. There was no difference in the prevalence of Luminex detectable DSA between humoral and cellular rejection episodes. In B+ with positive Luminex screening, 14 (56%) had DSA (single antigen Luminex test), in B- only 2 (20%). In CDC test 11 (B+) and 0 (B-) positive DSA results were found. In B-, GFR was not different between Luminex positive or negative screening results (67, 8-114 versus 67, 32-115 ml/min/1.73 m^2 resp, ns). In B+, GFR was lower (38, 6-71 ml/min/1.73 m^2) in the Luminex class I and/or class II positive patients in comparising to the Luminex negative patients (52, 16-74 ml/min/1.73 m^2). The GFR of children with positive DSA was 10 (5-66 ml/min/1.73 m^2) versus 51 (16-74 ml/min/1.73 m^2) in the DSA negative group ($p<0.05$).
Conclusions:
In B+, Luminex DSA were more prevalent and GFR was lower than in the B- group. Therefore, performing biopsy on indication seems to be justified in children. More Luminex and/ or CDC DSA were found in the B+ group compared to B- group. Luminex screening test only does not differentiate in GFR outcome. The necessity of routinely Luminex screening in all children after tx is subject to debate. When clinical indication of biopsy is made, additional testing for Luminex detectable DSA gives more insight in GFR outcome and might be useful in the decision what rejection treatment should be given.

P - 465 HOSPITAL ADMISSIONS BEFORE AND AFTER PAEDIATRIC RENAL TRANSPLANTATION

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Introduction:
Renal transplantation (RT) is the best form of renal replacement therapy and improves quality of life in children. Recent data however suggests that there are increased hospital admissions due to infections rather than rejection following RT in children
Material and methods:
To study hospital in-patient (IP) admissions in the year before RT and the 2 years following RT in 35 consecutive children who underwent RT atRoyalManchesterChildrenHospital from July 2009 to June 2011.
Results:
There were increased hospital admissions in the year following RT when compared to the year before RT. Comparison Pre-RT vs Post-RT: Number of episodes of hospital admissions 18 vs 37, total number of IP days 149 vs 173, percentage of patients requiring IP admission 31% vs 57%, average length of stay per-patient 4.2 vs 4.9 days. However the increased IP stay was predominantly in the first 6 months after RT and decreased subsequently. IP admissions were significantly lower in the second year following RT when compared to the year before RT (mean IP days 2.7 days vs 4.9 days). Infection, predominantly bacterial, was more common than acute rejection as the reason for IP admission.
Conclusions:
Hospital admission is increased in the year following RT when compared to the year before RT. This is mainly in the first 6 months and is significantly less in the second year after RT. Bacterial infection is the main reason for IP admission.

P - 466 CHARACTERISTICS OF RENAL TRANSPLANT CHILDREN WITH CHRONIC ALLOGRAFT NEPHROPATHY: EXPERIENCE OF A TERTIARY REFERRAL CENTER

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Introduction:
The short term outcome of kidney transplant has improved in recent years. However, there has been little progress in improving the long term survival of allograft. The aim of this study is to delineate the characteristics of chronic allograft nephropathy (CAN) patients.
Material and methods:
Medical files of renal transplant children with biopsy proven CAN were evaluated.
Results:
Between years 1982-2014, 210 renal transplant children were followed. During follow-up, 23 children were diagnosed as CAN with renal biopsy. Mean age of the patients at renal transplantation was 11.4±3.0 years. Maintenance immunosuppression consists of prednisolone, mycophenolate mofetil and tacrolimus/cyclosporine (CNI) in 20 patients and prednisolone, azathioprine and CNI in three patients. Posttransplant hypertension and posttransplant hyperlipidemia was diagnosed in 20 and 10 patients, respectively. During follow-up, 11 patients were treated with the diagnosis of acute rejection (AR) episode. In 14 patients, immunosuppression was converted to mTORi based regime after the diagnosis of CAN. And the rest of the patients continued to non-mTORi based regime. At the time of biopsy, median GFR values of mTORi and non-mTORi groups were 64.6 and 55.4 ml/min/1.73m^2, respectively (p=0.84). At last visit, patients under mTORi had better GFR when compared to non-mTORi group (p=0.041). After biopsy, median change of GFR in mTORi and non-mTORi groups were %28 and -41.9%, respectively (p=0.022). The number of AR episode did not have an effect on GFR at last visit (p=0.58). Median follow-up after histological diagnosis of CAN was 24 months (IQR; 5-48 months). Median GFR of all patients at last visit was 52.9 ml/min/1.73m^2 (IQR; 33.6-94.3 ml/min/1.73m^2) and graft loss was observed in 4 patients (18.1%).
Conclusions:
Chronic allograft nephropathy is an important cause of graft loss in our cohort and conversion to mTORi based regime resulted in a better outcome.

P - 467 BK VIRUS INFECTIONS IN PAEDIATRIC RENAL TRANSPLANT RECIPIENTS: A SINGLE-CENTRE RETROSPECTIVE STUDY

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Introduction:
BK virus (BKV) is a common complication after renal transplantation, which can result in BK virus associated nephropathy (BKVAN) and graft loss. Data on BKV in paediatric renal transplant recipients (RTRs) is still limited. In a single-centre retrospective study we measure the incidence and outcome of BKVAN.
Material and methods:
Since 11/2011, local guidelines indicate monthly surveillance during the first year post transplant. If BKV reached 10,000copies/ml in two consecutive blood tests, biopsy was performed (if concomitant decline in renal function) and immunosuppression reduced to allow BKV clearance. An audit of RTRs between 1/11/2011 and 31/10/2014 looked at surveillance level achieved, BK viremia and BKVAN incidence and management of those breaching the specified level.
Results:
38 RTRs were included in the analysis. Median surveillance levels were 75%. BK-viremia incidence was 17.5%. Median presentation was at 2 months (range 1-4 months). Three patients (A, B and C) reached threshold in 2 consecutive tests (first positives at months: A:3, B:2 and C:3) which prompted renal biopsy. BKVAN was diagnosed in 2 cases (Patient Bs' biopsy was inconclusive due to lack of medulla tissue). Calcineurin inhibitors (CNI) and purine antagonists were reduced in patients A and B. In C, who was receiving steroid and CNI, the CNI was reduced. Patients A and B were clear of BKV within 6 months. Patient C had low levels of BK-viremia at month 10. Renal function at 6 months post biopsy declined in patients A and C (eGFR (ml/min/1.73m^2): 60.1 to 51.6 and 59.2 to 53.4) and improved in patient B (eGFR (ml/min/1.73 m^2): 55.0 to 65). No graft loss during the audit period.
Conclusions:
In our cohort, BK-viraemia incidence is similar to rates previously reported for paediatric RTR. Monthly surveillance has allowed early detection of BKV and facilitated prompt action to promote BKV clearance.

P - 468 URINARY TRACT INFECTIONS (UTI) IN CHILDREN WITH KIDNEY TRANSPLANT (KT)

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Introduction:
UTI represent a main complications after KT and could have an important role in graft outcome. We evaluated the incidence of UTI in children with KT and estimated the role of UTI in graft impairment
Material and methods:
We included 75 children who underwent KT: 42 males and 33 females, mean age: 11.6 +/- 5.3. Four children received a graft from a living related donor and 71 from a deceased donor. First morning sterile urine sample to the microbiology laboratory was obtained when attending the Hospital for its usual medical control or immunosuppressive drug detection levels.
Results:
In 41 patients (54.7%) ESRD was secondary to CAKUT. Thirty-six patients (48%) presented at least one episode of UTI occurred in the first six months from KT, mainly in females (1.2:1). UTI developed in the first period were caused mainly by Gram negative bacteria (91%). E.Coli was the main agent (66.1%), the other uropathogens involved were: Proteus (9%), Enterobacter Cloacae (9%), Pseudomonas Aeruginosa (6%), Candida Albicans (3.3%). Later infections were caused mainly by Candida, Klebsiella, Proteus and Enterobacter Faecalis. One patient at the 15th month after KT manifested UTI by Corinebacterium Urealyticum associated with concretions of bladder mucosa. Eight patients (5 M) experienced graft loss: 4 patients were affected by CAKUT and had febrile UTI post-KT. One patient left the second KT by an acute deterioration of renal function during an UTI by BKV.
Conclusions:
UTI in KT children represent a main complaint as demonstrated by the high incidence (48%) in total population, mainly in females. A significant role is played by primary CAKUT and by immunosuppression as demonstrated by the high frequency also in patients without CAKUT. The role of UTI in long term survival of KT remains controversial.

P - 469 LONG-TERM OUTCOME OF PEDIATRIC KIDNEY TRANSPLANTATION: A SINGLE CENTER EXPERIENCE FROM GREECE

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Introduction:
Single-center experience studies may provide information about the factors affecting the outcome of pediatric kidney recipients with similar population characteristics. The aim of the present study was to investigate the determinants of graft survival in the long-term in a homogeneous ethnic population.
Material and methods:
A single center retrospective study was conducted at a tertiary affiliated institution. We reviewed the medical charts of all pediatric kidney transplants performed between 1990 and 2012. Demographic, laboratory, clinical data, and immunosuppression protocols, as possible factors associated with outcome, were recorded.
Results:
Forty-six (33.6%) grafts were lost, including 7 deaths with a functioning graft. The 5-, 10-, and 20-year graft survival was higher in living related donor transplantation (Tx) compared to deceased donor Tx (86.7% vs. 72.6%, P<0.05, 77.3% vs. 69.4%, P<0.05, 69.3% vs. 64.5%, P<0.05, respectively). The differences remained significant after adjustment for the decade of Tx. The 10- and 20-year graft survival increased from decade 1 to decade 2 (70.1% vs. 77.1% and 56.7% vs. 77.1%, respectively), but the difference was not statistically significant (figure). In univariate analysis risk factors for poor 5-year graft survival were graft primary non-function (HR: 32.333, CI:6.526-160.197), HLA mismatch (HR: 0.649, CI: 0.423-0.996), and DD Tx (HR: 2.417, CI:1.103-5.294). Cold ischemia storage, and duration of dialysis before Tx were not associated with graft survival at any time. Induction treatment with basiliximab vs. ALG was also associated with improved graft survival at 5 years (HR:4.635, CI1.392-15.432), but the effect attenuated at 10-years post Tx.
Conclusions:
A survival advantage at 5 years after Tx was observed among patients who received basiliximab as induction therapy compared to those treated with ALG. However, on the univariate models the effect of type of induction therapy on graft survival outcomes did not persist in long-term, suggesting that the role of induction treatment is not independent of the immunosuppression maintenance protocol.

P - 470 CHANGES IN CARDIOVASCULAR RISK FACTORS OVER TIME IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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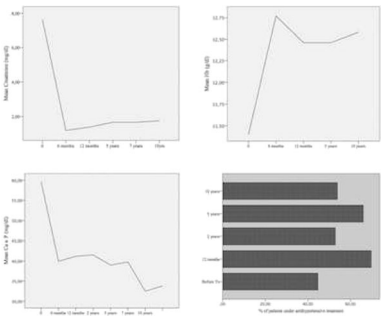
Introduction:
Anemia and calcium to phosphorus product are recognized as non-traditional risk factors associated with chronic kidney disease and have been associated with subclinical cardiovascular damage. The aim of the present study was to assess the changes over time in hematologic and biochemical parameters, as well as in hypertension prevalence after Tn in a single center pediatric kidney recipients' cohort.
Material and methods:
We reviewed the medical charts of 69 consecutive pediatric kidney transplant recipients followed-up in our department between 1990 and 2012. Demographic, laboratory, and clinical data, were recorded. Hypertension was defined as the use of antihypertensive medication.
Results:
The age range of the study population was 2-18 years. A statistically significant increase in hemoglobin (Hb) levels was observed after Tn compared with Hb levels at 12 months and 5 years after Tn (11.4 g/dl vs. 12.46 g/dl, P< 0.001, and 11.4 g/dl vs. 12.46 g/dl, P< 0.001, respectively). Thereafter, the levels of Hb did not show any significant changes. Creatinine levels presented a significant increased at 5 years compared with 12 months post Tn (1.38 mg/dl vs. 1.19 mg/dl, P < 0.001) and small non significant, but continuous increases during the following years. Calcium and Phosphorus product decreased significantly from 12 months to 5 years, and from 5 to 10 years post Tn (39.95 vs. 41.17 mg/dl, P <0.02, and 41.7 vs. 32.5 mg/dl, P<0.05, respectively). The percentage of patients who were receiving antihypertensive treatment increased from 44.7 % before Tx to 69.7% at 12 months, 66% at 5 years, and 53.8% at 10 years post Tx (Figure).



Conclusions:
Hemoglobin and calcium and phosphorus product presented a stable improvement in our cohort signifying a significant reduction of cardiovascular risk over time. On the other hand we hypertension remains a frequent complication in pediatric kidney recipients even years after kidney Tn.

P - 471 LEFT VENTRICULAR HYPERTROPHY IN CHILDREN AND ADOLESCENTS BEFORE AND AFTER SUCCESSFUL KIDNEY TRANSPLANTATION

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Introduction:
Left ventricular hypertrophy (LVH) is associated with premature death in children with chronic kidney disease (CKD). The aim of this prospective study was to compare echocardiographic (ECHO) findings in dialysed (DX) children with the consequent findings after successful KTX and to assess the impact of KTX on the occurrence of pre-existing LVH as well as influence of variables on the left ventricular mass.

Material and methods:
The sample concerned 17 children after KTX in whom ECHO was followed prospectively (x=2.2±0.8 years after KTX; function of the graft x=74.3±25.2 ml/min/1.73m^2). In all children the change of left ventricular mass index (LVMI), presence/absence of LVH was assessed and important risk factors for LVH were analysed (blood pressure, BP >95th percentile; hemoglobine <5th percentile; function of the graft; CaxP >4.4).
Results:
Prevalence of LVH was 23.5% and 29.4% on DX and after KTX respectively (p=0.06). Surprisingly, considerable intraindividual changes in the occurrence of LVH (i.e. reversibility of LVH after KTX and de novo occurrence) were observed. Principal change in ECHO finding occured in one third of children (n=6; reduction in 4, de novo appearance in 2). Statistically significant association was shown between LVMI and systolic hypertension (p<0.03). Changes in calcium phosphate metabolism, creatininemia and the degree of anemia did not correlate with the presence of LVH or its severity.
Conclusions:
LVH is common after pediatric KTX and the reversibility of already present LVH seems to be problematic even in the individuals with the functioning graft. Significant changes of LVMI on the individual level suggest that partial regression is feasible with thorough control of (systolic) BP and of other risk factors. Management of all DX and KTX patients should include regular ECHO examination.

P - 472 SUCCESSFUL KIDNEY TRANSPLANTATION IN A PATIENT WITH HEREDITARY XANTHINURIA

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Introduction:
Hereditary Xanthinuria (HX) is a rare genetic disorder caused by the enzyme xanthine dehydrogenase or oxidase deficiency. Although some patients can be asymptomatic, others may have kidney failure due to recurring kidney stones. Here, we present a patient with HX who was performed a renal transplantation, which was not reported before.
Material and methods:
18 month-old boy was presented with a febrile UTI, after when a 10 mm kidney stone was detected in the right kidney. There was consanguineous between his parents. Serum uric acid level was very low (0.1 mg/dl); urinary uric acid excretion was also low (0.44 mg/kg/day N: 9±3.75). Chemical analysis of the stone which was removed during an operation when he was 16 years old revealed a xanthine stone. Genetic analysis for HX showed a novel homozygous mutation (c.306+1 G>A) in the intron of xanthine dehydrogenase gene. His mother also had the same homozygous mutation, whereas his father had only one allele affected. The mother's serum uric acid level was also very low (0.1 mg/dl); she had no stones on ultrasonography. A therapy with a purine restricted diet and urine alkalinization with potassiumcitrate was started. His renal functions deteriorated and he developed end-stage renal failure at the age of 15.
Results:
A pre-emptive renal transplantation was performed; donor was his haploidentical mother. An immunosuppressive protocol containing prednisone, tacrolimus and mycophenolate mofetil was given. After 1 year of follow-up period, his graft functions were preserved (serum creatinine: 1.3 mg/dl, estimated GFR: 64 ml/min/1.73m^2). Serum uric acid leves were still very low; no sign of stone in ultrasonography.
Conclusions:
Renal transplantation should be considered as a good treatment option in patients with HX who developed end-stage kidney failure.

P - 473 10-YEAR OUTCOME OF PEDIATRIC RENAL TRANSPLANTATION: A SINGLE CENTER STUDY IN BRAZIL.

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Introduction:
The objective of this study was to describe the experience of pediatric renal transplantation at Hospital da Criança Santo Antônio - Porto Alegre-Brazil, consisting of a large number of Brazilian transplanted children.
Material and methods:
The center database was evaluated for patient and graft survival rates and post-transplant complications.
Results:
373 renal transplants (121 living donations-LD) were performed in 360 children between 2004 and 2014 (191 males, mean age 11.0±4.7 yr). The main causes of end stage renal disease were congenital anomalies of the kidney and urinary tract (CAKUT-39%) and glomerulopathies (27%). Initial immunosuppression consisted mainly of tacrolimus, mycophenolate, steroids and induction therapy with anti- IL-2R antibodies. The patient survival at 1, 5, and 10 yr was 97%, 94%, and 90%. The graft survival at 1, 5, and 10 yr was 92%, 82%, and 71%. For patients receiving LD, the graft survival at one, five, and 10 yr was 93%, 83%, and 71% respectively, and for patients receiving deceased donor transplant (DD) was 92%, 80%, and 68%respectively. The LD and the DD rate of graft survival was not different (Log rank test p=0.54). The most common cause of graft loss (n=67) were recurrence of primary disease (21%), chronic allograft injury (17%) and death with a functioning graft (16%). Mortality rate was 5% (n=20) and infection was the most important cause (40%) and CMV was the most prevalent (37.5%). Infection was also the most common post-transplant complication, and 33% of the total recipients had CMV infection. In our population infection was an important cause of complications and death, greater than that observed in the literature.
Conclusions:
The strategies for preventing the risk factors for bacterial or viral infections, in particular CMV infection, are crucial for better outcomes for pediatric renal transplant recipients in the future.

P - 474 WHICH HAS THE HIGHER MORBIDITY RATE AFTER RENAL TRANSPLANTATION? COMPARISON OF NEUROGENIC BLADDER, POSTERIOR URETHRAL VALVE AND VESICO-URETHERAL REFLUX

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Introduction:
Congenital abnormalities of the urinary tract (CAKUT) is one of the most common causes of chronic kidney disease among children. In this study, we aimed to determine the urinary tract infection (UTI) incidence and graft survival in pediatric renal transplant recipients with CAKUT, with specific attention to neurogenic bladder, posterior urethral valve (PUV) and vesico-uretheral reflux (VUR).

Material and methods:
All pediatric renal transplant recipients who were transplanted between January 2005 and December 2014, were enrolled in the study. Patients were grouped according to primary diseases as CAKUT and non-CAKUT cases. The UTI incidence in the post-transplant first and second 6-month periods were investigated. Estimated glomeruler filtration rate (eGFR) was calculated at post-transplant 6th, 12th and 24th months using Schwartz formula.
Results:
A total of 58 cases out of 133 (43,6%) had CAKUT, 25 of whom had PUV, 24 VUR and 9 neurogenic bladder. Age distribution was similar among the groups. The incidence of UTIs were higher in children with CAKUT than that with non-CAKUT in the post- transplant first year (34.0% vs 9.2% p=0.01); in the first six-month period, it was higher in children with VUR (20%) and neurogenic bladder (77%) compared to PUV (8%), but in the second six-month period it was higher in children with neurogenic bladder (55%) compared to VUR (16%) and PUV (16%) (p=0.001 and p=0.006) Average eGFR was lower in children with neurogenic bladder compared to children with VUR and PUV (Table). eGFR in 6-month, 1-year and 2-year time periods were similar in children with VUR and non-CAKUT case

	PUV	VUR	Neurogenic Bladder	Other Etiology
6 month avarage GFR (ml/dk/1,73m2)	70.83	78.20	43.33	70.94
1 year avarage GFR (ml/dk/1,73m2)	63.86	82.87	40.66	69.21
2 year avarage GFR (ml/dk/1,73m2)	57.82	77.00	35.00	68.22

Conclusions:
Children with neurogenic bladder have the worst outcome at post-transplant period.

P - 475 GROWTH AFTER RENAL TRANSPLANTATION

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Introduction:
Growth is impaired in children with chronic kidney disease. Renal transplantation may improve linear growth failure; however, catch-up growth after transplantation is generally not sufficient. In the present study, we evaluated growth velocity in pediatric renal transplant recipients.
Material and methods:
A total of 34 children (20 males) transplanted under the age of eighteen years and followed at least one year were enrolled in the study. Anthropometric measurements at the baseline, first, second and third year of transplantation and pubertal stages at the time of transplantation were recorded from the patients' file. Height standard deviation score (SDS)s and height velocities were calculated. Transplant data were also recorded; triple immunosuppressive therapy was used in all patients except one with steroid-free protocol. All children received alternate-day steroid therapy one year after the transplantation. None of the patients received growth hormone therapy before or after transplantation.
Results:
The median duration of renal replacement therapy before transplantation was 30 (2-147) months. Transplant age was 11.4±4.0 (2.3-16.7) years with a median follow-up of 40 (13-95) months. Three patients received preemptive transplantation and 28 (82%) received a kidney from living donor. There was a significant difference in height-SDS between the baseline and the first year (-2.98±1.98 vs. -2.59±1.93, p=0.002); however, the difference disappeared thereafter. In the first year, the mean growth velocity was 11.0±2.9, 6.8±2.6 and 4.4±2.8 cm/year in patients aged between 2-6, 6-12 and >12 years, respectively; p=0.004). Growth velocity was negatively correlated with transplant age (r=-0.708, p<0.001). Children transplanted before the puberty showed higher growth velocity as compared to children transplanted after puberty (7.7±3.1 vs. 4.2±2.8 cm/year, p=0.004). (7.7±3.1 vs. 4.2±2.8 cm/year, p=0.004).
Conclusions:
Even an improvement of growth after renal transplantation, catch-up growth is not enough and children remain far from their targets. Transplant age is a primary factor affecting growth velocity; pre-pubertal transplantation has a beneficial effect on growth.

P – 476 DE NOVO DONOR-SPECIFIC HLA ANTIBODIES IN LOW RISK PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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Introduction:
Antibody-mediated rejection (AMR) is a significant complication of kidney transplantation. Development of de novo donor-specific HLA antibodies (dnDSA) is reported to be associated with AMR and poor graft outcome even in low-risk kidney recipients. The risk factors are for the development of dnDSA are retransplantation, young age, deceased donor transplantation, nonadherence, insufficient immunosuppression, HLA alloantibodies before transplantation, DR or DQ mismatch, inflammation, T-cell mediated rejection. Serial monitoring of dnDSA has been proposed after renal transplantation. Therefore, we evaluated the DSA levels in our pediatric kidney transplant patients.
Material and methods:
DSA were evaluated in the 26 pediatric kidney transplanted patients followed actively in our outpatient clinic. The HLA typing (A, B, DRB1, DQB1) was performed by the polymerase chain reaction sequence-specific oligonucleotide method (PCR-SSO) combined with Luminex technology, using an SSO-LABType commercial kit (One Lambda, Inc., Canoga Park, CA, USA). The percentages of panel-reactive antibodies (PRA) and the specificity of anti-HLA antibodies were determined using LABScreen commercial kits (One Lambda, Inc.).
Results:
Mean age at transplantation was 11.5±4.55 years. Renal transplantation was performed from living related donors in 22 of our patients and from deceased donors in 4 patients. Blood group was ABO-compatible with the donor in all patients. None of the patients had DSA before transplantation. All patients received corticosteroids. Cyclosporine and mycophenolate mofetil were used in 13 patients, tacrolimus and mycophenolate mofetil in 10 patients and azathioprine and cyclosporine in 3 patients. The number of matched HLA antigens was 1 in 3 patients, 3 in 16 patients, 4 in 5 patients, 5 in one patient. After the mean follow-up period of 36.63 ±30.93 months, the patients were evaluated and dnDSA was negative in all our patients. At the time of evaluation, all patients had functional graft although 2 patients had chronic allograft nephropathy and 2 patients had a history of acute cellular rejection. Three months after the study, acute cellular and humoral rejection was diagnosed in a patient with poor adherence to immunosupression and dnDSA was found to be positive.
Conclusions:
Majority of our patients had low risk for the development dnDSA. Our results suggest that nonadherence is the major risk factor for development of dnDSA in low risk pediatric kidney transplant recipients especially in adolescents.

P - 477 SEVERE ACUTE TACROLIMUS ASSOCIATED NEPHROTOXICITY FOLLOWING RENAL TRANSPLANTATION

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Introduction:
Tacrolimus, commonly used as the main immunosuppressant following renal transplantation, has wide pharmacokinetic variability. A balance between adequate drug concentrations and the avoidance of nephrotoxicity is paramount. Genetic variability in enzymes which metabolise tacrolimus can affect response, with single nucleotide polymorphisms in the cytochrome P450, specifically CYP3A4/A5 subfamily, leading to high blood tacrolimus concentrations with low dose administration.
Material and methods:
A 12 year old haemodialysis dependent boy with Senior Loken syndrome underwent a living related donor transplant from his mother. Immunosuppression was by the TWIST protocol with basiliximab day 0+4, tacrolimus 0.15mg/kg bd (aiming for trough levels 8-12mcg/l), mycophenolate mofetil 600mg/m2 bd and prednisolone day0-4. Graft function was excellent with plasma creatinine 80umol/l by day4. Due to high tacrolimus trough levels on day4 and rising creatinine, tacrolimus was reduced and subsequently discontinued on day7. Blood pressure was normal, with no features of infection or obstruction. Ultrasound and MAG3 demonstrated normal kidney and perfusion. Renal biopsy demonstrated no evidence of acute rejection.
Plasma creatinine returned to baseline by day10 and tacrolimus recommenced. Within 15 hours of commencement creatinine was 257umol/l and peaked at 634umol/l despite discontinuation of tacrolimus. Maximum tacrolimus level following recommencement was 2.1mcg/l. A further graft biopsy showed irregularity of tubular epithelium with vacuolation in keeping with tacrolimus toxicity. Renal function returned to baseline following tacrolimus cessation. The patient was switched to sirolimus and is on long-term steroids with MMF 600mg/m2 bd.
Results:

Day	0	3	4	6	7	9	11 (am)	11 (pm)	15	18
Tacrolimus dose (mg bd)	5	5	0 (am) 4 (pm)	3	0	0	1	1	0	0
Tacrolimus level (mcg/l)	-	15.1	19.9	12.1	15.8	7.8	1.2	2.1	<1.5	-
Creatinine (umol/l)	823	82	80	132	143	378	86	257	634	84

Conclusions:
This patient developed severe nephrotoxicity initially with moderately elevated tacrolimus levels which improved following medication discontinuation. On re-introduction of lower dose tacrolimus, there was rapid deterioration of graft function within 12 hours, despite low trough levels. We are currently performing CYP3A4/5 genetic analysis in our patient and his mother to ascertain if genetic factors are a potential cause for the extreme tacrolimus toxicity observed in our patient.

P - 478 BK VIRUS INFECTION IN PEDIATRIC RENAL ALLOGRAFT RECIPIENTS

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Introduction:
BK nephropathy occurs in up to 10% of kidney transplant (KTx) recipients and up to 80% of these patients lose their graft. In the present study, we aimed to evaluate BK virus infection and nephropathy in pediatric KTx patients.
Material and methods:
A total of 40 KTx children still being followed-up in our center were retrospectively evaluated. Twenty nine patients (17 male, 6 cadaveric transplantations), regularly screened for BK virus, were included in the study. Immunosuppression therapy consisted of prednisolone, tacrolimus and mycofenolat mofetil (MMF). Induction therapy with ATG was used only in cadaveric transplantation. Screening for BK virus was conducted by quantitative polymerase chain reaction (PCR) in urine and blood samples. Renal biopsy was performed in patients who had persistent viremia and/or unexplained serum creatinine rise.
Results:
The mean transplant age was 11.9±4.1 years and median follow-up 37 (13-93) months. Viral replication was detected in 6 patients (3 male, 2 cadaveric transplantations and total number of HLA mismatches between 3 and 5). None of the patients received anti-rejection therapy before BK infection. When viruria was detected, tacrolimus was replaced by love dose cyclosporine. MMF was withdrawn and leflunomide was administered in patients with BK viremia (n= 4). Cidofovir was used in two patients with persistent viremia and biopsy-proven nephropathy. Ciprofloxacin and iv immunoglobulin were added to the therapy in only one patient with BK nephropathy. Among patients with BK infection all still suffer from viral load (viruria in 4, and viremia in 2 patients). GFR is preserved in one patient with BK nephropathy and in the other one a GFR decrease of 5 ml/min/1.73m^2 was noted.
Conclusions:
Polyoma virus BK infection is quite frequent among pediatric KTx patients. Early detection of viral replication and suitable therapy alterations may prevent graft lose.

P - 479 A SEVERE CASE OF ANTIBODY MEDIATED REJECTION. HOW SHOULD WE TREAT ?

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Introduction:
Antibody-Mediated Rejection (AMR) is a recognised cause of acute kidney allograft loss, especially in recipients presenting anti-HLA Donor-Specific Antibodies (DSA). The current range of therapies target removal of circulating DSA, blocking their effect or reducing their production. The complement activation in the AMR is implied by the C4d deposits in peritubular capillaries of allograft biopsy. Recent reports suggest the efficacy of Eculizumab in the treatment of AMR in highly sensitized patients. However, the multiple therapeutic agents used with Eculizumab in these single case reports makes it difficult to draw solid conclusions.
Material and methods:
We report a case of a 7 year old boy, with end-stage renal failure secondary to severe bilateral hypodysplasia, who received a deceased donor kidney transplant at the age of 5. Anti-HLA DSA (antiDR7, antiDR53) were detected by Luminex analysis 2 months after transplantation despite the association of Cellcept, Tacrolimus and Prednisone. 17 months post transplantation acute AMR was diagnosed, classified as BANFF 3B with circulating DSA (serum creatinine 3.21 mg/dl).
Results:
The patient was treated with Methylprednisone (6 shots), Intravenous Immunoglobulin (18 shots), Plasmapheresis (7 sessions), Antithymoglobulin (1 shot) and Azathioprine was substituted with

Mycophenolate Mofetil. No improvement was obtained and because active lesions were ongoing on the kidney biopsy Eculizumab was attempted as a salvage treatment (13 shots: loading dose 45 mg/kg, maintenance 30 mg/kg/week). Unfortunately, clinical outcome was not favourable. Anti-HLA antibodies were undetectable 4 months after AMR onset but kidney function did not improve and the patient was restarted on peritoneal dialysis.

Conclusions:

We present a case of aggressive AMR resistant to immunosuppressive treatment. Eculizumab was not efficient in improving AMR in our patient. More cilinical evidence is needed to determine its eventual role and its optimal timing in the treatment of AMR in highly sensitized patients.

P - 480 PEDIATRIC KIDNEY TRANSPLANTATION: RETROSPECTIVE EVALUATION OF SINGLE CENTER EXPERIENCE

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Introduction:

Pediatric renal transplantation has been performed in Istanbul University Istanbul Medical Faculty for 23 years. The immunosuppressive protocol was changed during this time. The aim of our study is to determine the effect of these protocol changes, especially administration of cyclosporine and tacrolimus regarding graft survival.

Material and methods:

Ninety (38 female, 52 male) pediatric kidney transplant recipients followed up between 1991-2014 in our unit were reviewed retrospectively. All patients received methylprednisolone. Azathioprine was used before 2001 and after 2001 mycophenolate mofetil was administered. All patients received cyclosporine before 2007. After 2007, some patients received cyclosporine and some others received tacrolimus.

Results:

The mean age of transplantation was 12.9±4.19 years and mean follow-up period was 57.75±43.29 months. Overall graft survival rate was 96.3% for one year and 94.5% for three years. The rate of graft failure and chronic allograft nephropathy were significantly higher before 2001 than in those after 2001 ($p < 0.05$). Fifty-nine patients received cyclosporine and 28 received tacrolimus. One-year graft survival was 96.5% in cyclosporine group and 94.7% in tacrolimus group ($p > 0.05$). Acute rejection was seen in 5 patients (8.4%) in the cyclosporine group and in 2 patients (7.1%) in the tacrolimus group. Chronic allograft nephropathy was detected in 10 patients (16.9%) in the cyclosporine group whereas in none of the patients in the tacrolimus group.

Conclusions:

Recently graft failure and chronic allograft nephropathy are uncommon with the new protocols. Although the number of patients who received tacrolimus is less and the follow-up duration is short, one-year graft survival and acute rejection rates are comparable with the patients who received cyclosporine.

P - 481 CYP3A5 GENOTYPE AND TACROLIMUS DOSING REQUIREMENTS IN RENAL TRANSPLANT. CASE REPORT.

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Introduction:

Tacrolimus is a widely used immunosuppressive agent in kidney transplantation. Children receive an initial standard dose and therapeutic drug monitoring is needed to maintain target levels and avoid nephrotoxicity and allograft reaction. The pharmacokinetic of tacrolimus is influenced by clinical and genetic factors requiring multiple dose modifications to reach target levels. One of the main determinants of these differences is a CYP3A5 gene polymorphism. We report a patient who required higher doses of tacrolimus to achieve therapeutic levels in which CYP3A5 genotype was determined.

Case description:

A 5 year-old boy, with end-stage renal disease secondary to Finnish Nephrotic Syndrome, received a renal transplant from a deceased donor in November 2014. He received standard immunosuppressive therapy (steroid, mycophenolate mofetil and tacrolimus) with basiliximab induction. He started on orally tacrolimus at seven day post-transplant at a dose of 0.17 mg/kg/day. Tacrolimus trough levels were obtained 12 hours after the last tacrolimus dose. Despite the progressive increased dosage up to 0.51 mg/kg/day, tacrolimus trough levels remained subtherapeutic (1.8-3.2 ng/mL) so we decided to study the CYP3A5 genotype.

Our patient was a CYP3A5*1*1 homozygous carrier, requiring higher tacrolimus dose to achieve target blood concentration 4 weeks after renal transplant. Hematocrit and albumin concentrations were consistent with baseline values. He is now on tacrolimus at a dose of 0.48 mg/kg/day, graft function is satisfactory and the patient is clinically stable.

Conclusions:

CYP3A5*1 produces the functional protein whereas CYP3A5*3 produces a truncated non-active protein. Homozygous CYP3A5*1*1 and heterozygous CYP3A5*1*3 genotypes (expresser phenotype) are known to require larger dose of tacrolimus to achieve target levels than homozygous carriers of the CYP3A5*3 allele (non expresser). In addition, the expresser phenotype may require a longer period to achieve target blood concentrations. A pre-emptive CYP3A5 genotyping might improve tacrolimus therapy individualization.

P - 482 TRAJECTORIES AND PREDICTORS OF ALLOGRAFT DYSFUNCTION AFTER RENAL TRANSPLANTATION IN CHILDREN

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Introduction:

Although the patient survival in renal transplant children is improving, it remains important to ensure optimal renal function over decades in order to optimize growth and development. It seems that both the number of functioning nephrons and the graft ability to adapt to an increasing

demand during body growth are important factors for long-term allograft function.

Material and methods:

The aim of this study was to examine the long-term progress of glomerular filtration rate in a pediatric kidney transplant cohort and the importance of the recipient and donor ages in predicting the risk of poor transplant outcome. Data on 67 transplant children who underwent 278 inulin clearance measurements between 2000 and 2010 were examined. A longitudinal latent class modeling technique was used to identify renal function trajectories and classify the children.

Results:

This technique identified three trajectories of renal allograft function after pediatric kidney transplantation: "low and decreasing", "moderate and stable", and "high and sharply decreasing" trajectories. The adjusted Odds ratio (CI 95%) to belong to the poor outcome group (low and decreasing) were of 0.03 (0.67, p=0.03) for living donor, 1.20 (0.99, 1.46, p=0.07) for an increase of one year of the age recipient, and 1.13 (0.99,1.31,p=0.07) for an increase of one year of the donor-recipient age difference.

Conclusions:

The present evaluation suggests that deceased donor, older age recipient, and large age difference between the donor and the recipient are important factors for bad long-term allograft function.

P - 483 DETERIORATING CARDIOPULMONARY FAILURE IN 8 YRS. OLD GIRL WITH ARPKD AFTER KIDNEY TRANSPLANTATION – A DIAGNOSTIC AND THERAPEUTIC CHALLENGE.

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Introduction:

Female patient G.K. (born 2007.) with ARPKD, treated with peritoneal dialysis (PD) due to early onset of ESRD from the age of 2.

Material and methods:

Cardiac examination at age 2 showed hypertrophy of ventricles walls, abnormal structure of left ventricle (LV) with transverse trabecula causing mitral valve (MV) dysfunction with obstructed left atrium blood inflow. PD was complicated by recurrent episodes of dialytic fluid leakage into pleural cavity followed by pleural hemorrhage. LRD kidney transplantation (KTx) was performed in 2009. After KTx, repeated respiratory infections were observed. In 2013, during subsequent pulmonary infection, the patient needed ICU treatment due to respiratory failure with pulmonary edema and severe pulmonary hemorrhage. The potential causes of this state were discussed and being considered cardiological, pulmonary or immunosuppressive complications.

Results:

At admission ECHO study revealed thickened muscular trabeculae on inflow tract into LV, increased mitral stenosis and LV outflow tract obstruction with preserved good contractility of LV. Angiography discovered an additional artery between left branch of pulmonary artery and left stomach artery; it was closed with coil device. Meanwhile, transient deterioration of transplanted kidney function was noted. The child was disqualified from cardiac surgery because of severe condition and followed up as outpatient. After a later pulmonary edema episode, the patient underwent urgent cardiosurgical intervention: removal of abnormal muscular trabecula and insertion of artificial mitral valve (9.05.2014). Post-operation, congestive heart and pulmonary failure were observed, complicated by massive bleeding to pericardium, pleural cavity and peritoneal cavity (probable due to warfarin toxicity). After 2,5 months of ICU intensive care, the child was discharged with normal kidney transplant function on Fraxiparine (nadroparin) anticoagulation therapy.

Conclusions:

The above case shows the rare coexistence and evolution of cardiac abnormalities in a child with ARPKD, after successful KTx and diagnostic and therapeutic challenge.

P - 484 RENAL GRAFT SURVIVAL AND RE-TRANSPLANTATION IN CHILDREN FOLLOWED INTO ADULTHOOD

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Introduction:

Renal transplantation in children has been performed at the children's hospital since 1986. The aim was to describe the long-term outcome after renal transplantation in childhood regarding graft survival and need of re-transplantation.

Material and methods:

Retrospective chart review of the 88 patients who underwent a first renal transplantation at our hospital 1986-2014

Results:

The median age at first transplantation was 8.9 years (range 1.1-17.6 years). 57 of the children (65%) were boys. In 62 patients (70%) the primary graft was from a living donor.

A total of 121 renal transplantations were performed in 88 patients (104 before transition at 18 years of age and 17 at the adult unit). Survival of first graft was 94% at one year, 86% at five years and 73% at 10 years. Thereafter the calculated graft survival decreased to 55% at 15 years and 29% at 20 years.

Today 70 of the 88 patients are alive with functioning graft. 11 patients have ongoing dialysis. 7 are deceased of whom one patient died before the age of 18 years. 35 of 36 patients <18 years of age have functioning grafts. Of the 51 patients transferred to the adult unit 35 are alive with functioning grafts: 21 with the first graft, 10 with the second, 3 with the third and 1 with the fourth graft. Of the 16 grafts transplanted at the adult unit 10 are functioning today.

Graft losses occurred in all ages but were more frequent during the teenage period. The primary diagnosis did not appear to have any impact on graft loss

Conclusions:

The overall results are very good. There is still a need to explore factors that affect the long-term graft survival such as adherence problems during the teenage years and the transition process. Adolescence is a vulnerable period with a peak of graft losses.

P - 485 RENAL TRANSPLANTATION IN CHILDREN- UAE EXPERIENCE

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Introduction:
Satisfactory rehabilitation of uremic children can be achieved by renal transplantation, with dialysis only bridging the period of terminal insufficiency, until transplantation becomes possible. We report our experience with renal transplantation in children with end-stage renal disease (ESRD) in a tertiary care centre of UAE.
Material and methods:
Retrospective study at a tertiary care centre of UAE over the last 5 years on 13 renal transplants which were performed on children below 15 years of age.
Results:
A total of 13 children transplanted of which majority were males(10/13). Six children had underlying glomerular disease while seven had tubulointerstitial renal disease. Extraperitoneal approach was used for graft placement. Basiliximab induction was followed by Triple immunosuppression with tacrolimus, mycophenolate and Steroids was used in all cases. Follow-up period ranged from 6 months to 5 years .Most cases of acute rejection responded to therapy. Surgical complications was encountered in one child as immediate graft thrombosis requiring graft removal . Graft survival was 100% at one year excluding the child with acute graft thrombosis and 100 % at two years. Satisfactory rehabilitation was achieved in children with functioning grafts.
Conclusions:
Renal transplantation in children in UAE offers an acceptable choice in ESRD and has a good success rate.

P - 486 OUR RESULTS OF PEDIATRIC KIDNEY TRANSPLANTATION; SINGLE CENTER EXPERIENCE, ULUDAG UNIVERSITY DEPARTMENT OF PEDIATRIC NEPHROLOGY

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Introduction:
Demonstrating demographics and results of 8-years of monitoring in patients followed due to kidney transplant was aimed in this study.
Material and methods:
A total of 45 patients followed in Uludag University Department of Pediatric Nephology; Dialysis and Transplantation Unit between 2006-2014 were evaluated for demographics and graft functions. Induction treatment was performed with basiliximab and metyl prednisolone whereas maintenance immunesupressive treatment was mostly performed with prendisolone, calcineurin inhibitors (CNI) and mycophenolic acid (MPA).
Results:
Mean age of our patients in the time of transplant was 13,3±4,9 and 24 (%53,3) and 21 (%46,7) of patients were girl and boy; respectively. Urinary tract infections (%28,8) was found to be most frequent cause of end-stage renal failure (ESRF). 30 patients (%66,6) had been transplanted from living donor whereas 15 patients (%33,4) had been transplanted from cadaver. Average post-transplant monitoring period of 42 cases with functioning graft was 31,4±25,2 months. During monitoring period, CMV infection occured in 11 cases (%24,4) whereas BKV infection occured in 1 case (%2,2). One case was returned to hemodialysis due to chronic allograft nephopathy. One case died due to sclerosing peritonitis as a complication of periton dialysis in second year of post-transplant period.
Conclusions:
Compared with dialysis treatment; kidney transplantation is a treatment with less complication and higher rates of survival in pediatric patients with end-stage kidney failure. Therefore, increasing number of kidney transplant is performed in our institution with favourable survival rates for both patient and graft.

P - 487 POST-TRANSPLANT VESICOURETERAL REFLUX MANAGED BY NONSURGICALLY IN A KIDNEY TRANSPLANTED CHILDREN

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Introduction:
Post-transplant (post-Tx) vesicoureteral reflux (VUR) is a common urologic complication after kidney transplantation, whereas its management is still controversial. Post-Tx VUR could be associated with urinary tract infections (UTIs) especially pyelonephritis in children with kidney transplanted. We report a child with post-Tx VUR in a graft managed by nonsurgically.
Results:
An 8-year-old girl with an end-stage renal disease (ESRD) secondary to nephronophthisis had been on chronic peritoneal dialysis program for three months. She underwent living-related kidney Tx from her mother. In first post-Tx year, she encountered 3 febrile and 8 afebrile UTIs caused by *Escherichia coli* and were treated with appropriate antibiotics. Voiding cysturetherography revealed grade 3 reflux into graft side and DMSA scan showed that a hypoactive area in the inferolateral of the graft. After that, prophylactic antibiotic and behavioral methods were started and in follow-up there was only one febrile UTI detected. After 12 months, there was no VUR in VCUG and hypoactive area in inferolateral of the graft was persisted in DMSA. Her 2nd year protocol biopsy revealed normal graft morphology. Her last serum creatinine and creatinine clerence were 0.7 mg/dl and 75 ml/min/1.73m^2, respectively.
Conclusions:
VUR into the graft is associated with recurrent UTI. Clinician should be considered non-surgical procedures like antibiotic prophylaxis and behavioral measures in normal or normal-like graft functions.

P - 488 C4D POSITIVITY IN A GRAFT WITHOUT MORPHOLOGICAL CRITERIA OF REJECTION IN A CHILD

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Introduction:
Antibody mediated rejection(AMR) has a bad prognosis which is resulted nearly 30% of graft lost. C4d is a marker of acute and/or chronic AMR due to anti-HLA antibody and considered by unrelated risk factor for graft lost. We report a child with C4d positivity in a graft without morphological criteria of rejection.
Material and methods: We transplanted from his mother with one unmatched HLA group to an 11-year-old boy with ESRD due to focal segmental glomerulosclerosis with biopsy-proven. Initial immunsupressive treatment was corticosteroid, cyclosporineA and mycophenolate mophetil.
Results:
At first year observation; his serum creatinine 1.1mg/dL, glomerular filtration rate(GFR) 100mL/min/1.73m2, proteinuria 2.2mg/m2/h and

non specific changes and C4d negative strain in protocol biopsy material. At second year observation his serum creatinine raised to 1.4mg/dL and minimal inflammation in interstitium(i1), arteriolar hyelinosis(ah1), diffuse positive C4d strain in peritubular capillaries(PTC), negative interstitial fibrosis and tubular atrophy(IFTA) in 2nd year protocol biopsy. Anti-HLADR16 and Anti-HLADQ5 were detected in donor. His serum creatinine levels at 3rd, 4th and 5th year were 1.2mg/dL, 1.4mg/dL and 1.5mg/dL, respectively. In yearly protocol biopsies; evidence of total inflammation(ti1), tubilitis(t1), CD3 prominent lymphocytic infiltration, diffuse C4d(+) strain in PTC and IFTA did not change. Proteinuria and Anti-HLADR16 and Anti-HLADQ5 levels showed no increment from 2nd to 5th years. Immunosuppressive treatment was not changed due to patient who does not meet characteristic clinical laboratory and histologic signs of graft dysfunction.

Conclusions:

In conclusion, in this 5-year observation period of normal functioning graft, we worried about leading to chronic graft dysfunction due to chronicAMR. Unlike in the interstitial fibrotic signs, the presence of PTC C4d staining in renal allografts may not have a predictive value regarding graft outcome. We emphasize that the need for further follow-up guidelines for renal allografts the presence of PTC C4d staining and do not meet the criteria of acute or chronic AMR.

P - 489 CMV INFECTION IN PEDIATRIC RENAL TRANSPLANTATION:A SINGLE CENTER EXPERIENCE

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Introduction:

Cytomegalovirus (CMV) is the most common opportunistic infection after solid organ transplantation leading to increased morbidity and mortality.

Material and methods:

Single-center, retrospective analysis of pediatric renal transplant patients of Uludag University Medical Faculty, Division of Pediatric Nephrology from January 1997 to December 2014 was assessed.

Results:

We enrolled 32 patients (17 females,15 males) with the mean age 13.03±5.31 at the time of transplantation. Ninety-seven percent of recipients and 65.6% of donors were seropositive pretransplant. Serology of 11 donors were not known. Twenty patients were given acyclovir prophylaxis and 9 patients were given valganciclovir prophylaxis whereas 3 patients were given both acyclovir and valganciclovir prophylaxis at different times. Mean duration of acyclovir and valganciclovir use were 13±8.1 months and 4.8±2.1 months respectively. CMV infection occured in 11/32 children (34%) with 5 patients (15%) developing CMV disease characterized by positive PCR (polymerase chain reaction) test in the presence of organ involvement. CMV infection recurred in 4 patients once and in 2 patients twice. Mean time to onset of CMV disease was 24.2±7.9 months post-transplant. Presenting symptoms in patients with CMV disease were diarrhea, nause and vomiting in 3 patients and nause,vomiting in 2 patients. There was no significant correlation between immunsupresive therapy and CMV infection.

Conclusions:

More studies are required to standardize preemptive therapy and prophylaxis duration as well as therapy choices for CMV infection in pediatric renal transplantion.

P - 490 PEDIATRIC RENAL TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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Introduction:

Renal transplantation is the treatment of choice for children with end-stage renal disease.

Material and methods:

We evaluated retrospectively of our 42 pediatric renal allograft recipients, including 25 boys and 18 girls from March 2010 to March 2015.

Results:

The overall mean age at transplantation was 12.56 ± 4.09 years. The majority of recipients received living donor grafts (79.5%). The mean duration of follow-up was 27.0 ± 14.6 months. The overall mean glomerular filtration rate at last checked time was 101.02 ± 36.95 mL/min/1.73m^2. Five acute rejection episodes were observed in 5 patients (12.8 %). Viral infections were developed in 4 recipients; cytomegalovirus (n= 2) and BK virus (n= 2). End stage renal disease was developed in 5 of the recipients; four from acute allograft dysfunction, one from cytomegalovirus infections. Two of the patients died; one from posttransplantion surgical complication and sepsis, and one from intra-operative cardiac complication. Thirty two of the recipients (82%) have normal renal functions.

Conclusions:

Our results showed that kidney transplantation is the best treatment of choice for end-stage renal disease in children.

P - 491 WHAT DO EUROPEAN YOUNG PEDIATRIC NEPHROLOGISTS LOOK LIKE? TOWARD A YOUNG PEDIATRIC NEPHROLOGY NETWORK (YPNN)

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Introduction:

As European pediatric nephrologists, we aim to obtain a high standard of patient care and scientific research. To reach this goal, high-quality post-graduate education is mandatory. Therefore we were interested to evaluate conditions for pediatric nephrology training in Europe, and to improve our knowledge of young European pediatric nephrologists and their expectations.

Material and methods:

On behalf of the European Society for Paediatric Nephrology, we launched a questionnaire for European Paediatric Nephrologists below 40 years of age to study different items: general characteristics, general medical education and specific education for paediatric nephrology in the country of origin, daily medical practice, research, teaching, conferences and publications, national and international societies, ESPN website and ESPN-IPNA Junior Classes.

Results:

During the ESPN conference we will present the preliminary results of this questionnaire.

Conclusions:
The EDTA has launched the Young Nephrology Platform (YNP in 2013) for all European nephrologists below 40 years of age. As such, they have a dedicated session at the EDTA conference every year, and they also organize a specific meeting on a yearly basis. Similarly, we would like to organize a Young Paediatric Nephrology Network (YPNN) among the ESPN; the results of this questionnaire will help us to bridge the gap, and to improve collaborations and networking among the future generation of Paediatric Nephrologists.

P - 492 GENDER AND OBESITY MODIFY THE IMPACT OF SALT INTAKE ON BLOOD PRESSURE IN CHILDREN

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Introduction:
The prevalence of high blood pressure (BP) in children has increased over the last decades. Most modifiable risk factors for high BP, such as obesity and salt intake, are imprinted in childhood and persist into adulthood, making it crucial to address these issues early in life. We aimed to evaluate the intake of salt in a cohort of children from Portugal, one of the leading countries in salt consumption, and to assess its impact on BP accounting for gender and weight status.
Material and methods:
We conducted a cross-sectional evaluation of 298 children aged 8-9 years, within the population-based birth cohort Generation XXI (Portugal). Anthropometric measurements were performed, BP was evaluated by 24-hour ambulatory monitoring and salt intake was determined by sodium excretion in 24-hour urine samples.
Results:
The average estimated salt intake was 6.5 ± 2.2 g/day, significantly higher in boys (6.8 ± 2.4 vs. 6.1 ± 1.9 g/day in girls, p=0.018) and in overweight/obese children (6.8 ± 2.4 vs. 6.1 ± 2.0 g/day in nonoverweight, p=0.006). Salt intake exceeded the WHO recommendation for adults (<5 g/day) in three quarters of the children. Daytime systolic BP increased by 0.94 mmHg (95% confidence interval [0.31-1.56], p=0.004) per gram of daily salt intake in overweight/obese boys, but not in nonoverweight boys or in girls.
Conclusions:
We showed an extremely high salt intake among 8-9 year-old Portuguese children. Higher salt consumptions were associated with higher systolic BP in boys, specifically in those who are overweight/obese. Our findings reinforce the importance of the interactions between obesity and salt intake in early childhood.

P - 493 COMPARISON OF AUSCULTATORY AND OSCILOMETRIC NORMATIVE VALUES FOR BLOOD PRESSURE EVALUATION IN CHILDREN

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Introduction:
The automated oscillometric blood pressure (BP) devices are widely used in children, but many physicians apply Fourth Task Force (4TF) normative values (Pediatrics 1994), which were obtained from auscultatory devices. This may yield incorrect BP percentiles/Z-scores and consequently incorrectly identify hypertensive children. Recently, oscillometric pediatric BP normative values have become available (Neuhauser et al, 2011). Aim: To compare auscultatory and oscillometric normative values for office BP evaluation in children
Material and methods:
We conducted a retrospective analysis of office and 24h BP measurements (ABPM) of 229 children (116 boys), median age 15.31 years (IQ range 12.94, 16.76). The office systolic BP (SBP) and diastolic BP (DBP) absolute values were converted into Z-scores using 4TF and oscillometric (Neuhauser) normative data. Results were compared using correlation analysis and the Bland Altman test. The accuracy of both normative values for prediction of hypertensive values on ABPM was analyzed using the receiver operator curve (ROC).
Results:
The comparison of the two normative methods for BP evaluation showed their good correlation (r= 0.9773 for SBP, r=0.9627 for DBP). Bland Altman test revealed only minimal difference in Z-scores between 4TF and Neuhauser for SBP (bias=-0.06±0.38, 95% LOA=-0.82 to +0.70), but a significant proportional error for DBP (Neuhauser underestimated DBP for DBP Z-scores lower than ¬1.65 and overestimated DBP at DBP Z-scores higher than 1.65; bias=0.18±0.60, 95%LOA=-1.0 to +1.36). However, 4TF and Neuhauser Z-scores yielded similar ROC AUC i.e. did not differ in prediction of ABPM systolic or diastolic hypertensive BP values defined as ABPM Z-scores ≥ 1.65.
Conclusions:
Auscultatory and oscillometric normative data are interchangeable for SBP evaluation, but significant differences were noted for DBP. Both methods were similar in the prediction of hypertensive BP values on ABPM. Supported by grant of the Czech ministry of health departmental program for research and development III (DPR III), code NT14335-/2013.