Established in 1871

SMW

Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

Supplementum 185

ad Swiss Med Wkly
2010;140
November 13, 2010

The European Journal of Medical Sciences

Annual meeting of the Swiss Society of Nephrology

Lugano (Switzerland), December 1–3, 2010

EMH FMH Schwabe
Editores Medicorum Helveticorum

Supported by the Swiss Academy of Medical Sciences (SAMS), the FMH (Swiss Medical Association) and by Schwabe AG, the long-established scientific publishing house founded in 1488

Official journal of the Swiss Society of Infectious Diseases, the Swiss Society of Internal Medicine and the Swiss Respiratory Society

Suppl. 185
ad Swiss Med Wkly
2010;140
November 13, 2010

Abstracted / indexed in
Index Medicus / MEDLINE
Web of science
Current Contents
Science Citation Index
EMBASE

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Cover image:
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All communications to:
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ISSN printed version: 1424-7860
ISSN online version: 1424–3997

Regular subscription price for 2010:
CHF 150.– (shipping not included)

12 issues per year

EMH FMH Schwabe

EMH Editores Medicorum Helveticorum, CH-4010 Basel
Schweizerischer Ärzteverlag AG, Editions médicales suisses SA,
Edizioni mediche svizzere SA, Swiss Medical Publishers Ltd.

1.1.

Renal sodium retention in cholestatic mice is independent of ENaC in CCD

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Purpose: The renal site of sodium retention in cirrhosis is still debated. Our previous study using cholestatic mouse model revealed an aldosterone independent stimulation of basolateral Na+,K+ATPase activity exclusively in cortical collecting duct (CCD). To explore the role of the apical amiloride sensitive sodium channel (ENaC) in the CCD we studied CCD specific aENaC KO (Hoxb7 cre; scnn1aloxlox).
Methods and Materials: Control (CTL) and CCD specific aENaC KO (KO) mice underwent bile duct ligation (BDL) or sham operation. Urinary sodium and potassium excretion was measured every 3 days in metabolic studies over 3-hours period and aENaC expression analyzed by immunofluorescence
Results: Two to three weeks after BDL, 30% (CTL and KO) mice displayed ascites (~20 ml, BDL(+)) whether the remaining ones did not (BDL(-)). Six groups were distinguished subsequently for analysis: CTL and KO; with sham operation, BDL without ascites (BDL(-)) and BDL with ascites (BDL(+)). At the time of evident ascites the urinary Na/K ratio (mean ± SEM) was as follow: CTL-sham 0.9 ± 0.2 (n = 6), CTL-BDL(-) 0.8 ± 0.3 (n = 7; ns vs CTL-sham), CTL-BDL(+) 0.1 ± 0.1 (n = 4; p <0.05 vs CTL-sham) and KO-sham 1.3 ± 0.2 (n = 6), KO-BDL(-) 1.2 ± 0.3 (n = 7; ns vs KO-sham), KO-BDL(+) 0.2 ± 0.1 (n = 5; p <0.01 vs KO-sham). The differences observed between CTL and KO groups were not significant. Immunofluorescence confirmed cre-mediated deletion of aENaC in the collecting duct of floxed mice. Aside from altered ENaC abundance in CCD, no other obvious changes were seen by immunofluorescence between CTL and KO mice.
Conclusion: ENaC activity in the CCD is not required for renal sodium retention in cholestatic mice.

1.2.

Successful cross-organ classification of fibrosis based on microarray metaanalysis applying a classifier model of renal transplant IF/TA

S. Rödder[1], A. Scherer[2], K. Körner[1], H. P. Marti[1]
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Purpose: We recently described a transcriptomic classifier consisting of 19 Metzincins and related genes (MARGS) discriminating biopsies from renal transplant patients with or without interstitial fibrosis/tubular atrophy (IF/TA), Roedder et al., AJT, 2009. In the present study, we tested the same algorithm in native organs with fibrosis using publicly available microarray datasets.
Methods and Materials: Microarray datasets of 326 human heart, liver, lung, kidney cortex, and pancreas microarray samples were analyzed; array samples with fibrosis: n = 266, and healthy controls: n = 60. Data were RMA normalized and batch effects were removed by mean adjustment where necessary. Probe sets were translated into Entrez IDs for comparability of features across different microarray platforms. Classifier performance was assessed as normalized correct rate with leave-one-out or partitioning. Commonly differentially expressed genes were identified in a 5-way VENN diagram. Expression of 9 genes was confirmed by low-density TaqMan PCR in independent patients from our institution with matched histological diagnoses (n = 50).
Results: Analyzing combined microarray data from five organs derived from 326 samples, our previously published 19-MARGS classifier for renal post-transplant IF/TA had an overall correct classification rate of 82%, with a sensitivity of 91% and a specificity of 73%. Microarray results were confirmed in independent patients by PCR of 9 MARGS. Importantly, 7 MARGS analyzed by PCR separated each fibrosis group from the corresponding control group in a principal component analysis.
Conclusion: Our 19-MARGS transcriptomic classifier not only detects IF/TA in renal allografts but also classifies native solid organ fibrosis, suggesting that the classifier represents a cross-platform, cross-organ classifier of tissue fibrosis irrespective of its etiology.

1.3.

Nephrotic range proteinuria induces inflammation and modulates sodium and water transport in collecting duct principal cells

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Purpose: Albuminuria is associated with renal failure progression and abnormal water and sodium handling. Effect of albuminuria is well described on proximal tubule but is unknown on distal nephron, where its concentration is high.
Methods and Materials: We investigated albumin uptake in nephrotic rats and the effects of apical albumin (from 0.01 g/L to 20 g/L) on two differentiated mouse cell collecting duct lines, mCCDcl1 and mpkCCDcl4.
Results: By immuno-histology albumin was taken up by principal cells in puromycin treated nephrotic rats. Similarly, FITC-albumin was rapidly uptaken by cultured collecting duct cells. Albumin, induced a dose dependent increase in abundance of proinflammatory and profibrotic cytokines mRNA (IKBα, TNFα and TGFβ) measured by RT PCR and activated NF-kB as assessed by luciferase reporter gene. Albumin also increased Snail and downregulated BMP7 expression in both cell lines. Apical albumin inhibited sodium transport assessed by measurement of amiloride-sensitive transepithelial current in a dose dependent manner in parallel with decreased expression of alpha-ENaC and SGK1 mRNA. Albumin exposure induced a clear membranous translocation of AQP2 in cultured cells that was also observed also in nephrotic rats. Both the inhibition of transport as well as the membranous expression of AQP2 were partly reversed by SB203580, a p38 kinase inhibitor.
Conclusion: Our data demonstrate that luminal albumin is uptaken by collecting duct principal cells, inducing a pro-inflammatory and pro-fibrotic response that very likely contributes to fibrosis progression. In parallel, albuminuria appears to modulate directly both sodium and water transport in the collecting duct by a mechanism involving p38 kinase.

1.4.

EphB4 forward signalling maintains podocyte homeostasis during Thy1.1 nephritis

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Purpose: Eph receptor tyrosine kinases and their ligands (ephrins) play a pivotal role in the development of the vascular and neuronal systems. They are also widely expressed in the adult kidney. The aim of our study was therefore to assess their role in the glomerular recovery from Thy 1.1 nephritis, a rat model of reversible mesangioproliferative glomerulonephritis.
Methods and Materials: Thy1.1 nephritis was induced in male Wistar rats. Animals were treated with vehicle or BHG712 (Novartis, Basel, Switzerland), a novel small molecular weight inhibitor of EphB4 phosphorylation, between days 5 and 9 of nephritis.
Results: EphB4 was expressed in healthy and nephritic glomeruli, however its forward signalling was initiated specifically around day 9 of nephritis at the apical membranes of podocytes. In contrast ephrinBs were located mainly at the podocyte foot processes. There was no morphological evidence of podocyte injury in vehicle-treated nephritic rats and podocyte number in this group was not different from healthy controls. On the other hand, podocytes of BHG712-treated nephritic rats showed evidence of maladaptation, such as formation of apical openings, pseudocysts and foot processes effacement. As a result, EphB4 inhibition led to podocyte loss partially due to apoptosis. Furthermore, BHG712 application to nephritic rats reduced the onset of intussusceptive angiogenesis suggesting a previously unrecognized role of podocytes in regulating intussusceptive vessel splitting.
Conclusion: Our results identify EphB4 forward signalling as a novel pathway allowing podocytes to adapt to transient capillary collapse observed during Thy1.1 nephritis and thus survive.

1.5.

Rational modulation of activated T cells apoptosis to prevent allograft rejection

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Zürich

Purpose: Pro-apoptotic BH3-mimetics are a promising new class of immunosuppressive agents. The small-molecule ABT-737 binds the anti-apoptotic Bcl-2, Bcl-XL and Bcl-w but not A1 and Mcl-1, and it thereby inhibits autoimmunity and suppresses allogeneic T cell responses in vitro. However, ABT-737 has only limited efficacy to prevent skin allograft rejection. The aim of this study was to understand apoptosis regulation after allogeneic T cell activation, and to pharmacologically interact with these mechanisms to control alloresponses.
Methods and Materials: The transgenic mouse model BM3.3 (transgenic TCR specific for the MHC class I molecule H2-Kb) was used to analyze the pro-apoptotic potency of ABT-737 alone or in combination with various immunosuppressive agents on a homogeneous population of allo-reactive CD8 T cells in either naïve or activated status. These data were correlated with the expression of anti-apoptotic Bcl-2 family members.
Results: Activated CD8 T cells were markedly more resistant to ABT-737 than naïve cells. This correlated with an increased expression of the anti-apoptotic A1 and Bcl-XL within the first hours after TCR engagement. Interestingly, exposure to cyclosporine A during

activation inhibited the up-regulation of A1 and Bcl-XL. As a consequence, cyclosporine A completely reversed the resistance of activated T cells and increased the immunosuppressive potency of ABT-737.
Conclusion: The physiological regulation of Bcl-2 proteins during lymphocyte activation reduces the immunosuppressive effect of ABT-737. However, rational apoptosis modulation in lymphocytes by pharmacological combination allows overcoming this resistance and represents a promising approach to prevent allograft rejection.

1.6.

Urinary calcium excretion is controlled by the circadian gene clock

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Purpose: Circadian rhythms have been described for plasma calcium, parathormone (PTH) and for urinary calcium in humans, and may play a role in nephrolithogenesis and osteoporosis. The mechanisms underlying these rhythms remain unknown and may include entrainment by systemic cues or by local molecular clocks.
Methods and Materials: Variations in plasma calcium, PTH, and calciuria were studied every 4 hours for 24h in regular C57/bl6 mice and correlated to renal mRNA and protein expression levels for the main partners involved in calcium reabsorption. Finally, mice deleted for the *clock* gene were studied.
Results: Plasma/urinary calcium, and PTH levels followed a cosine function with amplitude of, respectively, 2.5, 20 and 40% over the 24 h mean under light/dark cycles and under constant darkness. TRPV5 and NCX1 renal mRNA levels were varying by 17 and 12% over the 24 hours mean, respectively, while calbindin-D28K and PMCA renal mRNA did not change. NCX1 protein levels variations were confirmed by Western Blot analysis. In metabolic cages, *Clock*-deficient mice displayed higher urine calcium excretion (35% higher in light/dark conditions and 46% in constant darkness) and exhibited disturbed circadian rhythm compared to wildtype. In *clock*-deficient mice, plasma calcium and PTH levels were not significantly different from wildtype mice.
Conclusion: We showed that plasma calcium, PTH and calciuria followed circadian rhythms in the mouse and that TRPV5 and NCX1 renal mRNAs expression were also varying over 24 hours. In addition, our data shows that the *clock* gene is involved in the regulation of calciuria, as *clock*-deficient mice are hypercalciuric.

Oral Presentations – General Nephrology

2.1.

Renal microcirculation assessment with contrast enhanced ultrasonography

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Purpose: Contrast Enhanced Ultrasonography (CEU) is a novel imaging technique allowing organ perfusion quantification. So far, it has been rarely studied as a tool for renal perfusion assessment. The main purpose of the study was to evaluate the ability of CEU to detect changes in renal perfusion induced by angiotensin II (AngII) and an ACE inhibitor, and secondly to compare it with renal plasma flow (RPF, ml/min) measurement.
Methods and Materials: Mean blood pressure (MBP, mmHg), RPF using para-aminohippurate clearances and renal perfusion indexes (RPI) using CEU were measured before and after one hour AngII infusion at 1 ng/Kg/min, one hour at 3 ng/Kg/min and finally one hour after captopril 50 mg. Regions of interest were selected in the outer cortex of the kidney. RPI were calculated with a software. 12 healthy male volunteers were included in the study.
Results: The study was overall well tolerated. Two volunteers were excluded for technical reasons.

Table 1
Effect of AngII infusion and captopril on MBP, RPF and RPI

N = 10	Baseline	AngII 1 ng/Kg/min	AngII 3 ng/Kg/min	Captopril
MBP	84 (81–87)	88 (84–90)	95 (90–98)*	84 (78–91)†
RPF	728 (572–759)	517 (448–661)	418 (387–458)*	686 (663–981)†
RPI	184 (115–252)	99 (79–169)	66 (43–127)*	272 (143–480)†

Values are medians and interquartile ranges. *p >0.05 vs baseline, †p <0.05 vs AngII 3 ng/Kg/min.

At high doses, AngII infusion increased MBP and decreased RPF (–39%, median decrease) and RPI (–61%, median decrease) compared to baseline measurements. Captopril increased RPF (+19%, median increase) and RPI (+69%, median increase) compared to baseline.
Conclusion: As para-aminohippurate clearances, CEU is able to detect changes in the renal circulation induced by a potent renal vasoconstrictor as well as a renal vasodilator. CEU merits further investigation as a tool for renal perfusion assessment.

2.2.

The Swiss Paediatric Renal Registry (SPRR): 1970–2010

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Purpose: End-stage renal failure in children is a rare but severe condition. In order to optimize management and surveillance of long-term follow-up, central registration of these patients is essential. We describe the Swiss Paediatric Renal Registry (SPRR).
Methods and Materials: Data collection started in 1970 at the University Children's Hospital Zurich and was extended to form the SPRR in 1980. Since 2008, the database is located at the Institute of Social and Preventive Medicine in Berne. In 2009 collaboration was established with the European registry of the European Society for Paediatric Nephrology (ESPN). Included were children and adolescents <16 years undergoing dialysis for more than 3 months and/or renal transplantation (TPL). Main data collected were primary renal disease, concomitant diseases, demographic data, laboratory values, treatment and long-term outcome. Data were annually collected by a central data manager visiting all centres.
Results: From 1970–2008, 432 patients were registered (11.4 patients per year). Most frequent primary diseases were renal dysplasia (16%), hypoplasia (10%), focal segmental glomerulosclerosis (10%), nephronophthisis (8%), other hereditary nephropathies (8%) and hemolytic uremic syndrome (7%). Treatment consisted of dialysis and TPL thereafter or preemptive: living donation: n = 241 (68%); cadaveric donation: n = 113 (32%); preemptive TPL: n = 60 (14% of all TPL). Seventy-one of all registered patients (16%) died.
Conclusion: This national registry is a valuable and important resource for national surveillance of incidence, treatment and long-term outcome in children and adolescents with end stage renal failure. Furthermore provision is given to compare data with other countries and to collaborate in international research projects.

2.3.

How young adult patients with Gitelman syndrome experience their disease in everyday life: the results of a qualitative explorative study

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[1]Lugano; [2]Merate-Lecco/IT; [3]Bellinzona

Purpose: Gitelman syndrome, a rather benign inherited salt losing disorder, presents with salt craving, musculoskeletal complaints, fatigue, and dizziness. Surprisingly, there is no clear-cut correlation between biochemical abnormalities (alkalosis, hypokalemia and hypomagnesemia) and symptoms. The purpose of this study was to investigate how young adult patients experience the disease in everyday life.
Methods and Materials: We conducted a qualitative study based on in-depth interviews with 12 Italian-speaking subjects (7 = ♀; ♂ = 5) aged between 20 and 37 years with the clinical and molecular diagnosis of Gitelman syndrome. The well recognized constant comparative method described by Glaser and Strauss was used: a) interviews were audio-recorded, fully transcribed and analyzed; b) statements were coded and organized within common categories; c) to ensure analytical rigor, the researchers engaged in regular discussions on emerging patterns; d) a typology of the experiences was developed and tested on each transcript with an explicit search for disconfirming cases.
Results: Patients fell into 4 main groups: 1) those considering Gitelman syndrome a disabling illness; 2) those considering it a normalized illness; 3) those considering it a different normality; and 4) those considering it an occasional disability. Based on their representation of Gitelman syndrome, patients developed peculiar

a) ways of managing their condition in everyday life; b) forms of relationship with their doctor; c) lifestyles; and d) risks.
Conclusion: Gitelman patients have a wide margin of interpretation of their health condition and develop different experiences of it. Health care providers would take advantage to consider patients' own conception of the disease in order to adjust care and information.

2.4.

Biopsy findings and outcome in children with renal involvement in Familial Mediterranean Fever (FMF)

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Purpose: To evaluate renal involvement in FMF. FMF constitutes a major health problem in Armenia.
Methods and Materials: During 1993–2009 we observed 68 patients (age 2–18 years, 38 males) with FMF and renal involvement. FMF was diagnosed clinically and by genetic analysis (in 64). Biopsies were evaluated in Yerevan and Zurich. 56 patients were nephrotic, 4 nephritic (2 with rapid progression) and 8 had proteinuria (± hematuria).
Results: Renal biopsy showed amyloidosis in 50 (74%) patients (group A). However, 18 (26%) had other nephropathies (B): 5 minimal changes (MC) nephrotic syndrome, 4 acute post-infectious glomerulonephritis (APGN) and 1 each FSGS, IgA nephropathy, ANCA-GN and crescentic membrano-proliferative GN (MPGN-I). Five (3 with ESRD) had non-classified renal histology. Follow-up was 5.9 ± 3 (2–13) years. In group A 22 died (5 on dialysis). Eight are on hemodialysis, 1 transplanted, 3 in renal insufficiency and 5 remained nephrotic. Proteinuria decreased under colchicine treatment in 11 (including 2 with renal insufficiency). Group B: One with MPGN-I died of ESRF, 3 receive hemodialysis and 2 were lost to follow-up. The remaining 12 patients had a benign course: Spontaneous remission in 4 APGN, steroid-induced in 5 MC/1 FSGS and remission after immunosuppression in 1 ANCA-GN, and 1 IgA nephropathy with recurrent hematuria and preserved function.
Conclusion: 1) Systemic amyloidosis is a preventable but often fatal complication of FMF, even under RRT; 2) Other renal diseases in FMF – mostly coincidental – were more frequent than expected and carry a better prognosis; 3) FMF *per se* does not influence prognosis of non-amyloid nephropathies.

2.5.

NTproBNP predicts acute kidney injury and death in patents with Community-acquired pneumonia

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Basel

Purpose: Community-acquired pneumonia (CAP) is common and associated with a considerable risk of acute kidney injury (AKI) and death. Early and accurate risk stratification is an unmet clinical need.
Methods and Materials: We prospectively enrolled 422 patients presenting to the Emergency Department with CAP (mean age 75, female 167). NTproBNP was measured in a blinded fashion at presentation. AKI was defined – according to AKIN guidelines – as an increase of creatinine over 0.3mg/dl that persisted for at least 24 hours. The median follow up was 900 days (366-1622).
Results: NTproBNP at presentation was significantly higher in patients who developed acute kidney injury within the first 48 hours of hospitalisation (1255 (1937-30828) vs 703 (185-3506) pg/ml, P <0.001). Admission NTproBNP levels were strong predictors of AKI. In a ROC curve analysis for prognostic accuracy of admission NTproBNP to predict AKI, the AUC was 0.79 (SD 0.062, 95% CI 0.670–0.913; P <0.001). Similarly, admission NTproBNP levels were higher in short- and long-term non-survivors compared to survivors (NTproBNP median 4052 (1273-10504) vs 944 (231-3948) pg/ml, P <0.001 (NTproBNP median 2707 (705-9361) vs 528 (123-1932) pg/ml, P <0.001;) The AUCs for prediction of short-term mortality and long-term mortality were 0.703 (SD 0.041, 95% CI 0.623-0.0783) and 0.730 (SD 0.025, 95%CI 0.681–0.781), respectively. The potential of NTproBNP to predict short-term mortality was comparable to the currently used PSI score (AUC 0.762, SD 0.033, 95% CI 0.697–0.827, p comparison 0.153).
Conclusion: In patients presenting with CAP admission NTproBNP predicts the development of AKI as well as short and long-term mortality.

2.6.

Pregnancy and neonatal-postneonatal outcome in inherrited hypokalemic renal tubular disorders: case series and review of the literature

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Purpose: The term inherited hypokalemic disorder denotes a set of renal-tubular diseases that present with normal blood pressure and hypokalemia. The management has improved over the last years and the issue of pregnancy has become important for the patients. We extensively review reported information on pregnancies and neonatal-postneonatal outcome in children born to affected females. Furthermore we report our experience.
Methods and Materials: Searches were conducted up to April 2010 in the National Library of Medicine database and in the search engine Google Scholar focusing the course of pregnancy and the neonatal-postneonatal outcome in the context of inherited hypokalemic salt-losing renal-tubular disorder. Our experience was also included.
Results: There were 96 pregnancies (literature, N = 90; our experience, N = 6) in 47 affected women. There were 12 spontaneous abortions and 6 terminations. Pregnancy was associated with a decline in potassium level. Drug management included supplementation with potassium in all, with magnesium in at least 18, and with potassium-sparing diuretics in 10 pregnancies. A term or near term birth without perinatal or neonatal alarm indicators was noted in the remaining 78 pregnancies. Babies exposed in utero to potassium sparing diuretics were also found to be normal. Somatic growth and neuropsychological development are currently normal in 5 of 6 subjects aged between 0.12 and 18 years born to 5 patients, who are on follow up at our institutions.
Conclusion: Females affected by hypokalemic disorders can become pregnant and the disorder may be managed without outward effect on the fetus and with an excellent long-term outcome.

Oral Presentations – Transplantation

3.1.

Correction of metabolic acidosis with potassium citrate in renal transplant recipients

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Zürich

Purpose: ≥Persisting disturbances in acid/base homeostasis may negatively impact on several metabolic pathways in renal transplant patients (RTP), specifically in muscle and bone mineral metabolism. The aim of this study was to prospectively examine the efficacy and safety of potassium citrate (K-Cit) versus potassium chloride (K-Cl) with regard to normalization of acid/base derangements in RTP with chronic metabolic acidosis.
Methods and Materials: 30 RTP with chronic metabolic acidosis (serum bicarbonate <24 mmol/L) and stable renal graft function were randomized to receive an individualized dose of either K-Cit (N = 19) or K-Cl (N = 11) to achieve a bicarbonate level of ≥24 mmol/L over 12 months of treatment.
Serum potassium did not reach critical concentrations at any time point in either treatment group. Adverse treatment effects consisted mainly of mild gastrointestinal symptoms in both groups.

Results	Baseline		Month 1		Month 6		Month 12	
	K-Cit	K-Cl	K-Cit	K-Cl	K-Cit	K-Cl	K-Cit	K-Cl
Bicarbonate, mM/L	21.3±	20.4 ± 2	24.9 ± 2*	21.9 ± 2	24.1 ± 3*	21.6 ± 2	24.3 ± 3*	21.4 ± 2
Potassium, mM/L	4.2	4.1	4.7	4.4	4.7*	4.2	4.4	4.3
eGFR, ml/min	51±13	60 ± 19	–	–	–	–	50 ± 11	56 ± 14
Citrate dosage, gr	0	0	3.3 ± 0.4	0	4.0 ± 2.3	0	4.7 ± 2.1	0
Potassium dosage, gr	0	0	58 ± 7*	25.4 ± 9	71 ± 41*	27.3±10	83 ± 37*	28.2 ± 10

*) P <0.05 vs. K-Cl

Conclusion: This is the first study demonstrating that metabolic acidosis can effectively and safely be normalized in patients with a renal graft. K-Cit was associated with a trend to slightly better preservation of renal graft function. In analogy to demonstrated benefits in patients with native CKD improving acid/base homeostasis may be advantageous in preserving GFR of grafted kidneys too. Further analysis of our data will focus on the impact of K-Cit on bone structure, mineral metabolism, physical performance and quality of life in RTP.

3.2.

Pre-transplant IgG subclasses of donor-specific HLA-antibodies and development of antibody-mediated rejection

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Purpose: Low-level donor-specific HLA-antibodies (HLA-DSA) represent a major risk for development of antibody-mediated rejection (AMR), but the clinical impact is variable. We investigated whether the pre-transplant IgG subclass pattern allows distinguishing harmful from presumably irrelevant HLA-DSA.
Methods and Materials: All patients who have been transplanted from 1999 to 2008 in the presence of HLA-DSA with a total strength >2000 MFI by single-antigen flow-beads (SAFB) were included (n = 74). Forty of these 74 patients (54%) experienced early AMR, 34 patients (46%) did not. Pre-transplant sera were analyzed using SAFB with IgG subclass specific secondary antibodies.
Results: The investigated 74 patients had in total 141 HLA-DSA. IgG1 was the most frequent subclass (111/141; 78%), followed by IgG2 (69/141; 49%), IgG3 (51/141; 36%), and IgG4 (28/141; 20%). When patients were grouped according to the IgG subclass pattern of HLA-DSA, only 4/74 patients (6%) had isolated weak complement-binding HLA-DSA (i.e. IgG2 and/or IgG4), 21/74 patients (28%) had isolated strong complement-binding HLA-DSA (i.e. IgG1 and/or IgG3), and 46/74 patients (62%) had a mixture of strong and weak complement-binding HLA-DSA. The incidence of early AMR was numerically but not statistically lower in patients with isolated weak complement-binding HLA-DSA than in the other two groups (25% vs 54% and 57%; p = 0.48).
Conclusion: The IgG subclass pattern of pre-transplant HLA-DSA is dominated by strong complement-binding antibodies. The IgG subclass composition is not predictive for development of AMR and thus does not provide additional information beyond the standard IgG SAFB assay for pre-transplant risk stratification.

3.3.

Chronic norovirus infection after kidney transplantation: molecular evidence for immune-driven viral evolution

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Purpose: Norovirus (NoV) infection is the most common cause of acute self-limiting gastroenteritis. In immunocompetent recipients norovirus infection is self-limited. Only three cases of chronic NoV infection in adult solid organ transplant recipients have been reported so far. Here we report on persistent norovirus infection in nine adult renal allograft recipients.
Methods and Materials: This case series describes nine consecutive kidney allograft recipients with chronic NoV infection with persistent virus shedding and intermittent diarrhea from 97–898 days. The follow-up includes clinical course, type of immunosuppression and NoV PCR. Detailed molecular analyses of virus isolates from stool specimens over time were performed.
Results: The intensity of immunosuppression correlated with the diarrheal symptoms, but not with viral shedding. Molecular analysis of virus strains of each patient revealed infection with different variants of GII.4 strains in 7 out of 9 patients. Another two patients were infected with either GII.7 or GII.17 strain, respectively. No molecular evidence for nosocomial transmission in our outpatient clinic was found. Capsid sequence alignments from follow-up specimens of 4 patients showed accumulation of mutations over time resulting in amino acid changes predominantly in the P2 and P1-2 region. Up to 25 amino acids mutations were accumulated over a 683-day period in the patient with a 898 days shedding history.
Conclusion: NoV infection may persist in adult renal allograft recipients with or without clinical symptoms. No evidence for nosocomial transmission in adult renal allograft recipients was found in our study. Molecular analysis suggests continuous viral evolution in immunocompromized patients unable to clear this infection.

3.4.

Virtual crossmatching for risk stratification in renal transplantation

P. Amico, P. Hirt-Minkowski, G. Hönger, D. Bielmann, M. J. Mihatsch, H. Hopfer, J. Steiger, S. Schaub
Basel

Purpose: Donor-specific antibodies (DSA) represent a major risk factor for antibody-mediated rejection (AMR) and allograft loss. The virtual crossmatch (virtual-XM) using single HLA-antigen flow-beads has been proposed for accurate identification of HLA-DSA, but large prospective studies assessing its value for pre-transplant risk assessment are lacking.
Methods and Materials: Two-hundred and thirty-three consecutive renal allograft recipients were prospectively stratified according to the virtual-XM. Virtual-XM negative patients (n = 190, 82%) received standard immunosuppression. Virtual-XM positive patients were only transplanted with negative CDC-crossmatches and received additional induction with anti-T-lymphocyte-globulin and intravenous immunoglobulins (n = 43, 18%).
Results: The cumulative incidence of clinical/subclinical AMR at one year was significantly lower in the virtual-XM negative than in the virtual-XM positive group (15/190 (8%) versus 18/43 (42%); p <0.0001). Out of the 15 patients experiencing AMR despite a negative virtual-XM, only 6 patients (3%) had early clinical AMR <3 months (4 due to presumed non-HLA-DSA; 2 due to missed HLA-DSA). The remaining 9 patients experienced either late subclinical (n = 7) or late clinical AMR (n = 2) likely related to de-novo DSA. Death-censored allograft survival at two years was 91% in the virtual-XM positive and 98% in the virtual-XM negative group. After a median follow-up of 2.6 years, serum creatinine was not different among the two groups (129 µmol/l vs 130 µmol/l; p = 0.58).
Conclusion: A negative virtual-XM is associated with a very low risk for early clinical AMR and its accuracy depends on a complete donor HLA-typing and full specification of recipient's HLA-antibodies. The outcome in patients with a positive virtual-XM is variable requiring further improvement for better clinical prediction.

3.5.

Immunofluorescence for plasmalemmal vesicle-associated protein-1 helps to identify transplant glomerulopathy in kidney transplant biopsies

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Basel

Purpose: Transplant glomerulopathy (TG) is a common finding late after kidney transplantation and contributes to the deterioration of graft function. While advanced stages are easily diagnosed on PAS sections, detection of early lesions is more difficult. The glomerular expression of Plasmalemmal Vesicle-Associated Protein-1 (PV-1) has been suggested as an ancillary tool in the diagnosis of transplant glomerulopathy.
Methods and Materials: Cryo sections of kidney transplant biopsies with a diagnosis of TG were double-stained with PV-1 and CD34 and compared to a group of 6 month protocol biopsies without relevant pathological findings and late indication biopsies without glomerular pathology. Photographs of all glomeruli were scored as negative, segmentally or globally positive. Image analysis was performed to obtain the area of each glomerular cross section, the PV-1 and CD34 positive area.
Results: Using a cut off of 0.01 PV-1+ area/glomerular area and at least two PV-1+ glomeruli 21/25 cases with TG were identified. 18 of these case had at least one globally affected glomerulus. Only 1 of 18 protocol biopsies showed PV-1 positivity above the cut off. 4/16 late indication biopsies were PV-1+. Interestingly, 1 of these cases had his transplant removed 6 months later and 2 others were retransplanted 31 or 45 months after the biopsies, while there was only 1 transplant nephrectomy in the remaining 12 patients.
Conclusion: PV-1 seems to be a sensitive marker of TG and may especially be useful to identify early cases. In addition, PV-1+ without established TG may have the potential to serve as a prognostic marker.

3.6.

Serum Angiopoetin-2 concentrations correlate with renal resistance index and outcome in renal allograft recipients

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Purpose: Renal allograft dysfunction and mortality are associated with the Renal Resistance Index (RI) as an indicator for impaired hemodynamics. Angiopoetin-2 (Ang-2), a circulating antagonistic vascular ligand of the endothelial-specific Tie2, has been identified as non-redundant primer for endothelial cell activation. We tested whether Ang-2 serum concentrations are associated with renal transplant function, arterial stiffness, RI and outcome.

Methods and Materials: We performed a prospective single centre cohort study in 200 renal allograft recipients (mean time after transplantation at inclusion 7.0 ± 6.2 yrs). At study inclusion, Ang-2 serum concentrations were measured by an in-house immune-luminometric assay. RI was determined in segmental arteries of the allograft by color-coded duplex ultrasound. Current mean follow-up time is 3.3 ± 0.5 yrs.
Results: Ang-2 correlated with renal resistance index (r = 0.32; p <0.001), eGFRNankivell (r = –0.29; p <0.001), recipient age (r = 0.27; p <0.005), serum albumin (r = –0.26; p <0.005); C-reactive protein (r = 0.26; p <0.01), Framingham risk score (r = 0.22; p <0.05) and mean arterial pressure (r = 0.23; p <0.05), but not with donor age, arterial stiffness, cholesterol, HbA1c or PTH. In a multivariate regression analysis, Ang 2 remained an independent predictor of RI (p <0.01). 16 patients died and 12 became dialysis dependent during follow-up. Mean Ang-2 concentrations were significantly higher in patients who died as compared to those who stayed alive (mean ± SD: 4.1 ± 1.9 ng/ml vs. 2.7 ± 1.6 ng/ml; p <0.01) and in those who became dialysis-dependent compared those who did not (5.6 ng/ml vs.2.6 ± 1.4 ng/ml; p <0.001).
Conclusion: In addition to established cardiovascular risk factors, circulating Ang-2 appears to be a relevant determinant of renal resistance index and allograft function and deserves consideration in prospective outcome trials in renal transplantation.

Oral Presentations – Dialysis

4.1.

Sodium thiosulfate pharmacokinetics in hemodialysis patients and in healthy volunteers

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Purpose: Vascular calcification is a leading cause of morbidity and mortality in patients with advanced renal failure. Human and animal studies indicate that sodium thiosulfate (STS) may prevent the progression of vascular calcifications. The pharmacokinetics of STS in hemodialysis patients has not been investigated yet.
Methods and Materials: STS was given iv to ten hemodialysis patients once on (8 g), and once off hemodialysis (8 g). In addition, STS was applied to nine healthy volunteers once iv (8 g) and once orally (5 g). Thiosulfate concentrations were measured in blood, urine and dialysate.
Results: In volunteers and hemodialysis patients, mean endogenous thiosulfate baseline concentrations were in the same range (5.5 ± 1.82 vs 7.1 ± 2.7 mmol/L, p = *ns*). Renal clearance was high in healthy volunteers (1.86 ± 0.45 ml/min*kg BWT) and reflected GFR. Non-renal clearance was slightly higher in healthy volunteers (2.25 ± 0.32 ml/min*kg BWT) than in anuric dialysis patients (2.04 ± 0.72 ml/min*kg BWT). Hemodialysis clearance of STS was 2.62 ± 1.01 ml/min*kg BWT. Based on the total body clearance and the thiosulfate steady-state serum concentrations, a mean endogenous thiosulfate generation rate of 1.05 ± 0.40 mmol/min was calculated for all participants. After oral application, only 4% of STS was recovered within 24 hours in the urines of healthy volunteers. This number correlates with a low bioavailability of 7.6% (0.8–26%).
Conclusion: Given the low and variable bioavailability of oral STS, only iv STS should be prescribed at the present time. The biological relevance of the high hemodialysis clearance for the timepoint of STS dosing awaits clarification of the mechanisms of action of STS.

4.2.

Haemodynamic consequences of changing potassium concentrations in haemodialysis fluids

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Purpose: A rapid decrease of serum potassium concentrations during haemodialysis produces an increase in blood pressure at the end of the session, even in the absence of intradialytic effects. Paradoxically, in animal models potassium is a vasodilator. The purpose of this trial is to study the haemodynamic consequences induced by acute changes in dialysate potassium concentration.
Methods and Materials: In 24 patients, 288 dialysis sessions, using a randomised single blind crossover design, we compared six dialysate sequences with different potassium profiles. The dialysis sessions was divided into 3 tertiles, modulating potassium concentration in the dialysate between the value normally used K and K+1 and K-1 mmol/l. Haemodynamics were evaluated using a finger beat-to-beat monitor.
Results: Comparing K-1 and K+1, differences were found within tertiles regarding systolic (+5.3, +6.6, +2.3 mm Hg, p <0.05, <0.05, ns) and mean BP (+4.3, +6.4, –0.5 mm Hg, p <0.01, <0.01, ns), as well as peripheral resistance (+212, +253, -4dyne.sec.cm-5, p <0.05, <0.05, ns). The stroke volume showed a non-statistically-significant inverse trend (–3.1, –5.2, –0.2 ml). 18 hypotension episodes were recorded. 72% with K-1, 11% with K and 17% with K+1 (p <0.01 for K-1 vs. K and K-1 vs. K+1).
Conclusion: A rapid decrease of serum potassium during dialysis -obtained by reducing the potassium in the dialysate- translated into a decrease of systolic and mean blood pressure mediated by a decrease in peripheral resistance. The risk of intra-dialysis hypotension inversely correlates to the potassium concentration in the dialysate.

4.3.

Estimation of creatinine clearance (CrCl) by determination of body composition from bioimpedance analysis (BIA) and anthropometric measurements

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Zürich

Purpose: Generally, kidney function is determined as measured CrCl from 24-hour urine collection (24hU), or estimated using established formulas such as MDRD and Cockcroft-Gault (CG). 24hU is laborious and frequently imprecise, whereas estimation formulas are not suitable for patients with abnormal body composition (i.e. obesity, cachexia, low/high muscle mass). The aim of this study was to test the accuracy of a method to determine CrCl using BIA and anthropometric measurements.
Methods and Materials: In 21 individuals (16 CKD patients, 5 healthy volunteers) body weight, height, waist and hip circumference, upper-midarm-circumference (MAMC), and standardized skin folds (SSF) were measured. Fat-free-mass (FFM) and body-cell-mass (BCM) were obtained from total-body-BIA (Akern®, BIA-101). CrCl from 24hU was determined concurrently. Using multiple linear regression a model to estimate 24-hour creatininuria (24hU-Cr) and CrCl [estimated 24hU-Cr÷1440×serum creatinine] was developed, using results from 24hU.
Results: Variables correlating best with 24hU-Cr were BCM, FFM, MAMC, height, SSF and body surface area (BSA). Stepwise backwards regression resulted in a model with BCM and BSA allowing most accurate prediction of CrCl (R^2 = 0.96, mean deviation: 2.1 ± 9 ml/min or 1.9 ± 15%). Agreement was clearly lower for MDRD and CG (R^2 = 0.91 and 0.85; 20 ± 17 and 9.5 ± 16 ml/min; 31 ± 14 and 9.2 ± 19%, respectively).
Conclusion: The model using BCM derived from BIA in combination with BSA allows a very accurate estimation of CrCl in a wide range of renal function in both CKD patients and normal controls. This method agrees better with measured CrCl than estimation by MDRD and CG formulas and is less laborious than measuring CrCl by 24hU collection.

4.4.

Successful intradermal hepatitis B vaccination in hemodialysis patients anergic to standard intramuscular vaccination

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Aarau

Purpose: To determine if intradermal hepatitis B vaccination can elicit an immune response in hemodialysis patients anergic to standard intramuscular HBs vaccination.
Methods and Materials: Hemodialysis patients who had not developed any anti-HBs antibodies after at least two complete courses of intramuscular HBs antigen (40 µg of Engerix® or HBVaxPro at months 0,1,2 and 6) were included in the study. Eligible patients received for eight consecutive weeks a 10 µg weekly dose of HBs antigen (Engerix B 10®), whereby half of the 10 µg dose was applied intradermally to the ventral side of each forearm as described by Barraclough et al. (Am J Kidney Dis 2009; 54:95–103). Antibody titers were measured at 3 and 9 months after vaccination. Antibody titers ≥10 IU/L were considered successes. Patients with 3 months› titers between 5 and 100 IU/L received a 40 µg i.m. booster at 3 months.
Results: 7 patients, none of whom was on immunosuppressive medication, were included in the study. The protocol was well tolerated. Results are presented below:

Patient	Anti-HBs (IU/L)			Success?
	before	3 months	9 months	
1	<5	111	(transplant)	yes
2	<5	39	310*	yes
3	<5	<5	<5	no
4	<5	62	26*	yes
5	<5	10	(died)	yes
6	<5	188	47	yes
7	<5	9	<5*	no

* 40 µg i.m. booster at 3 months

Conclusion: The intracutaneous HBs vaccination protocol was surprisingly successful in achieving a HBs immune response in hemodialysis patients anergic to intramuscular HBs vaccination.

4.5.

Technique failure of peritoneal dialysis (PD): What were the reasons for switching to hemodialysis (HD) during the last decade?

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St. Gallen

Purpose: Technique failure remains a problem despite new PD solutions and automated PD. The aim of our study was to analyse the reasons for failure of the method during the last decade.
Methods and Materials: All prevalent PD patients in our center between January 2000 and June 2010 were analyzed retrospectively (n = 118). Incidence of technique failure, reasons for PD-failure and switch to hemodialysis were analysed. A change of PD catheter allowing to resume PD therapy was not considered as a technique failure.
Results: Median patient follow-up was 2 years. 80% (95/118) stopped PD during follow-up: 22% (26/118) due to death, 29% (34/118) due to transplantation and 30% (35/118) due to technique failure. Technique failure occurred after a median of 5.3 years. The cumulative incidence was 10% at one year and 23% at 3 years. The cause was peritonitis in 40% (14/35), inadequate dialysis or ultrafiltration in 31% (11/35), peritoneal leakage or catheter problems (incl. local infection) in 16% (6/35). Further 10/118 PD-patients were switched to temporary HD but went back to PD after a median of 54 days (6 due to change of cathether, 4 due to abdominal surgery).
Conclusion: 1 in 3 prevalent PD patients still experienced a technique failure during the last decade. Peritonitis and insufficient dialysis remain the major causes of switch to HD. To increase technique longevity of PD an increased effort in continuous patient education might have a positive impact on the prevention of peritonitis.

4.6.

Elderly patients on hemodialysis (HD): Sense or Nonsense?

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St. Gallen

Purpose: Incident HD patients become older and the benefit of renal replacement therapy (RRT) for elderly patients can be questioned. We investigated if elderly patients required more effort of care or caused a higher burden to the health system.
Methods and Materials: Since 01.01.2007 all dialysis treatments at our centre are prospectively recorded in a database. We analyzed all consecutive patients starting HD between 01.01.2007 and 30.06.2010 for nursing effort rating, catheter treatment and hospital stay. Patients were divided by age with a cut-off of 75 years old.

Results:	All patients		Patients on HD >30 days	
	<75 yrs.	>75 yrs.	<75 yrs.	>75 yrs.
N	100	39	47	20
Follow-up (days, mean ± SD)	189 ± 322	209 ± 339	392 ± 379	400 ± 387
Age (years, mean ± SD)	60.1 ± 13	79.8 ± 3.7	57.7 ± 13.6	80.7 ± 4
Nursing effort rating:				
Easy / medium / hard	64 / 32 / 4	61 / 35 / 4	65 / 32 / 3	62 / 34 / 4
Catheter treatments	29%	55%*	27%	54%*
Hospital stay (per patient-year):				
Admissions	3.7	3.7	2.7	2.9
Inpatient days	67.8	61.6	38.2	36.7

* p <0.001

Conclusion: Patients >75 years old had more frequent dialysis catheter treatments. However there was no difference regarding nursing effort rating, number and length of hospital stay compared to <75 years old. Therefore it seems not a question of age but of general condition if an elderly patient benefits from RRT without needing an increased amount of health resources.

Poster Presentations – Basic Science

1

PA21, a new iron-based phosphate binder prevents arterial calcification in chronic renal failure (CRF) rats

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Purpose: The use of calcium-based phosphate binders to control hyperphosphatemia can induce hypercalcemia and has been associated with progression of vascular calcifications. The purpose of the study was to evaluate the effects of PA21, a new iron-based-non-calcium phosphate binder, on the development of vascular calcifications in uremic Wistar rats.
Methods and Materials: CRF was induced by feeding rats with an adenine-enriched diet for 4 weeks. Then CRF-rats were randomized to receive either PA21 5% or calcium carbonate (CaCO3) 3% in the diet or a placebo for another 4 week period. Drugs were added to the food and control non-CRF rats received the same diet (n = 6-11/group). Vascular calcifications were assessed blinded on random sections of several vessels (aorta, carotid and femoral arteries). The degree of Von Kossa positivity was scored semi-quantitatively with scores ranging from 0 to 3 depending on the surface of Von Kossa positivity.
Results: At randomization, no difference was observed for serum Ca, phosphate, creatinine and body weight between the CRF groups. At sacrifice, phosphate was similarly decreased by CaCO3 3% and PA21 5% (to 2.02 and 2.21 mmol/l respectively) compared with CRF-control rats (2.86 mmol/l, p <0.005). Calcium, creatinine and weight were similar between the CRF-groups. Preliminary results show that despite comparable effects on phosphate and Ca, PA21 5% was associated with a significantly lower score of vascular calcifications (p = 0.043, chi-square test) when compared with CaCO3 3%-treated-CRF rats and controls.
Conclusion: These preliminary results suggest that PA21 reduces the development of vascular calcifications in rats with CRF beyond the control of phosphatemia and hypercalcemia.

2

Dlifferential effects of immunosuppressive drugs on effector and regulatory T cells

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Purpose: Current experimental data suggest that CD4+CD25+Foxp3+ regulatory T cells (Tregs) based immunotherapy would be of great interest to promote donor-specific immune tolerance in transplantation (Tx). Whether and how adoptive transfer of Tregs could be best combined with current immunosuppressive regimens in clinical settings remains to be defined. Using an experimental Tx model, we had previously shown that the transfer of antigen-specific Tregs promoted long-term skin allograft acceptance in lymphopenic mice, in the absence of any immunosuppressive drug. However, allograft survival was only slightly prolonged when Tregs were transferred alone into non-lymphopenic mice, suggesting that in more stringent conditions such as in clinical settings adjuvant therapies may be needed to effectively control alloreactive T cells (Teff).
Methods and Materials: Here we have investigated the effects of various immunosuppressive drugs on the survival, proliferation and effector function of Teff and Tregs in response to alloantigens in *in vitro* assays and in our *in vivo* Tx model.
Results: Teff proliferation was inhibited in a dose-dependant manner by rapamycin and cyclosporine A, while anti-CD154 only marginally affected Teff proliferation and survival *in vitro*. Rapamycin promoted apoptosis of Teff as compared to Tregs that were more resistant under the same culture conditions. *In vivo*, the transfer of donor-specific

Tregs could be advantageously combined with rapamycin and anti-CD154 to significantly prolong MHC-mismatched skin allograft survival in non-lymphopenic recipients.
Conclusion: Taken together, our data indicate that immunosuppressive drugs differentially target T-cell subsets and could promote Tregs expansion and/or function while controlling the Teff pool.

3

Regulation of podocyte survival and endoplasmic reticulum stress by fatty acids

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Purpose: Apoptosis of podocytes occurs during the course of diabetic nephropathy. As free fatty acids (FFA) are elevated in states of insulin resistance we examined the effect of palmitic, oleic and palmitoleic acid on apoptosis/necrosis and endoplasmic reticulum (ER) stress in podocytes.
Methods and Materials: Podocytes were incubated with FFAs complexed to BSA. Apoptosis/necrosis was determined by flow cytometry (Annexin V/propidium iodide staining) or by Western blots for activated caspase 3. ER-stress was assessed by RT-PCR analysis of XBP-1-splicing and by Western blots of BiP (heavy chain binding protein) and CHOP (C/EBP [CCAAT/enhancer binding protein] homologous protein). A lentiviral system was used for gene silencing of CHOP. RT-PCR analysis for BiP, and CHOP was performed to assess their expression in glomeruli from patients with DN and pre-transplant biopsies.
Results: Palmitic acid induced apoptosis/necrosis in a dose- and time-dependent manner. Similarly, palmitic acid strongly induced CHOP and BiP. XBP-1-splicing was increased already 4 h after exposure to palmitic acid implying a potential role of XBP-1-splicing in transcriptional activation of CHOP. Oleic and palmitoleic acid strongly attenuated the induction of CHOP and prevented the apoptotic/necrotic effect of palmitic acid. Similarly, gene silencing of CHOP was protective. Finally, BiP expression was significantly upregulated in glomeruli from patients with DN.
Conclusion: These studies identify saturated and monounsaturated FFAs as antagonistic regulators of podocyte survival, ER-stress, and imply a critical role of CHOP. They offer a rationale for interventional studies aimed at testing whether dietary shifting of the FFA balance towards unsaturated FFAs can delay progression of DN.

4

Enteroviral mesangial cell tropism is enhanced by selection pressure

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Purpose: Case reports, animal and *in vitro* studies indicate a link between enteroviral infections and renal diseases (Pasch & Frey, NDT 2006). Viruses of the genus enteroviridae cause non-specific flu-like symptoms. Such symptoms typically precede IgA nephropathy. Here we assessed whether selected “nephrotropic” enteroviruses are capable of lytically infecting mesangial cells *in vitro*.
Methods and Materials: An echovirus strain 30 (echo 30), was isolated from a child with hand-and-mouth disease and hematuria. Primary human, murine and rat mesangial cells were exposed to high titers of this virus, and to 6 reference and 6 clinical coxsackievirus B1-B6 strains. Lysis of cultured mesangial cells was monitored and virus titers quantified. To enhance mesangial cell tropism, all viruses were passaged ten times in mesangial cells. The echo 30 genome was sequenced before and after passaging.
Results: Murine mesangial cells were permissive towards infection with all tested enteroviruses, whereas rat mesangial cells were not. In human mesangial cells, the picture was heterogenous. Some viruses – including the echo 30 strain - caused cell lysis, an effect enhanced after repeated passaging. Some viruses did not affect cell morphology, but showed stable virus titers, indicating ongoing chronic replication. A third group of viruses did not at all replicate in mesangial cells. Sequence comparison of the echo 30 before and after passaging revealed exchange of 7 amino acids.
Conclusion: Enteroviruses infect human mesangial cells acutely, chronically, or not at all. Passaging enhances the mesangiolytic properties of selected enteroviruses *in vitro*. Selection pressure may select mesangiotropic, nephritis-causing enteroviruses *in vivo*.

5

Intrinsic APRIL and BLyS production in human lupus nephritis (LN)

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Purpose: APRIL and BLyS are two important B cell survival factors. Large clinical trials for systemic lupus erythematosus are underway investigating interference with B cell function by targeting these molecules. However, the local expression of APRIL and BLyS has not been studied in detail in kidneys with LN.
Methods and Materials: We analyzed the mRNA expression of APRIL, BLyS and the corresponding receptors BCMA, TACI and BAFF-R in microdissected human biopsies with proliferative LN (n = 25) and compared it with pretransplant biopsies of living donors (n = 9). To identify the cells expressing the respective proteins, APRIL, BLyS and BAFF-R were also studied immunohistochemically in renal biopsies with proliferative (n = 21) or membranous (n = 8) LN.
Results: APRIL and BLyS mRNA levels were increased in glomeruli of patients with proliferative LN (12 ± 22- [p <0.05] and 30 ± 47-fold [p <0.01], respectively). Tubulointerstitial expression of APRIL, BLyS, BCMA, and TACI was also elevated (13 ± 25- [p <0.01], 58 ± 94- [p <0.01], 136 ± 332-[p <0.01], and 109 ± 305-fold [p <0.05], respectively); BAFF-R showed low basal expression. APRIL stained prominently in glomeruli with proliferative, but not membranous LN and the pattern was consistent with mesangial cells. An accumulation of CD68 positive cells was present in glomeruli in association with APRIL expression. APRIL, BLyS and BAFF-R could also be localized to interstitial inflammatory cells.
Conclusion: This is the first study to provide detailed data on local expression of APRIL and BLyS in glomeruli and tubulointerstitium of human proliferative LN. Future studies should aim to clarify intrarenal effects of APRIL and BLyS inhibition.

6

Identification of periostin as a novel matricellular protein linked to progression of glomerulonephropathies

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Purpose: Matricellular proteins (MP) are known to be involved in the pathogenesis of chronic nephropathies.
Methods and Materials: To identify MP contributing to the progression of lomerulonephropathies (GN), glomerular gene expression was studied by microarrays on patients with focal-segmental glomerulosclerosis (FSGS, n = 19), membranous GN (MGN, n = 21), minimal change disease (MCD, n = 5) and confirmed by real-time RT-PCR on additional biopsies. Immunohistochemistry (IHC) was performed on routine kidney biopsies.
Results: Fifteen out of 19 known MP were found to be induced on transcriptional level in proteinuric GN. The highest induction was seen for periostin (POSTN), specifically in the progressive diseases FSGS and MGN. Real-time RT-PCR on glomerular samples confirmed the POSTN mRNA induction in progressive GN. POSTN mRNA expression showed a negative correlation with renal function in a larger set of glomerular and tubulointerstitial specimen (r = –0.18, p = 8.1E-03, r = –0.47, p = 6.9E-14, respectively; n = 221). By IHC on healthy kidneys a discrete positivity for periostin was found in the glomerular tuft, surrounding the vascular pole, and along the Bowman›s capsule; no expression in the tubulointerstitium was detected. A prominent mesangial periostin staining was present in biopsies with progressive GN. Furthermore, periostin was found in areas of interstitial fibrosis. Co-immunofluorescene for smooth muscle actin and periostin suggests mesangial cells as the source of glomerular periostin.
Conclusion: In sum, periostin is constitutively expressed in healthy glomeruli and is linked to progression of GN and renal failure.

7

Uroguanylin excretion is compromised in salt-sensitive children but not adults

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Purpose: Several explanations have been proposed to explain blood pressure increases due to oral salt intake. In response to oral salt intake prouroguanylin, a gastrointestinal peptide, is secreted and activated by peptidases to uroguanylin in the gut and renal tubules to reduce Na+-uptake or -reabsorption, respectively. Intestinal maturity and renal integrity is frequently compromised with reduced birth weight. We hypothesized a disturbed uroguanylin availability with low birth weight.

Methods and Materials: Caucasian children born with low or normal birth weight and being either small or appropriate for gestational age and young adults (n = 28 each, mean age 11.3 ± 2.1 and 25.7 ± 0.9 years, respectively) were investigated. Salt sensitivity was assigned if mean 24-hour blood pressure increased by >3 mm Hg on a high as compared to a controlled salt diet. Uroguanylin was determined by ELISA, renal size by ultrasound and intestinal maturity by a panel of postpartal nutrional parameters.
Results: Urinary uroguanylin excretion steeply increased with rising salt intake during a low salt diet (p <0.001), yet not during a high salt diet in adults and in children. Salt-sensitive and -resistant children, but not adults, demonstrated a reduced uroguanylin excretion (p <0.0187) in low salt conditions. The uroguanylin excretion was inversely correlated to the change of 24-h mean arterial pressure during low and high salt diet (r^2 = 0.23, p <0.01) and positively with kidney length (p <0.03) in these children. Parameters of intestinal maturity did not correlate with uroguanylin excretion in these children.
Conclusion: We conclude that renal size but not intestinal maturity at birth determine urinary uroguanylin availability in low birth weight children.

Poster Presentations – General Nephrology

8

High incidence of hemolytic uremic syndrome in Switzerland is associated with indicators of livestock farming intensity

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Purpose: Survey of age-specific incidence rate of childhood hemolytic-uremic syndrome (HUS) in Switzerland and association of Shiga-toxin associated HUS (Stx-HUS) with indicators of livestock farming intensity.
Methods and Materials: Epidemiological-ecological analysis based on nationwide data through the Swiss Pediatric Surveillance Unit (1997-2003) and the national census (Swiss Federal Statistical Office).
Results: One hundred-fourteen cases were registered, 88% were ≤5 years old. The annual incidence rate was 1.42 (0.60–1.91) and 4.23 (1.76–6.19) per 10›000 children ≤16 and ≤5 years, respectively (*P* <.01). Stx-HUS was more frequent compared to non-Stx-HUS and more frequent in patients ≤5 years compared to the entire cohort (*P*<.01). The incidence rate of non-Stx-HUS did not significantly vary with age. The present incidence rate in Switzerland is higher compared to data from most other national studies. Strong association was found between incidence rate of Stx-HUS and indicators of rural density (livestock breeding/population, cattle/cultivated area), *P*<.05 and *P*<.01 in children ≤16 and ≤5 years, respectively.
Conclusion: HUS is frequent in young Swiss children and is mostly associated with Shiga-toxin producing *Escherichia coli* (STEC). The incidence rate significantly correlates with livestock farming intensity, supporting the impact of direct and indirect contact with animals or fecal contaminants in transmission of STEC to humans.

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Toxic Fanconi's syndrome after zoledronate overdose

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Purpose: Intravenous bisphosphonates have been reported to cause FSGS and acute tubular necrosis.
Methods and Materials: We describe two patients who developed Fanconi›s syndrome after receiving high doses of i.v. zoledronate. Tubular thresholds for glucosuria (ThrG) and phosphaturia (ThrP) were calculated as described by Brodehl (Pediatr Nephrol 1988;2:183-189).
Results: Case 1: An 80 y old woman with known primary hyperparathyroidism was admitted with hypercalcemia (3.4 mmol/l). She had moderate renal failure (eGFR 43) but negative urinalysis for protein and glucose. To treat hypercalcemia, 4 mg of i.v. zoledronate was given not only on admission, but erroneously also on each of the following 3 days (total dose 16 mg). 5 days later, she developed renal glycosuria (ThrG 2.3 mmol/l), phosphaturia (ThrP 0.1 mmol/l), proximal tubular acidosis, aminoaciduria, uricosuria (FE >100%) and severe tubular microproteinuria with unchanged GFR. All of these defects completely resolved in 6 weeks.
Case 2: A 69 y old man was referred for evaluation of impaired renal function. Subsequent to chemotherapy for Hodgkin›s disease >15 years ago, severe osteoporosis had developed, which was treated by monthly i.v. doses of 4 mg zoledronate over 6 years (total dose >250 mg). During this time, his previously stable GFR deteriorated from 70 to 22 ml/min/1.73 m^2 and he was found to have renal glycosuria (ThrG 5.7 mmol/l), phosphaturia (ThrP 0.26 mmol/l), uricosuria (FE 80%), proximal tubular acidosis and significant tubular proteinuria, none of which had been present before zoledronate.
Conclusion: This is the first report of toxic Fanconi's syndrome caused by high doses of intravenous zoledronate.

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Salt intake and reversed salt sensitivity in pregnancy

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Purpose: Blood pressure decreases in pregnancy. Simultaneously, plasma volume increases. In non-pregnant individuals, salt intake leads to plasma volume expansion and increased blood pressure. We hypothesize that improved placental perfusion with salt-dependent plasma volume expansion reduces placental-derived vasoconstrictory signaling thus lowering blood pressure.
Methods and Materials: In young normotensive women (n = 25 non-pregnant, n = 33 pregnant between gestational week 7 through 20), office blood pressure, body weight gain and sodium uptake as calculated by urinary sodium excretion were assessed before and at the end of 7 days of salt supplementation (9 g salt/d). In contrast to non-pregnant, pregnant women were not subjected to a salt-reduced diet (3 g salt/d) due to concerns regarding placental perfusion. This additionally allowed us to assess spontaneous salt intake in pregnancy. Serum samples and 24-h urinary collections were obtained after informed consent. Pregnant matched time controls (n = 3) remained untreated for a similar observation period.
Results: Compliance was 100% in non-pregnant, yet only 71% in pregnant women mostly due to hyperemesis. Body weight and urinary sodium excretion increased in actively treated pregnant (also compared to time controls) and non-pregnant women. Spontaneous urinary salt excretion in pregnant women was as high as of salt-supplemented non-pregnant women and further increased by high salt diet. With increased urinary sodium excretion, mean office blood pressure increased in 68% of non-pregnant, but decreased in 75% of pregnant women (X^2 = 6.04; p <0.02) (+3.2 ± 1.3 vs. –2.9 ± 2.2 mm Hg, respectively).
Conclusion: We conclude that spontaneous salt intake is increased and increased salt intake lowers blood pressure in pregnancy for reasons yet to be determined.

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End-stage renal failure in a young adult: an unusual presentation of late-onset cobalamin C disease

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Purpose: The cblC type of methylmalonic aciduria and homocystinuria (cblC) is a rare autosomal recessive disorder leading to defective intracellular cobalamin metabolism. Late-onset disease in adolescent and young adults has been reported in less than 20 cases, characterised by neuro-psychiatric and/or thrombo-embolic manifestations and a more favourable outcome than in early-onset cases.
Methods and Materials: In this report, we describe the clinical, biochemical and molecular findings in a 23-year- old man who was initially misdiagnosed as essential malignant hypertension with haemolytic uremic syndrome (HUS). He progressed to end-stage renal failure 15 days after admission. Thereafter, the finding of hyperhomocysteinemia prompted further studies in fibroblasts leading to the diagnosis of the cblC disorder. Sequencing of the *MMACHC* gene showed the homozygous missense mutation c.565C>A. Hyperhomocysteinemia decreased rapidly under intensive treatment with i.v. hydroxycobalamin, oral betaine, folate and carnitine, allowing the patient to undergo a living related renal transplantation. Eighteen months post-transplant, biochemical parameters had improved dramatically and kidney function is normal.
Results: Renal complications such as thrombotic microangiopathy, proximal renal tubular acidosis, and chronic renal failure have been described mainly in early-onset CblC disease. To our knowledge, this is the first case of end-stage renal failure with HUS in a young adult, presumably secondary to thrombotic microangiopathy, although this could not be confirmed since hypertensive crisis precluded a diagnostic kidney biopsy.

Conclusion: cblC disease should be included in the differential diagnosis of malignant hypertension and/or HUS in adults, as cblC disease, although rare, is a treatable disorder.

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Vascular inflammation in patients with stage 4 chronic kidney disease and sleep apnea

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Purpose: Unrecognized sleep apnea syndrome (SAS) is highly prevalent in obese patient or in patient with chronic kidney disease (CKD). Both CKD and SAS are associated with vascular endothelial inflammation and increased risk for cardiovascular diseases. We investigated whether the endothelial alterations that are attributed commonly to CKD are in fact related to SAS.
Methods and Materials: Thirty-one non-obese patients with stable stage 4 CKD and 40 subjects with normal kidney function and a body mass index ranging from normal to obese underwent attended polysomnography. To assess vascular inflammation and oxidative stress directly, we quantified the expression of NF-kB and nitrotyrosine by immunofluorescence in freshly harvested venous endothelial cells. To evaluate basal NO production and activity, we quantified the expression of eNOS and phosphorylated eNOS (pheNOS). Vascular reactivity was measured by brachial artery flow-mediated dilation.
Results: Expression of eNOS and pheNOS and flow-mediated dilation were significantly lower, whereas expression of nitrotyrosine was significantly greater in SAS patients (stage 4 CKD: n = 26; obese [BMI ≥30 kg/m^2]: n = 34) than in SAS-free subjects (n = 13) regardless of central adiposity. Expression of NF-kB was greater in stage 4 CKD an obese SAS patients than in obese SAS-free subjects (p = 0.002). After 4 weeks of continuous positive airway pressure therapy, flow-mediated dilation and expression of eNOS and pheNOS significantly increased in both SAS populations whereas expression of nitrotyrosine and NF-kB significantly decreased.
Conclusion: As in obesity, untreated SAS in stage 4 CKD is a major determinant of vascular endothelial dysfunction, inflammation, and elevated oxidative stress in these patients.

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Cystatin C at birth in neonates with congenital kidney malformation diagnosed on prenatal ultrasound

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Purpose: Congenital kidney malformations (CKM) accounts for 20% of all significant anomalies diagnosed on prenatal ultrasound. Csytatin C (Cys C) is proposed as a sensible marker for renal function in neonates. We compared Cys C at birth in neonates with prenatal diagnosed of CKM to a control group.
Methods and Materials: Cystatin C was drawn on cord blood in 100 term neonates (control group) with normal prenatal ultrasound to define a reference interval values for Cys C of [1.55–2.66 mg/l] and mean Cys C of 2.04 mg/l ± 0.28 SD. During the same period, 29 neonates with prenatal diagnosis of kidney malformation (KM) had cord blood Cys C evaluation at birth. The KM group was divided in unilateral kidney malformation (UKM) and bilateral kidney malformation (BKM). We compared Cyst C (mg/l) in the different groups (univariate analyses) and analysed impact of group with adjustment on gender, age, weight and size in a multivariate regression model of Cys C.
Results: The CKM group have a median (M) gestational age of 39 weeks ± 1.03, a M size of 51 cm ± 2.0 and M weight of 3.526 kg ± 0.48 and this parameters were comparable to controls. 18 pts /29 have UKM, 11/29 BKM. Mean Cys C in the 3 groups were 2.12 mg/l ± 0.44 for KM, 1.96 mg/l ± 0.38 for UKM and 2.4 mg/l ± 0.37 for BKM (p = 0.007). In the multivariate analysis BKM was statistically different from control group (p = 0.008) but not UKM group (p = 0.11).
Conclusion: Cystatin C measured on cord blood to estimate renal function in neonates with CKM was statistically increased in patients with bilateral kidney malformations at birth compared to controls.

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Patients' education in chronic kidney disease (CKD) based on the sense of coherence: does it help?

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Purpose: Patients often do not understand CKD and consequently experience problem coping with renal replacement therapy (RRT). A course was built for CKD patients to address information, coping and sense of coherence according to the pedagogical concept of dynamic learning.
Methods and Materials: The course is free for patients and close relatives. Designed and led by a nephrology nurse trained in education and group dynamics it addresses kidney function, CKD, RRT, psychological issues, social aspects, diet, collaboration with professionals. Participants answer a questionnaire with validated questions regarding sense of coherence (normal values 55–60) and quality control questions.
Results: Over 5 courses 51 questionnaires were analyzed from 69 participants. The average sense of coherence was 46 before the course (range 29–60) and 51 afterwards (range 30–62), the mean increase per course was 7% (range –2% to +17%). Participants who could hardly imagine life with RRT dropped from 39% before to 19% after the course, whereas after the course 72% could quite well imagine life with RRT. Knowledge about CKD was self-rated as average or good by 49% of the participants before the course and 88% afterwards. Before the course 51% of the participants stated they did not possess the tools to live well with CKD, after the course 90% declared having acquired these tools.
Conclusion: A structured course can increase the knowledge of CKD patients and relatives, leading to an increased sense of coherence. The acquisition of information and comprehension tools should allow CKD patients and their relatives to live a better life despite the burdening disease.

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Gordon's syndrome; rare and tricky

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Purpose: Background: Gordon's syndrome (GS), is a rare genetic disorder, characterized by hypertension, hyperkaliemia, acidosis and normal eGFR. We present the case of a patient with GS revealed by severe hyperkaliemia and masked hypertension.
Methods and Materials: Case: A 25-year-old boy with a chronic courses of schizophrenia was referred because of hyperkaliemia of unknown origin. His growth was normal, he had no past history of palsy but sometimes he complained about cramps. The diagnostic work-up disclosed hyperkalemia (7.1 mmol/l), acidosis (pH 7.29, HCO_3– 19 mmol/l), hyperchloremia (113 mmol/l) and normal eGFR (100 ml/min). Plasma renin was in the reference range, aldosterone (1.04 nmol/l) slightly elevated. Office blood pressure was normal. However, a 24-h ambulatory blood pressure monitoring revealed stage I arterial hypertension without nocturnal systolic physiological dip. Laboratory values normalized (K+ 4.9, pH 7,37, HCO_3– 27 mmol/l, Cl– 80 mmol/l) on hydrochlorothiazide 12.5 mg/day. Daily urine K+ excretion increased from 6 to 96 mmol/l.
Results: Discussion: The diagnosis of GS could be postulated in this case by the presence of a hyperchloremic metabolic acidosis with hyperkalemia, normal renal function, masked hypertension and finally the response to low doses of thiazides, which is a hallmark of the disease.
Conclusion: The diagnosis of GS deserves consideration in young patient with "true hyperkaliemia" and hyperchloremic metabolic acidosis. Hypertension should be actively searched for in all these patients even if we know that the metabolic disorders always precede hypertension, which rarely manifests itself until patients are 30 years of age. Treatment with thiazides is a very satisfactory management.

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Tubular dysfunction in idiopathic nephrotic syndrome

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Purpose: To evaluate the degree of tubular involvement in INS at various stages of the disease.
Methods and Materials: 19 patients with INS were studied. 13 were steroid responders (group 1). 6 patients were non responder to steroid or were steroid dependant (group 2). Biopsies showed 3 FSGS and 3 MCD. Protein, microalbumin (ALB), alpha-microglobulin (AMG), N-acetyl-beta-D-glucosaminidase (NAG) and creatinine (cr) were measured in each urine sample. Patients were considered in remission if prot/cr ratio (g/mol) was <20 (group 1a and 2a), and in relapse if the ratio was >200 (group 1c and 2c). Some patients in group 1 had non nephrotic proteinuria (group 1b). Tubular dysfunction was defined by NAG/cr ratio (mg/mmol) >0.86 or by AMG/cr ratio (mg/mmol) >1.58.
Results:

	Prot/cr	ALB/cr	NAG/cr	AMG/cr
Group 1a	10.3 ± 4.1	1.1 ± 1.0	0.19 ± 0.12	1.40 ± 0.97
Group 1b	60.4 ± 63.4	42.8 ± 66.7	0.39 ± 0.21	1.20 ± 0.56
Group 1c	713.3 ± 276.8	799.8 ± 534.9	2.25 ± 1.86*	4.25 ± 2.09*
Group 2a	11.3 ± 6.1	4.7 ± 5.7	0.26 ± 0.19	1.18 ± 0.60
Group 2c	914.9 ± 718.6	682.9 ± 589.3	3.00 ± 2.72*	5.47 ± 4.30*

Results are mean SD, p <0.001 compared to group 1a and 2a
No difference was observed between group 1 and group 2 neither in remission nor in relapse.

Conclusion: These data indicate that tubular dysfunction occurs in INS but only in patients in relapse. In this population, tubular dysfunction was independent of the severity of the nephrotic syndrome, the treatment protocol and the histopathology.

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Hypertensive crisis as first presentation of retroperitoneal fibrosis (RPF): a case report

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Purpose: A 62-year-old woman with a history of untreated hypertension (stage 1) presented with hypertensive crisis to the medical department. She did not take regular medication. Blood pressure was 230/120 mm Hg on admission.
Methods and Materials: Laboratory evaluation revealed a sedimentation rate of >110 mm/h (with CRP normal), serum potassium of 3.2 mmol/l, creatinine of 213 umol/l, serum protein of 91 g/l, ASAT 33 U/l, phosphatase alcaline 247 U/l and g-GT of 272 U/l. Urine analysis revealed 800 mg proteinuria in 24 h and a urine-sodium of 33 mmol/l.
Results: Analysis of immunological markers revealed negativity for anti-mitochondrial- (AMA), anti-nuclear- (ANA) and anti-neutrophil-cytoplasmatique (ANCA) antibodies. The patient's serology was negative for Hepatitis B, -C and HIV. Renal ultrasound revealed bilateral hydronephrosis with normal renal parenchyma. An abdominal CT scan showed a peri-aortal infrarenal mass that extended to the common iliac arteries, including the middle sacral artery and the two ureters.
Conclusion: The principal diagnosis was hypertensive crisis due to a retroperitoneal fibrosis (Morbus Ormond) with obstructive uropathy and secondary acute renal failure. The patient was treated with 60 mg prednisone daily, followed by 100 mg azathioprine daily; hypertension was treated by a betablocker, a calcium-channel-blocker (CCB) and an ACE inhibitor. Three months after initiating the treatment, the creatinine was 97 umol/l and the hypertension well controlled (114/79 mm Hg). Due to a cushingoid presentation prednisone was stopped after 6 months. Azathioprine could be stopped after one year of therapy. Four years later the patient is well without recurrence of RPF.

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Inflammatory markers and associations with kidney function in the general population

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Purpose: Increased levels of inflammatory markers such as C-reactive protein (hsCRP), tumor necrosis factor α (TNFα), Interleukin 1b (IL1b) and Interleukin-6 (IL6) have been reported in stage 3-5 CKD. In this study, we assessed levels of inflammatory markers across all ranges of kidney function.
Methods and Materials: Population based, cross-sectional study in a random sample of 6174 Caucasian subjects aged 35 to 75 years in Lausanne, Switzerland. The EPI-CKD formula was used to calculate estimated glomerular filtration rate (eGFR).
Results: There were only slight variations in plasma concentrations of inflammatory markers across eGFR quintiles (table). In multivariate logistic regression analysis adjusting for confounders, with CKD as a dichotomized dependent variable (eGFR <60 (n = 283) or ≥60 ml/min/1.73m² (n = 5892)), MAU (OR: 2.09; 95% CI 1.45–3.02; p <0.005) and log-transformed TNFα (1.17; 1.02–1.35; p = 0.027) were associated with CKD, whereas IL1b, IL6, and hsCRP were not.

CKD-EPI quintiles	1	2	3	4	5
eGFR (ml/min)	66.0 (9.1)	77.6 (4.9)	86.2 (4.0)	94.5 (4.2)	105.5 (7.2)
hsCRP (mg/dl)	1.5 (2.2)	1.3 (2.1)	1.2 (2.2)	1.2 (2.9)	1.2 (2.3)
Il6 (pg/ml)	1.37 (2.4)	1.33 (2.6)	1.36 (2.7)	1.23 (2.7)	1.30 (2.9)
Il1b (pg/ml)	0.29 (1.2)	0.45 (1.7)	0.39 (1.7)	0.40 (1.6)	0.47 (1.9)
TNFα (pg/ml)	3.11 (2.8)	2.96 (2.7)	2.96 (2.7)	2.66 (2.6)	2.68 (2.7)
MAU (mg/mmol)	6.2 (9.6)	5.5 (5.8)	5.5 (5.6)	5.8 (5.9)	5.8 (7.0)

Values are medians with interquartile range in brackets

Conclusion: In this population-based study we found an association between kidney function, MAU and TNFα. The absence of an association between kidney function and Il-6, Il1b and hsCRP suggests that these markers do not play a major role in the development and progression of CKD, and/or that actual dosing techniques are not refined enough to detect small differences in concentrations. The association between kidney function and TNFα merits further study.

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Peripheral facial nerve palsy in children with severe arterial hypertension: report of two cases and systematic review of the literature

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Purpose: In childhood peripheral facial nerve palsy may result from various conditions. However, most cases are classified as idiopathic. Less recognized is the association between peripheral facial nerve palsy and severe arterial hypertension.
Methods and Materials: We report on two children (5-year-old boy with segmental cortical hypoplasia in the upper part of the right kidney; 11-year-old girl with fibromuscular dysplasia of the left renal artery) in whom peripheral facial palsy led to the detection of severe hypertension. Furthermore we review the literature.
Results: The literature disclosed 23 further cases (15 female and 8 male subjects). Twenty-three (92 percent) of the 25 cases (literature, N = 23; our experience, N = 2) were ≤15 years of age. The peripheral facial palsy was unilateral in 19 and bilateral in 6 cases. In addition to the peripheral facial palsy, signs of central nervous system dysfunction were observed in 17 patients: headache, vomiting, convulsions, hyperactive reflexes, positive Babinski sign, altered level of consciousness, and visual disturbances. In the patients blood pressure reduction after correction of the underlying disorder or antihypertensive medication was followed by resolution of the facial palsy. Eight further cases of peripheral facial palsy were found in three case series specifically addressing the neurological signs of arterial hypertension in a total of 74 severely hypertensive children.
Conclusion: The association between severe arterial hypertension and peripheral facial nerve palsy merits wider recognition and assessment of blood pressure is recommended in every child with facial palsy. With effective antihypertensive therapy the prognosis of this form of peripheral facial palsy is excellent.

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Rituximab treatment in hyperigG4 related systemic disease

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Purpose: HyperIgG4 systemic diseases are described as tissue infiltration by IgG4 positive plasma cells and IgG4 hypergamma-globulinemia.
Methods and Materials: We report the case of a 83 year old Chinese male presenting with weight loss, peripheral adenopathies, interstitial lung disease, renal failure with tubular proteinuria, retroperitoneal fibrosis, hyperproteinemia with hypergammaglobulinemia, asymptomatic dysthyroidia and pancreatic tests anomalies.
Results: The clinical picture was similar to hyperIGg4 related disease given diffuse organ infiltration including idiopathic pancreatitis, 50 fold elevation of IgG3 (19.5 mg/ml) and IgG4 (17.5 mg/ml) subclasses, absence of monoclonal component and T/B cell clonality and negative immunologic and virologic testing. Examination of two adenopathies showed a follicular lymphoid hyperplasia with major plasma cells infiltration and no argument for a lymphoproliferative disease. A kidney biopsy revealed interstitial nephritis and tubulitis with a polyclonal interstitial lymphocyte and plasma cells infiltration mainly composed of IgG4 containing plasma cells. To avoid corticosteroid side effects and given the polyclonal nature of the infiltrate, we undertook Rituximab treatment with a classic scheme (375 mg/m² over four weeks). The evolution was rapidly favorable. Within one month the patient gained seven kilos, dyspnea regressed, pancreatic tests, thyroid tests, CRP and renal function normalized, hypergammaglobulinemia normalized. More than one year after the treatment the patient is still in remission and has experienced no safety issue.
Conclusion: This demonstrates that renal and systemic hyperIgG4 related disease can successfully be treated with Rituximab alone, with sustained regression of the hypergammaglobulinemia and organ infiltration.

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Protein and energy intake in patients with chronic kidney disease stage ≥3

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Purpose: Patients with chronic kidney disease (CKD) present high risk for undernutrition. Depending upon the method used and the population studied, 40 to 70% of patients with CKD are undernourished. The aim was to assess protein and energy intake in patients with CKD ≥3.
Methods and Materials: A cross-sectional study was performed in the outpatient clinic of nephrology and hypertension in our University Hospital. All patients with residual renal function ≤60 ml/min/1.73 m² MDRD were included. Their protein and energy needs were

determinated according to EDTNA/ERCA guidelines. Dietary intakes were assessed by dieticians using patients' 7-day self-weighted foods and drinks diaries. Nutritional assessment was based on weight history, mid-arm muscle circumference and tricipital skinfold thickness. Undernutrition was defined as weight loss ≥5% of usual body weight and reduced muscle or fat mass below 25th percentile.
Results: Forty-eight patients were included, aged 65 ± 13, mainly of hypertensive and diabetic etiology. Mean energy and protein intake were respectively 72 ± 24% and 117 ± 38% of recommendations, with 1/3 of patients meeting less than 2/3 of energy needs. Mean Body Mass Index (BMI) was 27 ± 5 kg/m² and mean lean mass was 25th to 50th percentile. Eight (16%) patients were undernourished, with BMI 21 ± 4 kg/m² and lean mass 5th to 10th percentile.
Conclusion: Despite meeting protein needs, the population studied lacks energy intake. Stable weight and high BMI often hide loss of lean mass. A more systematic and thorough nutritional assessment could prevent undernutrition in CKD patients.

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Evaluation of a renal risk score in the Swiss population: consolidated results from a screening project in pharmacies in the years 2008–2010

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Purpose: Prevalence of chronic kidney disease in the Swiss population is not really known. The mostly asymptomatic progression and the low grade of awareness about kidney disease in the general population motivated a pilot project for information and detection. In the context of the World Kidney Day (WKD) a renal risk score was developed in 2008. During the past 3 years, this score was evaluated in screening activities in 62 pharmacies of 6 cantons/regions.
Methods and Materials: 800 people were screened and their scores analysed. The responsible pharmacists were specifically trained for screening activities and consulting. Participants were interviewed in the pharmacies. Points were attributed to each item and the sum corresponded to the risk score. Less than 2 points was defined as a low risk for kidney disease, between 2 and 4 a moderate risk and >4 an increased risk. A visit to the general practitioner was recommended for persons with at least moderate risk.
Results: Participants' characteristics (items) and renal risk scores

Characteristics	n (N = 800)	%
Age >50 years	537	67
Sex: female	562	70
Family history		
Chronic kidney disease	74	9
Diabetes	158	20
Cardiovascular disease: myocardial infarction	172	22
Cardiovascular disease: vascular diseases	249	31
Personal history		
Chronic kidney disease	137	17
Diabetes (treated)	35	4
Cardiovascular disease (treated)	196	25
Systolic blood pressure >140	210	26
Diastolic blood pressure >90	132	17
Microalbuminuria >2 mg/mmol	175	22

Results renal risk scores

	n (N = 800)	%
Low risk (<2)	199	25
Moderate risk (2–4)	289	36
High risk (>4)	312	39

Conclusion: 75% of the participants showed a moderate or high renal risk score. Participants in this screening program in pharmacies were mostly women >50 years old. Concerns due to the high proportion of FH or PH of kidney disease, diabetes or cardiovascular disease might have motivated these participants to undergo the risk evaluation.

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An unusual cause of secondary amyloidosis

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Purpose: We report on a case of a 70 y/o woman with CKD stage 4 admitted with acute-on-chronic renal failure triggered by diarrhea. Hyperkalemia, severe hypochromic microcytic anemia and an elevated C-reactive protein of 76 mg/L were detected. The patient presented with oliguria, pleural effusions, ascites and diffuse leg edema combined with extended ulcerations of the lower extremities. Her personal history revealed chronic leg ulcers to be persisting for more than 20 years.
Methods and Materials: Laboratory tests were performed at time of admission, showing nephrotic range proteinuria of 6.5 g/g (protein to creatinine ratio) with concomitant hypoalbuminemia of 19 g/L. A diagnostic procedure with a percutaneous renal biopsy was performed.
Results: Renal amyloidosis with extensive involvement of the glomerula and the vessels was seen in combination with extracapillary proliferation. Material from biopsies of the stomach and colon revealed congo-red positive tissue. Serum amyloid (SAA) protein concentration was elevated to 409 mg/L (<6.8 mg/L) before initiation of renal replacement therapy by intermittent hemodialysis and decreased to 18.4 mg/L after resolution of the chronic leg ulcers after 1 year of dialysis. Clinical and radiological workup did not reveal any other source of systemic inflammation. Unfortunately, kidney function did not recover. However, recurrent bleeding diathesis from the intestinal tract could be effectively managed by citrate anticoagulation during dialysis treatment.
Conclusion: Secondary amyloidosis is a rare condition, resulting mainly from chronic inflammatory processes. Chronic leg ulcers as the main cause of secondary AA amyloidosis have been reported only in a few case reports in the literature.

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Indications and outcome of plasma exchanges (PEX) – a single center experience during the last decade

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Purpose: PEX is an expensive and cumbersome procedure with limited evidence-based benefit. We reviewed the indications and outcome of PEX during the last decade.
Methods and Materials: All PEX performed in in-patients at our centre between January 2000 and August 2010 were analyzed retrospectively for the number of exchanges, indications, complications and outcome at discharge. Successful outcome included renal function recovery, neurological or hematological response. Unsuccessful outcome included death, need for dialysis or the absence of neurological or hematological improvement.
Results: 894 PEX occurred in 76 patients of which 74 could be analyzed. On average 12 PEX/patient were performed (range 1–94). Main indications were thrombotic microangiopathy in 30% (22/74), multiple myeloma in 22% (16/74), auto-immune disease (ANCA vasculitis, lupus, Goodpasture syndrome) in 18% (13/74), neurological disorder in 14% (10/74) and acute humoral rejection in 8% (6/74). Overall PEX was successful in 62% (46/74), unsuccessful in 38%. 7% (5/74) of the patients died and 19% (14/74) remained on dialysis. A successful outcome was registered in 77% (17/22) of the thrombotic microangiopathy cases and in 83% (5/6) of the humoral rejection cases. Of the myeloma cases 50% (5/10) remained on dialysis. Major complications occurred in 15% (11/74) of the patients, mainly catheter-related problems.
Conclusion: As reported in the literature PEX is still used in a broad spectrum of diseases with variable short-term outcome. A successful outcome was observed in conditions where there is evidence of benefit such as thrombotic microangiopathy and humoral rejection. However the effect of PEX in myeloma remains doubtful.

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Does vitamin B6 (pyridoxine) deficiency contribute to anemia in patients with chronic kidney disease stage ≥3?

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Purpose: Pyridoxine deficiency may contribute to renal anemia in patients with chronic kidney disease (CKD) stage ≥ 3 because of poor dietary intake, increased needs and pyridoxine metabolism disturbances. We tested the hypothesis whether blood pyridoxine levels were associated with anemia in non-dialyzed patients with CKD stage ≥3.
Methods and Materials: A cross-sectional study was performed in the outpatient clinic of nephrology and hypertension in our University Hospital. All patients with residual renal function ≤60 ml/min/1.73 m² MDRD were included. Pyridoxal-5-phosphate (P5P), blood

haemoglobin (Hb), vitamin B12 and folic acid were measured. Anemia was defined as Hb <120 g/l for women and <135 g/l for men and/or need for an erythropoietic stimulating agent or iron therapy. Nutritional assessment included weight, mid-arm muscle circumference and tricipital skinfold thickness. Undernutrition was defined as weight loss ≥5% usual body weight and reduced muscle or fat mass below 10th percentile.
Results: Of the 48 patients included, aged 65 ± 13, mainly of hypertensive and diabetic etiology anemia's prevalence was 54%. Mean blood P5P was 82.3 ± 54.4 nmol/l. Blood P5P levels were correlated with vitamin B12 (Spearman r: 0.346; p = 0.016) and folic acid levels (Spearman r: 0.553; p <0.001). No correlation was found between P5P and Hb levels. High nutritional risk was found in 27% patients. Only 8 (16%) patients were undernourished.
Conclusion: Neither pyridoxine deficiency nor undernutrition is present in the population studied, despite a high nutritional risk. Therefore, in those patients we were unable to explore the association between pyridoxine deficiency and renal anemia.

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Radiological renal artery embolization with a vascular plug as rescue therapy for uncontrollable nephrotic syndrome

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Purpose: Background: Nephrotic syndrome in patients with renal amylodosis is a common problem and sometimes delicate to treat. First step treatment are salt-diet, therapy with loop diuretics and ACE-inhibitors or ARB. In case of resistant nephrotic syndrome chemical nephrectomy with non-steroidal anti-inflammatory drugs, calcineurin-inhibitors or aminoglycosides can be tried to minimize proteinuria. The last option is surgical nephrectomy or radiological embolization of renal arteries.
Methods and Materials: n/a
Results: Case: We report a 63 years old patient with uncontrollable nephrotic syndrome and coagulation disorder. He had biopsy proven diagnosis of a renal amyloidosis due to a monoclonal gammopathy of uncertain significance (lambda light chains). Chemotherapy with cyclophosphamide, thalidomide and dexamethasone was initiated. Despite the treatment he progressed to end stage renal failure, starting hemodialysis. The patient had sustained severe nephrotic syndrome, with massive proteinuria (>40 g/day), low serum albumin (9 g/l), anasarca and orthostasis. In addition he suffered from coagulation disorder with an intracavitary left ventricular thrombus after myocardial infarction. Despite anticoagulation a pelvic vein thrombosis and embolic cerebral infarction due to the cardiac thrombus occurred. Several therapies were tried to control proteinuria (treatment with non-steroidal anti-inflammatory drugs and cyclosporine) but severe nephrotic syndrome persisted. Finally the patient was considered for renal artery embolization. After occlusion of both renal arteries with a vascular plug the patient became anuric and serum albumin rose to normal values with subsequent disappearence of anasarca and orthostasis.
Conclusion: In patients on hemodialysis with uncontrollable nephrotic syndrome embolization of renal arteries with a vascular plug is a feasible treatment option.

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Post liver transplant glomerulonephritis: a case report

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Purpose: Glomerulonephritis is frequently associated with liver disease and rises several issues when liver transplantation is indicated. New-onset renal failure is often linked to calcineurin inhibitors toxicity after liver transplantation. We describe here an unusual case of early rapidly progressive IgA glomerulonephritis occurring in a previously normal renal function liver recipient.
Methods and Materials: A 66 year-old man underwent deceased donor liver transplantation for alcoholic cirrhosis. Immunosuppression regimen consisted of basiliximab, tacrolimus, mycophenolate mofetil and corticosteroids. An autoimmune deficit of factor V in the coagulation pathway led to a switch from tacrolimus to everolimus at day 21. Renal failure and albuminuria appeared 45 days later followed by glomerular microhematuria. Everolimus withdrawal and ciclosporin introduction did not improve renal abnormalities. As creatinine increased up to 382micmol/l, a renal biopsy was performed 5 months post transplant. Light microscopy showed a mesangio-proliferative glomerulonephritis with crescents and tubulo-interstitial nephritis. Immunofluorescence was positive for IgA and C3 deposits. Electron microscopy confirmed IgA glomerulonephritis.
Results: The patient received IV methylprednisolone 500 mg for 3 days at month 0-2-4, oral prednisone 0.5 mg/kg on alternate day for 6 months than progressive tapering over 4 months. Proteinuria and glomerular microhaematuria disappeared completely 4 months after the first bolus. One year later, creatinine is stable at 144 micmol/l.
Conclusion: The occurrence of rapidly progressive IgA glomerulonephritis after liver transplantation is unfrequent. It raises several issues including the possibility of a quiescent IgA disease before liver transplantation. The mechanisms involved are unknown but everolimus might have been the trigger. Corticosteroids treatment is the first option and has been successful in this case.

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Angioplasty of renal-artery stenosis can still be the best solution: a case report

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Lugano

Purpose: Renal artery stenosis, a possible cause of hypertension and ESRD, is a consequence of atherosclerosis or fibromuscolar dysplasia. Whereas it is generally accepted that fibromuscular dysplasia is effectively treated by angioplasty, the optimal management of atherosclerotic renal-artery stenosis is currently under debate. Treatment options consist of medical therapy or revascularization (surgical endarterectomy or angioplasty with stenting). The role of endovascular therapy remains however controversial since data from randomized trials have not shown a benefit from revascularization over medical therapy.
Methods and Materials: A 88-years-old woman with a single functional kidney showed an acute rise of beforehand stable blood pressure that was resistant to more than three drugs of different classes, episodes of pulmonary edema and oligo-anuric ARF requiring hemodialysis. Angiography showed a subocclusive right renal artery stenosis (>90%). An angioplasty with stenting was performed.
Results: We observed an instant reduction of blood pressure and of the number of antihypertensive drugs required, and re-establishment of diuresis with quick correction of fluid overload and with significant improvement of renal function (GFR 36 ml/min).
Conclusion: Despite the results of the recent ASTRAL-trial angioplasty can be a reasonable procedure in individual patients with hemodynamically significant lesions (bilateral or in a single functional kidney), inability to tolerate medication, recurrent flash pulmonary-edema or ARF (according to 2005 ACC/AHA-guidelines). One of the limitations of most randomized trials is the fact that due to the presence of multiple exclusion criteria the results are not always applicable to 'real world' cases

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Cardio-respiratory arrest caused by vitamin D deficiency rickets: A case report

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Purpose: Clinical manifestations of vitamin D deficiency rickets are widely described; however cardio- respiratory arrest is rare.
Methods and Materials: We report a case of a 16 months old infant who initially presented with stridor that was misdiagnosed as viral laryngitis. He presented, two weeks later, a cardiorespiratory arrest related to a laryngospasm secondary to severe hypocalcemia. He was successfully resuscitated and vitamin D deficiency rickets was diagnosed.
Results: Medical history revealed that the infant was exclusively breast fed without vitamin D supplementation till the age of 10 months and also deprived from other milk due to cultural habits. Physical exam revealed a frontal bossing, widening of the wrists and rachitic rosary. Laboratory test revealed a severe hypocalcaemia (ionized calcium: 0.42 mmol/l, total calcium: 1.15 mmol/l), an elevated alkaline phosphatase level of 1300 U/l, a normal serum phosphorous level of 2 mmol/l, a decreased 25 (OH) cholecalciferol of 5.7 mcg/l, a normal calciuria level of 0.35 mol/mol of creatinine and an increased parathyroid hormone level of 325 ng/l. X-ray radiography of the wrist showed evidence of metaphyseal widening, and demineralization of the distal radial and ulnar metaphyses. Bone mineral density (BMD) of the lumbar spine was 0.298 g/cm^2, corresponding to a Z-score (standard deviation from the mean) below -2 SD.
Conclusion: The aim of this presentation is to highlight the symptoms of vitamin D deficiency rickets that could be life threatening and the importance of vitamin D supplementation for some ethnic minority population who are faced with the risk of developing this disease.

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Anti-hLAMP2-antibodies and dual positivity for anti-GBM and MPO-ANCA in a patient with relapsing pulmonary-renal syndrome

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Purpose: One third of patients presenting as anti-glomerular basement membrane (GBM) antibody positive pulmonary-renal syndrome or rapidly progressive glomerulonephritis are also tested positive for anti-neutrophil cytoplasmic antibodies (ANCA). Whilst anti-GBM disease is considered a non-relapsing condition, the long-term course of double-positive patients is unknown.
Methods and Materials: We report a patient with such dual positivity, who presented with pulmonary hemorrhage and crescentic glomerulonephritis. Plasmapheresis in combination with immunosuppresive therapy led to a rapid remission but the disease relapsed after two years.
Results: The serum of the patient was tested positive for antibodies to human lysosomal membrane protein 2 (hLAMP2), a novel autoantigen in patients with active small-vessel vasculitis (SVV).
Conclusion: Thus anti-hLAMP2 antibodies may indicate decisively a clinical course similar to ANCA-associated vasculitis in double-positive patients and could therefore be of clinical utility to direct therapy.

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Hyperpigmentation without Addison's disease: melanocortin-induced anorexia/cachexia syndrome in a renal allograft recipient with chronic inflammation: a case report

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Purpose: Cheung and coworkers demonstrated that CKD-associated anorexia/cachexia are caused by a defective hypothalamic regulation of appetite. The defect is attributed to an alteration in the hypothalamus response to leptin and inflammation. This neural circuitry is known as the central melanocortin-system. The melanocortins (a,ß,Y-MSHs and ACTH) constitute a family of pro-opiomelanocortin(POMC)-derived peptides and have progressively revealed an incredibly wide range of physiological functions including pigmentation, adrenocortical steroidogenesis, energy homeostasis and a protective anti-inflammatory response.
Methods and Materials: A 64-year old male received a renal transplant and developed a delayed insufficiency of the vascular anastomosis with a subsequent retroperitoneal hemorrhage. After explantation of the graft and placement of a stent into the left-external-iliac artery, the clinical course was complicated by multiple opportunistic infections (CMV/Clostridium/Pulmonary-Aspergillosis) and recurrent sepsis from stent-infection by Pseudomonas (5x).
Results: The patient developed a severe decay of his general status, with asthenia, lack of appetite, severe diffuse muscular atrophy and a significant weight loss (16Kg). Contemporarily an intense brown hyperpigmentation of the skin was observed. Synacthen-test excluded insufficiency of the hypothalamic-hypophysiary-corticoadrenal-axis. After positioning of a naso-gastric-tube for enteral nutrition and under therapy with antibacterial and antifungal antibiotics we observed a gradual improvement with weight gain, increase of muscular strength, appetite, walking capacity, regression of inflammatory parameters and normalisation of skin pigmentation.
Conclusion: Inflammatory stress and chronic diseases activate the melanocortin-system, which can induce anorexia/cachexia and a diffuse brown hyperpigmentation. Aggressive nutrition and control of the infective diseases can disactivate the system. New drugs should be developed to interrupted the neural circuitry.

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Health economic modelling of the cost-effectiveness of microalbuminuria screening in Switzerland

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Purpose: End-stage renal disease (ESRD) is coupled with high cost, making CKD an important economic burden for health care systems. In Switzerland, ESRD patients on dialysis represent 0.05% of the population. The yearly dialysis cost for these patients comprises 1.1% of health care expenditure covered by the obligatory part of the health insurance. Several studies have demonstrated that an early treatment of CKD can slow the progression of renal decline. CKD can be detected by simple tests at acceptable reliability. However cost-effectiveness data of a CKD screening approach are not available for Switzerland.
Methods and Materials: Hoerger et al. published recently a comprehensive health policy model (Am J Kidney Dis 55: 463-473, 2010) which allowed them to model the cost-effectiveness of microalbuminuria screening in the USA. The Markov simulation model consists of 7 mutually exclusive stages of CKD. The model of Hoerger et al. will be run with Swiss data for parameters including prevalence of risk factors, cost of screening test, cost of medical visits, cost of medical treatment, cost of drugs and medical practice.
Results: The model will predict the costs, quality-adjusted life-years and incremental cost-effectiveness ratios for the total population and different sub-populations/risk groups at varying screening intervals. Costs will be reported from a health care system perspective.
Conclusion: We will calculate the cost-effectiveness of microalbuminuria screening in high-risk groups for CKD. Our results may provide medical experts, policy makers and health insurance funds with guidance for possible prospective pilot CKD screening programmes and the development of local CKD guidelines.

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Cinacalcet in the treatment of secondary hyperparathyroidism: a pharmacoeconomic evaluation in the swiss healthcare setting

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Purpose: Secondary hyperparathyroidism (SHPT) is a common condition in dialysis patients, characterized by unbalanced levels of parathyroid hormone (PTH), serum calcium (Ca) and phosphorous (P) associated with increased mortality and morbidity. Cinacalcet is effective in controlling metabolism parameters and may improve outcomes. An economic evaluation comparing cinacalcet with standard treatment (mainly vitamin D sterols and phosphate binders) is done to assess cost-effectiveness.
Methods and Materials: The analysis is conducted with a Markov model with probabilistic patient-level simulation. The model simulates lifetime dynamics of PTH, Ca and P under two therapeutic alternatives: standard treatment (ST) and cinacalcet plus ST. The simulation of metabolic parameters changes over time is based on the OPTIMA study, a European multicentre, open-label, 23-week study. Published correlations between these levels, mortality and morbidity (CV events, fractures, and parathyroidectomy) were incorporated as well as Swiss cost data for dialysis, drugs and events management. The effectiveness was measured as life expectancy and quality-adjusted life expectancy. Health Utility Indexes were derived from literature and considered dialysis, CV events and fractures.
Results: Simulated patients in the cinacalcet group gain an average (SD) 1.40 (4.36) life-years (LYs) and 1.01 (3.00) QALYs at a differential cost of CHF 48,908 (87,759), not considering the cost of dialysis. When taking that into account the differential cost rises to CHF 164,003 (411,810). The incremental cost-effectiveness ratio, which indicates the incremental money necessary to buy the unit benefit, is 34,858 CHF/LY and 48,310 CHF/QALY.
Conclusion: This study suggests that cinacalcet treatment in SHPT could be cost effective in the Swiss Healthcare System.

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Eculizumab in atypical hemolytic uremic syndrome: long-term clinical course and histological findings

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Purpose: background: Atypical hemolytic uremic syndrome (aHUS) has been associated with defective regulation of the alternative complement pathway. Plasma exchange is an efficient therapy for treatment and prevention of relapses.
Methods and Materials: Eculizumab, a monoclonal humanized anti-C5 antibody, inhibits activation of the terminal complement pathway and has been shown to be effective and well-tolerated in patients with paroxysmal nocturnal hemoglobinuria. Treatment of patients with aHUS with eculizumab is supported by recent reports on its successful use in pediatric and adult patients with aHUS.
Results: case: A 9 year old girl with relapsing aHUS due to factor H mutation (Cys611Tyr in SCR 10) was treated with plasma exchange three times per week with an exchange volume of 150% plasma volume. A reduction of the plasma exchange frequency induced repeatedly relapses of aHUS, manifest with blood pressure increase, worsening of the renal function, thrombocytopenia, anemia and modest increase in LDH. Due to the high frequency of plasma exchange needed to stabilize aHUS, we decided to treat the patient with Eculizumab, 600 mg every two weeks. 13 months after starting Eculizumab, the girl did not suffer aHUS relapses, the renal function improved (GFR from 45 to 60 ml/min/1.73 m^2), the number of antihypertensive medications decreased from 5 to 3 with a substantial improvement of myocardial hypertrophy, EPO amount / week was reduced and the quality of life increased substantially. A renal biopsy performed 2 months after start of Eculizumab showed the absence of thrombotic microangiopathy.
Conclusion: The optimal duration of treatment remains to be determined.

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The missing ion

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Purpose: Hypocalcemia may develop for various resasons including hypoparathyroidism. Here, we describe a case of inappropriate hypoparathyroidism in the presence of severe hypomagnesemia.
Methods and Materials: A 51 y/o white male diagnosed for acute myeloid leukemia was treated with two cycles of induction chemotherapy including idarubicin, amsidyl, and cytarabin. Subsequently, he developed diarrhea and a progressive hypocalcaemia. Despite treatment with Ca (4 g/d) and 800 IU cholecalciferol, the hypocalcaemia worsened. He was referred to our Department.

Results: Parameter	Value	Unit
Ionized calcium	0.81	mmol/l
Magnesium	<0.2	mmol/l
Sodium	142	mmol/l
Potassium	2.5	mmol/l
Phosphate	0.78	mmol/l
eGFR	>90	ml/min/1.73 m^2
PTH	15	pg/ml
25-OH-Vit D3	17	nmol/l
1, 25-(OH)2-Vit D3	55	pmol/l

The urinary FECa, FEMg and FEPO4 were very low corresponding with diarrheal loss. Unexpectedly, no compensatory hyperparathyroidism, but rather an inappropriately low PTH was present. Following substitution the potassium and the magnesium rose to 4.0 and 0.52 mmol/l, respectively. Calcium and 25-OH vitamin D3 supplementation increased calcium serum levels to 2.0 mmol/l. Now, still hypocalcemic, hyperparathyroidism developed (146 pg/ml).
Conclusion: Two major explanation might account for this inappropriate hypoparathyroidism: First, similar observations in patients treated with cytarabin suggest a direct drug toxicity, and second, more intriguing a dysregulated parathormon secretion might have occured due to hypomagnesemia. In favor of this assumption, we observed a prompt recovery and rise of the iPTH level with magnesium correction. Though magnesium as type 1 agonist of the calcium-sensing receptor on the parathyroidal glands triggers parathormon secretion the opposite holds true if magnesium is absent. Then, PTH secretion is directly reduced. A magnesium-dependent PTH resistance involving impaired adenylate cyclase stimulation in low magnesium conditions further aggrevates hypocalcemia.

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Early diagnosis and complete recovery with plasma exchange in a 6 months old infant with familial atypical hemolytic uremic syndrome

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Purpose: Hemolytic uremic syndrome (HUS) is a leading cause of acute renal failure in childhood. The majority of the cases are preceded by an episode of diarrhea mostly due to Shiga-toxin-producing Escherichia coli. Atypical HUS associated with defective regulation of the alternative complement pathway should be considered in children without diarrhea, with relapsing HUS or with positive familial history for atypical HUS and plasma exchange should be immediately started in order to prevent long term renal complications.
Methods and Materials: We report on a 6 months old female with acute presentation of hemolytic anemia (hemoglobin 63 g/l , LDH 3523 U/l, Haptoglobin <0.1 g/l), thrombocytopenia (60 G/l) and oliguric acute renal failure (creatinine 66 µmol/l , urea 11.1 mmol/l).
Results: Familial history disclosed several relatives with unclassified lethal renal diseases and a cousin of the infant's father with a genetically proven factor H mutation (heterozygous CFH/CFHR1 hybrid gene in which exons 1-21 are derived from CFH and exons 22/23 from CFHR1). Therefore, plasma exchange was immediately started (1x day, 150% of plasma volume). Renal replacement therapy was not necessary and after one week all blood parameters were within normal range.
Conclusion: After 3 months of follow-up without plasma exchange, normotension and normal kidney function without proteinuria or arterial hypertension was observed. Genetic analyses confirmed the same mutation in the child and child's father.

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Successful treatment of steroid-dependent minimal change disease by mycophenolate mofetil in a patient with HIV-infection

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Purpose: Management of kidney disease causing nephrotic syndrome, such as minimal change disease (MCD) in HIV-positive patients is challenging, as this involves not uncommonly immunosuppressive therapy, and there is no consensus on the treatment strategy.
Methods and Materials: We report on a successful treatment of steroid dependent MCD in a patient with HIV infection.
Results: A 31-year-old female patient with well-controlled HIV infection on HAART for 2.5 years presented with severe nephrotic syndrome (urine albumin/creatinine ratio 1523 mg/mmol) and acute renal failure (serum creatinine 243 mmol/L). She was taking lamivudine, efavirenz, and tenofovir, and denied the use of any other drugs. The kidney biopsy revealed MCD and the patient was treated with prednisone 50 mg once daily (1 mg/kg bw). In the following course over 1 year, steroid withdrawal was not achievable due to 4 relapses upon reduction of steroid. After addition of mycophenolate mofetil (MMF) (500 mg bid), steroid was for the first time successfully withdrawn. However, after stop of MMF a relapse occurred within 1.5 months. After restart of prednisone partial remission was achieved and because of increasing proteinuria under reduction of prednisone MMF was added again. Complete remission was achieved, steroids were withdrawn and MMF was given for further 7 months and stopped thereafter. Three months later the patient is still free of any relapse. Her immunologic state has been stable and no opportunistic infection has occurred.
Conclusion: MMF can be used safely and successfully for the treatment of steroid-dependent MCD in patients with HIV infection.

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An unusual case of nephrotic syndrome after treatement with bevacizumab

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Purpose: A 65-year-old man with metastatic cancer of the coecum was treated with bevacizumab (anti-VEGF-antibody) because of tumor progression. Twenty months after starting of anti-VEGF-therapy, he developed edema, shortness of breath, and hypertension. On admission, serum creatinine was 228 µmol/l and increased to 400 µmol/l in the following. Heavy proteinuria and decreased serum albumin were noted. Laboratory test concerning hemolysis were normal.
Methods and Materials: Renal biopsy showed acute extracapillary glomerulonephritis with fresh cellular crescents in up to 50% of the glomeruli and strong diffuse IgA deposits in mesengial areas as well as capillary-loop double contours, and prominent electron-dense deposits in the mesangium and subendothelial space. Marked foot process effacement and glomerular endothelium swelling was also noted.
Results: These histologic findings were interpreted as proliferative IgA glomerulonephritis associated with thrombotic microangiopathy. Bevacizumab was discontinued. Immunosuppression with cyclophosphamid and steroids was started for 6 months. The renal function improved to a serum creatinine of 265 µmol/l, and proteinuria decreased significantly. A follow-up renal biopsy revealed fibrous transformation of the crescents in 30% and some globally sclerotic glomeruli.
Conclusion: Renal biopsy demonstrated glomerular capillary endothelial injury typical for thrombotic microangiopathy and consitent with the current assumption that VEGF is essential for glomerular capillary integrity. The additional observation of a proliferative IgA glomerulonephritis was surprising, and difficult to explain in the context of the current known biological activity of VEGF. We hypothesize that the IgA glomerulonephritis was a secondary IgA nephropathy because of the gastrointestinal tumor. Despite the general recommendation to stop bevacizumab when proteinuria appears, early renal biopsy is mandatory to identify treatable concomitant renal pathology.

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Tubulointerstitial Nephritis and Uveitis (TINU) Syndrome

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Purpose: Tubulointerstitial nephritis and uveitis (TINU) syndrome is a rare entity of unknown etiology. It is more frequent in women and its median age of presentation is 15 years. The nephritis usually precedes the uveitis (65%). The long-term prognosis is generally good, but relapses of the uveitis are frequent. First line therapy consists of systemic corticosteroids, but spontaneous recovers have also been reported.
Methods and Materials: –
Results: Case report
A 14 year-old female adolescent complained about fever and headache. The symptomatic therapy did not improve the subjective complaints and five weeks later leucocyturia, tubular proteinuria and glucosuria ensued. The clinical examination was normal and blood analysis revealed a moderate anemia (hemoglobin 107 g/L) together with thrombocytosis (platelets 573 G/L) and elevated marker of inflammation (C-reactive protein 87 mg/L, sedimentation rate 76 mm/h). Acute renal failure (creatinine 120 µmol/L) and persistent signs of tubular damage induced us to perform a renal biopsy, which highlighted an acute tubulointerstitial nephritis. At that time the ophthalmological examination was normal and the etiology of the interstitial nephritis was unknown. A therapy with systemic corticosteroids was immediately started and two months later, still under systemic corticosteroids (0.5 mg/kg/d), the patient presented with pain and redness of both eyes. An ophthalmological examination revealed an anterior bilateral uveitis, which was successfully treated with topic corticosteroids.
Conclusion: TINU syndrome is a rare diagnosis which should be suspected when a young patient presents with interstitial nephritis followed or preceded by uveitis. This case demonstrates that the uveitis can also appear during the systemic corticosteroid therapy.

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Nephrology teaching in the Newly Independent States (NIS) – a continuing challenge

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Purpose: Despite many efforts by nephrological societies and others to advance nephrology in the NIS results are often transient, since local nephrologists are only rarely involved in RRT and old concepts persist. Our aim was to apply a new strategy for training and education.
Methods and Materials: Our strategy is based on 3 pillars: I) A strong partnership programme (Zurich/Yerevan), existing since 1989; II) a joint teaching programme in the Ukraine (Lviv) and Moldova (Chisinau), 2001–2008, and III) a new concise nephrology textbook in Russian (2010) specifically designed for Russian speaking countries. (I) is mainly sponsored by the Canton of Zurich and (II) and (III) by the SNSF.
Results: Based on (I) a joint teaching programme (II: nephrology, imaging, biopsies) was carried out in Lviv, Chisinau and Yerevan. However, effects in Lviv and Chisinau were limited because of poorly motivated Hospital Directors and limited duration. The new textbook (III) edited together with a renowned nephrologist in Moscow (A. Tsygin) is directly based on the experience obtained from (I) and (II). European co-authors (5 Swiss) were highly motivated and readily accepted the special concept incorporating many Editorial comments. Special attention was paid to renal biopsies (M. Mihatsch) and RRT. The first reactions in Russia were very positive.
Conclusion: To train a new generation of nephrologists in the NIS takes much time and efforts. Occasional teaching courses and short-term sister programmes are important but not sufficient. Other concepts like ours may be more effective.

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Prevalence of reduced renal function in laboratory tests

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Purpose: To analyse the prevalence of reduced renal function (RF) in the tests performed by private laboratories in 2008.
Methods and Materials: Data from two laboratories (*Labor Dr. Güntert* and *Labormedizinisches Zentrum Dr. Risch*) were available. Patients with a creatinine test were included in the analysis. Prevalence of reduced RF was assessed by creatinine-based estimates of the glomerular filtration rate (eGFR), calculated with the CKD-EPI equation. In case of multiple tests for the same patient, only the test reporting the highest creatinine value was taken into account. Prevalence was also analysed for different commissioners.
Results: 22945 patients were included. 57% were women and the mean age was 55 ± 20 years. Normal RF was reported by 47.7% of the patients, whereas 34.3% showed a mildly (60–89 ml/min/1.73 m^2) and 15.6% a moderately (30-59 ml/min/1.73 m^2) decreased RF. 443 patients (1.9%) had a severely decreased RF (15–29 ml/min/1.73 m^2) and 106 patients (0.5%) suffered from end stage renal disease (<15 ml/min/1.73 m^2). Reduced RF was more frequent and severe among patients in hospital, rehabilitation, or nursing homes, as well as among patients visiting a nephrologist or urologist. Nevertheless, patients seen by GP's or other specialists had reduced RF prevalences oscillating between 20% (gynaecology) and 52% (internal medicine).
Conclusion: Although such analyses are subjected to high selection biases, these results emphasise the high prevalence of reduced RF. Whereas severe renal dysfunctions are usually known, mildly to moderately reduced RF are probably under-diagnosed and therefore at high risk for progression. Screening and prevention programs may become a basic necessity.

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A Kayexalate-associated gatric ulcer in a patient with hyperkalemia

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Purpose: Kayexalate, a cation-exchange resin, has long been used in the treatment of hyperkalemia. Nonetheless its efficacy is largely unproven. There is an increasing number of reports of kayexalate-induced gastrointestinal tract lesions, mostly colonic.
Methods and Materials: A 84-year-old female patient presented to the emergency department with a 3-day history of diarrhea and abdominal pain. Her history included hypertension, type 2 diabetes mellitus and stage 3 chronic kidney disease. Her medications included 100 mg of aspirin, enalapril, furosemide, and pantoprazol. On physical examination the patient was conscious, her blood pressure was 137/45 mm Hg, and her heart rate 86 bpm. The ECG was normal. The lab tests showed acute renal failure with a creatinine blood level of 403 umol/l and an urea level of 46.4 mmol/l. The serum potassium level was 5.8 mmol/l. The patient was started on IV fluids, ACE inhibitors were discontinued and 30 g of kayexalate with 20 ml of lactulose were given orally.
Results: An upper gastrointestinal endoscopy performed 12 hours later revealed antral mucosal erosions; on biopsy basophilic kayexalate crystals were observed in a mucosal ulcer (H&E stain). After a complicated hospital course the patient eventually recovered and was dismissed home.
Conclusion: We report a case of kayexalate-associated upper gastrointestinal tract injury. Concurrent use of aspirin could have initiated mucosal damage; uremia and gastroparesis are possible exacerbating factors. Based on its unproven efficacy and its association with gastrointestinal tract lesions kayexalate should not be used in the treatment of hyperkalemia if other approaches such as renal replacement therapy are available.

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ANCA positive vasculitis with rapid progressive glomerulonephritis (RPGN) in adolescents: Plasmaexchange (PEX) to recover and preserve renal function?

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Zürich

Purpose: Treatment and outcome of ANCA pos. vasculitis and RPGN in childhood are presented.
Methods and Materials: BOY: 13 years old at onset of an acute pyelonephritis. Three days thereafter pneumonia was diagnosed. Unsuccessful antibiotic treatment and rapid impairment of renal function (GFR: 14 ml/min). Additional symptoms: Arthralgia, recurrent epistaxis, petechiae. Vasculitis associated findings: C-ANCA-titer (1:1280). Renal biopsy(RB): Extracapillary proliferative and necrotizing GN. Treatment: 9 sessions of PEX within 13 days. Induction therapy with 3 doses methylprednisolone (M-PDN) i.v., followed by prednisolone (PDN) p.os., cyclophosphamide (CyP) pulses i.v. After 3 months (m): GFR: 62 ml/min, proteinuria: 1000 g/mol, C-ANCA-titer: 1:10. Current treatment: Daily PDN (tapering, orally), CyP i.v. every 4 weeks (in total 6 dosis), thereafter switched to azathioprine (AZA).
Results: GIRL: 13 years old at onset with parvovirus-infection with fatigue, gonarthritis, anemia. Within 8 weeks renal function decreased (GFR: 35 ml/min). ANCAtiter(1:640). RB: Extracapillary proliferative GN with fibrosis and crescents. Treatment: 14 sessions of PEX within 40 days. Induction therapy with 3 doses M-PDN i.v, thereafter PDN and CyP p.os during 12 weeks. After 3 m: GFR 60 ml/min, ANCA neg. Switch from CyP to AZA and tapering of PDN. After 2 years(y): Recurrence of arthralgia and manifestation of cutaneous lesions: Switch from AZA to MTX p.os. (15 mg/m^2 weekly). After 6y: In remission (GFR of 65 ml/min), mild proteinuria and borderline ANCA-titer. Current treatment: PDN 2.5 mg every second day and MTX 10 mg/week p.os.
Conclusion: Early and adequate treatment with immunosuppressiva and PEX may prevent development of RPGN preserving renal function in ANCA pos. vasculitis.

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Are we able to estimate kidney function in elderly inpatients?

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Purpose: Estimating GFR in the elderly, taking into account the additional difficulty of evaluating their muscle mass, is a hard task. The purpose of this study was to verify the reliability of (i) selected kidney function markers other than creatinine and (ii) currently used prediction algorithms in an elderly inhospital population.
Methods and Materials: In an elderly population of an internal medicine ward, using inulin clearance (single shot) as gold standard, the algorithms of Cockcroft, MDRD, Larsson (Cystatin C), White (beta-trace) and Macdonald (creatinine, muscle mass by bioimpedance) were evaluated.
Results: 69 patients were included in the study: age 78.0 ± 7.0 y; weight 77.3 ± 15.2 kg, muscle mass 19.1 ± 6.1 kg, creatinine 134 ± 62 µmol/l, cystatin C 1.71 ± 0.87 mg/l, beta-trace 1.33 ± 0.64 mg/l, GFR inulin 34.1 ± 19.9 ml/min. The error in the estimation of GFR (median and interquartile range) and the area under the ROC curve (cut off ± 15 ml/min) were respectively: Cockcroft 14.3 (5.55–23.2) ml/min and 0.763 ± 0.059, MDRD 16.3 (6.4–27.5) ml/min and 0.717 ± 0.065, Larsson 12.8 (4.50–25.3) ml/min and 0.844 ± 0.051, White 17.6 (11.5–31.5) ml/min and 0.680±0.066, Macdonald 32.2 (13.9–45.4) ml/min and 0.883 ± 0.41.
Conclusion: Currently used algorithms overestimate GFR in elderly inpatients (P <0.001). The best results were obtained with Larsson (cystatin C) (P <0.05) and Cockcroft (P = 0.05) algorithms. The determination of muscle mass by bioimpedance did not provide any significant contribution.

Poster Presentations – Transplantation

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Pattern of reduction in plasma immunoglobulins during Immunoadsorption

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Purpose: Immunoadsorption (IA) is a procedure consisting in treating filtered plasma of the patient through columns of beads. These beads have physicochemical properties that allow the adsorption of immunoglobulins (Ig). Columns contaning staphylococcal protein A can adsorb the Ig through their Fc fragment. Unlike plasma exchange (PE), other plasma protein fractions are not lost. We aimed to evaluate the pattern of reduction of plasma Ig during IA treatments.
Methods and Materials: Immunoglobulins were measured by nephelometry before and after IA in three high-risk sensitized patients awaiting a kidney transplantation. We next compared the efficacity of the epuration of Ig during IA and during a PE administered to a patient with acute kidney rejection. Indeed, the latter treatment is performed without giving plasma, which brings Ig and other proteins. Finally, we compared the impact of both treatment on the coagulation, knowing that regional anticoagulation was given during the PE.
Results: Measurements of the rate of reduction (RR%) of Ig were performed in 14 out of 24 IA treatments. The RR% of total Ig in 5 AI treatments was 64% and was 67% in one PE. RR% of classes IgG, IgM and IgA were 73%, 46.5% and 24% respectively. During the PE, RR% were 70%, 51% and 66% respectively (table 1). Coagulation was altered following the PE only.
Conclusion: IA seems as much effective as PE in eliminating IgG, this more specifically and probably with a better safety profile. The elimination of IgA and IgM classes is less important with IA than with PE.

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Assessment of bone quality in renal transplant patients by DXA and micro-computed tomography (µCT)

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Purpose: Renal transplant patients (RTP) are at risk of developing bone abnormalities due to preexisting renal osteopathy and immunosuppressive therapy. The changes in bone structure and their pathogenesis are poorly described so far.
Methods and Materials: Bone quality was investigated in 29 RTP with stable graft function. Bone mineral density (BMD) was assessed by dual energy x-ray absorptiometry (DXA) and compared to cancellous bone micro-architecture of iliac crest bone biopsies analyzed by micro-computed tomography (µCT). Follow-up (FU) DXA measurements and biopsies were performed 1 year after baseline (BL) evaluation.
Results: Cumulative BL and FU assessments resulted in 46 pairs of DXA and µCT measurements. Comparison of BMD at lumbar spine, hip and femoral neck determined by DXA versus µCT revealed no significant correlations. None of the other micro-architectural parameters including cancellous bone volume density, bone surface density, connectivity density, trabecular number, separation and thickness obtained by µCT correlated with BMD from DXA. BL and FU DXA measurements revealed individual changes in absolute BMD ranging from –5 to +11%. Nevertheless, these relative alterations did not result in significant shifts in the WHO-classifications of osteoporosis (T-score, Z-score) in most patients. In contrast, FU biopsies of 18 patients showed prominent quantitative micro-architectural changes ranging from –42 to +288% versus BL for some parameters.
Conclusion: In conclusion, DXA and µCT analyses revealed changes in BMD and cancellous bone micro-architecture of RTP within a 1 year FU. The findings suggest that assessment by DXA does not adequately reflect the type, degree and dynamics of structural bone alterations in these patients.

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Splenectomy as a rescue therapy for refractory humoral rejection after ABO-incompatible kidney transplantation

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Purpose: Treatment of acute antibody-mediated rejection (aAMR) includes steroids, plasmapheresis or immunoadsorption, IVIG, and in some cases rituximab. In refractory cases, splenectomy has been proposed as a rescue therapy.
Methods and Materials: We describe a 41-year-old caucasian man, who received an AB0-incompatible second renal allograft from his brother. The common Swiss protocol for ABO-incompatibility (including rituximab, immunoadsorption, and oral immunosuppression with tacrolimus, steroids and mycophenolate) was applied.
Results: From the surgical point-of-view the postoperative phase was uneventful, but renal allograft function was delayed. A biopsy at d4 post-transplant revealed aAMR. Despite further solumedrol pulses and immunadsorptions, renal allograft function deteriorated. Due to a pre-existent low-level anti-class1 antibody (anti-HLA-A2 MFI656) immunoadsorption was replaced by plasma exchange. Nevertheless a second biopsy at d15 showed refractory aAMR. Creatinine rose to 507 µmol/L, and the patient became oliguric. On d17 we decided to perform splenectomy. Three days later renal function started to improve (creatinine dropped from 507 to 207 µmol/L), and urine production normalized. Plasma exchange was continued for 5 sessions every other day, and basic immunosuppression with tacrolimus, mycophenolate and steroids was maintained. The patient was discharged on d45 with a serum creatinine of 197 µmol/L. Over the next 6 months renal function remained stable (serum creatinine 170–200 µmol/L, proteinuria 0.5–0.8 g/d). A protocol biopsy 6 months post-transplant showed chronic- active AMR. Therefore 5 solumedrol pulses, and another course of rituximab and IVIG were given. The patient was vaccinated against Haemophilus and Pneumococcus. No infectious complications were seen so far.
Conclusion: Splenectomy is a useful rescue therapy for severe refractory aAMR.

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Two cases of Nocardia in renal transplant recipients

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Purpose: –
Methods and Materials: –
Results: Case 1
A 39 year old kidney transplanted woman was hospitalized because of an upper lobe pneumonia. The chest CT revealed a necrotizing pneumonia in the right upper lobe and *Nocardia veterana* was found in the culture of the bronchoalveolar lavage fluid. A brain CT was normal.
Case 2
A 42 year old kidney transplanted man was admitted for breathing-dependent chest pain after two episodes of non resolving pneumonia. The chest CT scan revealed multiple infiltrates and a lung abscess. A punction of the latter was positive for *Nocardia farcinica*. A brain CT showed multiple lesions consistent with cerebral involvement. Both patients received trimethoprim-sulfamethoxazole at an induction

dosage of 15 mg/kg iv, followed by a maintenance dose of 10 mg/kg. Because of the cerebral involvement, the second patient also received moxifloxacin at a dosage of 400 mg/day. Both patients recovered after a prolonged course of antibiotics.
Conclusion: Nocardiosis, an infection caused by aerobic gram-positive actinomycetes, is mostly observed in immunocompromised patients. In solid organ transplant recipients, the incidence varies between 0.7% and 3.5%. Inhalation of the organism is considered the most common route of entry and the lungs are the primary site of infection in more than two-thirds of the cases. Nocardia pneumonia can frequently be initially misdiagnosed as tuberculosis, invasive fungal disease or malignancy. Tendency to progression and relapse requires prolonged treatment and close clinical monitoring. Brain involvment is common and should be excluded even in asymptomatic patients.

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Experience with early high-dose mycophenolic acid in renal transplantation – a case series

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Purpose: Concomitant cyclosporine interacts with mycophenolic acid (MPA). This leads to a reduced MPA exposure in cyclosporine- versus tacrolimus-treated patients after renal transplantation. Patients with low MPA exposure are at risk for rejections. With conventional dosing, MPA area-under-the-curve (AUC) is adequate only after 3 months posttransplant. We report our clinical experience with initial high-dose MPA (myfortic) treatment to optimize early MPA-AUC.
Methods and Materials: We treated 10 consecutive standard-risk kidney-transplant recipients as follows:
– MPA (myfortic) [mg]: day 0–14: 1440 b.i.d., day 15–28: 1080 b.i.d., from day 29: 720 b.i.d.
– Cyclosporine A according trough level [µg/l]: week 0–5: 200–250, week 6–12: 180–220, week 13–52: 150–200
– Prednisone: initially 1 mg/kg/day, then tapered to 10 mg qd at 6 months.
Results: Nine patients experienced primary transplant function, one had delayed graft function. Three patients had steroid-sensitive rejections (all BANFF IIA). At 1 year all patients remained on MPA and had a functioning graft (12-month creatinine 134 ± 53 µmol/l). Seven patients developed CMV reactivation during the first 3 months. Transient BK-viremia occurred in 2 patients three months after transplantation. Gastrointestinal disturbances were rare: one patient developed microsporidia-associated diarrhea, starting 4 weeks after transplantation. Diarrhea improved after MPA dose reduction. In all other patients, MPA could be fully dosed over the entire study period without side effects.
Conclusion: The early administration of high-dose MPA in clinical routine is feasible, safe and effective. Gastrointestinal side effects are not more frequent than with standard MPA dosing. Close monitoring for viral reactivations (CMV, BK) is recommended.

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Calcineurin-inhibitor induced pain syndrome after kidney transplantation – a rare, but disabling condition

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Purpose: End stage renal disease (ESRD) is an increasing health burden, leading to severe morbidity and mortality. Kidney transplantation represents the preferred treatment for ESRD. Nevertheless, the use of the essential immunosuppressive agents may be associated with various side effects. Musculoskeletal pain after kidney transplantation most often is a manifestation of high dose steroid therapy, steroid withdrawal, renal osteodystrophy or osteoporosis. Apart from these common pain causes, in 1989 the intake of cyclosporine has been identified for the first time as a novel reason for severe skeletal pain. It has been reported that cyclosporine may induce bone marrow oedema leading to severe and disabling bone pain mainly located in the lower limbs. Due to its relation to high CNI serum levels, the syndrome was named calcineurin-inhibitor induced pain syndrome (CIPS) by Grotz and colleagues in 2001.
Methods and Materials: Here we report a patient who suffered from progressive disabling bilateral pain in his feet and knees due to CIPS evolving two months after kidney transplantation. Interestingly, shortly after the first patient had been diagnosed of suffering from CIPS, another patient presented with almost exactly the same symptoms and radiologic findings.
Results: n/a
Conclusion: Musculoskeletal pain is a common symptom after solid organ transplantation. In the case of disabling pain preferentially located in the lower extremities in a patient with a CNI-containing immunosuppressive regimen, one should consider the differential diagnosis of CIPS. Reduction or replacement of CNI therapy and administration of calcium channel blockers help to ameliorate symptoms and improve live quality.

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Single center evaluation of efficacy and safety of methoxy polyethylenglycol-epoetin beta in renal allograft recipients

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Zürich

Purpose: Methoxy polyethylenglycol-epoetin beta (Mircera®) is a continuous erythropoietin receptor activator (CERA) with a long half-life, allowing extended dosing intervals in patients with renal anemia. We reviewed our experience in renal transplant patients (RTP) under CERA given every 4 weeks.
Methods and Materials: We studied 7 stable RTP with a mean time after transplantation of 109 ± 109 months (median 84 months), a mean GFR of 28 ± 6 ml/min (median 30 ml/min) and a baseline Hb level of 10.2 ± 0.5g/dL. At the time of conversion to CERA, 3 patients were erythropoesis-stimulating agent (ESA) naïve and 4 patients were on darbepoetin alfa (30-50 µg weekly) for at least the previous 3 months. All patients received CERA at the calculated monthly dose from the beginning.
Results: After conversion to CERA the Hb level changed from 10.2 ± 0.5 g/dL to 10.8 ± 1.9 g/dL after 3 months, to 11.6 ± 0.9 g/dL after 6 months and to 11.2 ± 1.4 g/dL after 12 months in all patients. The mean required CERA dose during follow-up ranged btw. 72 and 92 µg per month (median doses were btw. 75 and 100 µg). An overcorrection of the Hb level (>12.5 g/dL) was seen in 2 patients. A drop of the Hb level (<10.5 g/dL) was seen in 4 patients. Reasons were infectious complications without dose adaptation of CERA, missed outpatient visits, and in one case inadequate dose adaptation. Overall there were no specific adverse events during the 12 months treatment period assigned to the CERA treatment.
Conclusion: Treatment with CERA administered every 4 weeks was effective in RTP with impaired renal function and seems to be a viable option in this complex patient population.

Poster Presentations – Dialysis

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Development of an erythropoietin prescription simulator to improve the abilities to prescribe erythropoietin stimulating agents: is it feasible?

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Purpose: The increasing use of erythropoietins with long half-lives and the tendency to lengthen the administration interval to monthly injections call for raising awareness on the pharmacokinetic and risks. The pharmacodynamic complexity and individual variability limit the possibility of attaining comprehensive clinical experience. In order to help physicians acquiring prescription abilities, we built a prescription computer model, to be used as simulator and education tool.
Methods and Materials: The model, developed using Visual Basic on Excel, was tested with 3 different ESA half-lives (HF: 24, 48, 138 h) and 2 administration intervals (AI: weekly, monthly). 2 groups of 25 nephrologists were exposed to 6 randomised combinations of HF and AI. They were asked to achieve and maintain the Hb target of 11–12 g/dL.
Results: The simulation using an ESA with a HF of 138 h administered monthly showed an overshooting tendency (percentage of Hb >13 g/dL: 15.8 ± 18.3 vs. 6.9 ± 12.2; P <0.01), quicly corrected with experience. The prescription ability appeared to be optimal with a 24 h HF and a weekly AI (ability score 1.52 ± 0.70 vs. 1.24 ± 0.37; P <0.05). The monthly AI was accompanied by less therapeutic adjustments (4.9 ± 2.2 vs. 8.2 ± 4.9; P <0.001); a direct correlation between Hb variability and number of therapy modifications was found (P <0.01). The “delta Hb” was a better indicator of Hb variability than the SD.
Conclusion: Computer-based simulation can be a useful tool for improving the ESAs prescription abilities among nephrologists by raising awareness about the pharmacokinetic characteristics of the various ESAs and recognizing the factors that influence haemoglobin variability.

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Stimulated sweating as a therapy to improve water and sodium balance in chronic hemodialysis patients: preliminary results

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Purpose: Controlling the extracellular volume and body sodium content in haemodialysis patients is a difficult task. The aim of this study is to evaluate the influence of stimulated sweating on the interdialytic weight gain (IWG), blood pressure regulation and potassium/urea balance.
Methods and Materials: Cross over design. One month without hot water baths, followed by one month during which the patient takes four hot water baths a week of 30 minutes each, on non-dialysis days at home. Patients are instructed to keep water at a constant temperature between 38 and 43°C, according to tolerance. Haemodynamic parameters are recorded, and weekly laboratory analysis (Na, K, urea, creatinine, Phosphate, Calcium, Hct) performed. Exclusion criteria are a cardiovascular event in the previous year, a tunnelled vascular catheter and residual diuresis ≥500 ml/day.
Results: So far, three patients-all men, mean age 62 years-have been included. Changes in monthly mean interdialytic weight gain and blood pressure are shown in the table. Overall, mean IWG decreased from 2.4 ± 1.1 to 2.0 ± .3 kg (p = 0.1). Mean weight loss due to sweating during a hot water bath was 460 ± 7 g. No differences were found in electrolytes or blood pressure, no side effects were reported.

	Patient 1		Patient 2		Patient 3	
Hot water bath	*No*	*Yes*	*No*	*Yes*	*No*	*Yes*
Dry weight (kg)	88.0	88.0	86.0	86.0	63.5	63.5
Mean SBP (mm Hg)	163 ± 12	167 ± 13	147 ± 8	144 ± 13	141 ± 11	142 ± 10
Mean DBP (mm Hg)	93 ± 7	87 ± 5	77 ± 9	68 ± 6	82 ± 6	83 ± 6
Mean interdialytic weigth gain (kg)	1.5 ± 0.5	0.4 ± 0.3	3.6 ± 0.9	3.3 ± 0.8	2.4 ± 0.8	1.8 ± 0.7

Conclusion: Stimulated sweating appears to be a safe, promising way to improve water and sodium balance in selected haemodialysis patients, but more data are necessary before definite conclusion can be drawn.

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Podoplanin positive cells are a hallmark of encapsulating peritoneal sclerosis

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Purpose: Encapsulating peritoneal sclerosis (EPS) and simple peritoneal sclerosis are important complications of long-term peritoneal dialysis (PD). Podoplanin is a glycoprotein expressed by mesothelial cells and lymphatic vessels, which might be involved in inflammatory reactions in the peritoneal cavity.
Methods and Materials: We studied 69 peritoneal biopsies including patients on PD (n = 16), patients with EPS (n = 18), and control biopsies taken at the time of hernia repair (n = 15) or appendectomy (n = 20). Immunohistochemistry was performed to localize podoplanin. Additionally, markers of endothelial cells, mesothelial cells, myofibroblasts (smooth muscle actin), proliferating cells, and double labelling for smooth muscle actin/podoplanin was performed on selected biopsies.
Results: Podoplanin was present on the endothelium of lymphatic vessels in the submesothelial fibrous tissue and on mesothelial cells. In patients on PD and in biopsies with appendicitis the mesothelial cells demonstrated a cuboidal appearance and circumferential podoplanin staining, with gaps between the cells. The number of lymphatic vessels was variable, but prominent at sites of fibrosis. In patients with EPS a diffuse infiltration of podoplanin positive cells with a fibroblastic appearance was present in 15 out of 18 biopsies. This pattern was focally present in 3 out of 16 on PD, and in none of the 35 controls. The podoplanin positive cells did not express the endothelial marker or the mesothelial marker (calretinin).
Conclusion: EPS is characterized by a population of podoplanin and smooth muscle actin double positive cells. Podoplanin might be a suitable morphological marker supporting the diagnosis and might be involved in the pathogenesis of EPS.

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An unexpected complication of buttonhole-cannulation – two cases of veno-cutaneous fistulae with severe repetitive bleeding episodes

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Purpose: Buttonhole (BH)-cannulation offers the advantage of an easy, quick and almost painless procedure with fewer "bad puncture-events" for the patient. It is reported to be safe and "fistula-preserving". We report two cases with potentially fatal bleeding complications requiring semi-urgent surgical intervention. Because of our "native-fistula-policy", fistula-cannulation is sometimes challenging. Consequently the BH-technique was started in 2009 as a nurse project with the intention to reduce unsuccessful needling episodes.
Methods and Materials: The protocol consisted of a break-in period (6–10 sessions) for the creation of the tunnel track with all cannulations carried out by the same nurse. In the following routine period the whole staff had to be involved. All punctures were performed with the routinely used standard sharp needles.
Results: 8 of 80 prevalent HD patients were selected for BH-cannulation. Almost all of them reported a marked pain reduction and the rate of missed cannulations clearly dropped. After 14 weeks respectively 1 year, in two patients repetitive bleeding episodes occurred directly after or between dialysis sessions and even during the night. In both cases surgical revision showed a large veno-cutaneous fistula (4–6 mm diameter) without any sign of infection, confirmed by histological examination.
Conclusion: Continued use of sharp needles in BH-cannulation may favour the formation of a large veno-cutaneous fistula with bleeding tendency. To our knowledge this potentially fatal complication has not been described so far. In agreement with the literature, we recommend the switch from sharp to blunt needles as soon as the needle-track is established.

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Can a score predict outcome in over 75 years old patients starting dialysis?

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Purpose: Couchoud [1] published a prognostic score including 9 independent risk factors which correlated with outcome in elderly patients >45 days on dialysis. The aim of this study was to apply this score to our patients and extend the use to those with dialysis duration <45 days.
Methods and Materials: Since 01.01.2005 all patients treated with haemodialysis at our centre are prospectively recorded in a database. 41 patients >75 years old at start of dialysis were identified with a subgroup of 20 patients on dialysis for >45 days. The Couchoud score was calculated retrospectively for each patient at start of dialysis and correlated with the individual outcome at 6 months. Score values are given in mean ± SD.
Results: In the whole group analysis the score was 1.4 ± 1.8 for patients still on dialysis at 6 months versus 3.3 ± 1.9 for those who died (p = 0.053), 3.9 ± 1.3 for those who recovered kidney function and 4.0 ± 2.8 for those withdrawn from dialysis. In the subgroup analysis ony one patient, whose score was zero, died, one patient withdrew from dialysis (score 9) and none recovered.
Conclusion: In the overall collective of >75 years old patients those who died within 6 months showed a higher score than those staying on dialysis. However patients recovering kidney function showed similiar high values, thus the score still does not predict individual outcome accurately. Either this prognostic score is insufficient or a selection bias took place before starting dialysis.
1 Couchoud C, et al. NDT 2009; 24:1553.

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Epoetin does not demonstrate anti-inflammatory properties after cardiac surgery

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Purpose: Erythropoietin has been thought to have nephroprotective as well as antiinflammatory properties. We have previously demonstrated that a-epoetin (EPO) does not modify renal function after cardiac surgery. In the same patients, we measured cytokines blood levels and compared the levels between the groups.
Methods and Materials: From June 08 to June 09, 80 patients having cardiac surgery were randomised to receive either 40 000 IU a-Epoetin (n = 20) or 20 000 IU a-Epoetin (n = 20) or saline injection after cardio-pulmonary bypass (CBP). To assess acute inflammatory response serum cytokines (Il6, Il8, Il1beta, Il10, TNFalpha, Il12p70) were measured using a luminex technique before Epoetin infusion and at day 4.

Results: Patient groups did not differ in terms of age, gender, comorbidities and baseline renal function. IL6, IL8, Il1beta, Il10, TNFalpha, Il12p70 were measured at day 0 and similar between groups. IL 6 and IL8 decreased at day 4 and this decrease was observed in all groups. The group treated with EPO 20 000 units, the decrease of IL6 was significantly less than in the control (77 ± 12 vs 135 ± 34 pmol/ml, p <0.05). IL8 also appeared to decrease less with EPO treatment but this trend did not reach statistical significance.
Conclusion: A single administration of either 20 000 or 40 000 IU a-Epoetin after cardiac surgery does not alleviate the inflammation observed in the post operative state rather appeared to impede the spontaneous decrease in proinflammatory cytokine, mostly IL6. These results, associated with the negative results on renal function do not support the use of EPO in acutely ill patients for nephroprotection.

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Protein-energy deficiency in hospitalized patients requiring haemodialysis

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Purpose: Patients on haemodialysis (HD) are at high risk of undernutrition. Among inpatients, dialysis- and acute disease-induced anorexia and hypercatabolism further increase nutritional risk. The aim was to assess prevalence and degree of protein-energy deficiency among inpatients requiring HD.
Methods and Materials: A cross-sectional study was performed in the acute dialysis unit of our University Hospital. All inpatients requiring HD were included independently from aetiology or chronicity of renal failure, excepted ICU patients. Patients' weight was obtained after HD session. Dietary intakes were visually quantified by dieticians based in consumed servings during the dialysis day and compared to protein and energy needs as defined by ESPEN guidelines. Undernutrition was defined as weight loss ≥5% of usual body weight in the last 3 months. Nutritional risk was assessed with the Nutritional Risk Screening (NRS-2002).
Results: Twenty-two patients (64% men, mean age 61.5 ± 18) were included. On HD day, 91% patients had protein-energy deficiencies. Energy intake reached 51.8±31.4% and protein intake 44.6 ± 27.3% of requirements including oral intakes for every patients, oral nutritional supplements (n = 7) and tube-feeding (n = 1). Undernutrition occurred in 64% of the patients with mean weight loss of 4.7 ± 4 kg (max. 11 kg). Sensibility and specificity for NRS-2002 to detect patients with protein-energy deficiency was respectively 60% and 50%.
Conclusion: Inpatients' protein-energy deficiency on HD day is frequent and significant. It seems to be a tendency to get worse after each HD day and can be partially compensated by nutritional treatment. In these patients, NRS-2002 cannot be considered as a screening tool.

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Effect of intradialytic resistance band exercise on physical function in patients on maintenance haemodialysis: a pilot study

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Purpose: Though physical activity is recommended in maintenance haemodialysis (MHD) patients, randomized controlled trials testing the effects of exercise in this population have given conflicting results. Aerobic exercises mostly failed to produce improvements in physical function while resistance exercise, although less studied, appeared to be more promising. The use of sophisticated materials such as leg press and free weights may preclude widespread application of resistance training in MHD patients. Simple and cheap elastic bands may thus be an attractive alternative. We tested the feasibility of a supervised intradialytic resistance band exercise training program, and its effects on physical function, in MHD patients.
Methods and Materials: 11 unselected adult MHD patients from our center, aged 70 ± 10.7 (mean ± SD) years, including 8 men and 3 women, accepted to follow the program under the supervision of qualified physiotherapists. 36 exercise sessions of moderate intensity (twice a week, mean duration 40 min each, during 4.5 to 6 months), mainly involving leg muscles against an elastic resistance, were performed.
Results: The exercise program was well tolerated and all patients completed it. Statistically significant improvements were observed in the Tinetti Test: 23.9 ± 3.9 points before vs 25.7 ± 3.5 points after the program (p = 0.022) and the Timed Up and Go (TUG) test: 12.1 ± 6.6 vs 10 ± 5.8 seconds (p = 0.0156). Improvements in the 6-minute walk distance (6-MWT) and in the one-leg balance (OLB) tests just failed to reach statistical significance.
Conclusion: In this single center pilot study an intradialytic resistance band exercise program was feasible, well tolerated and showed encouraging results on physical function.

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A self-administered food frequency questionnaire for a rapid quantification of calcium intake

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Purpose: Excessive calcium intakes is associated with increased cardiovascular mortality in dialysis patients. It is usually assessed through dietician interviews. A simplified self-administered food frequency questionnaire (FFQ) has been validated in the general population for calcium intake. We examine validity of this FFQ in patients on hemodialysis.
Methods and Materials: The validity was assessed comparing the results of the FFQ to those of the 3-day food diary (DR). Test-retest reliability was assessed by having subjects complete the questionnaire at recruitment and 1 month later. Both evaluations included the FFQ and the DR, with permutation one month later. We planned to include 40 hemodialysed patients. Daily calcium intake quantified by the two methods was compared by a paired Student t-test, and linear regression. Agreement between the two methods was evaluated according to Bland-Altman. We compared the difference in variance for paired data with Pitman's permutation test.
Results: We report the results of 24 patients. The mean calcium intake assessed by DR was 742 ± 339 mg daily (mean ± SD) and was not statistically different of the one evaluated with the FFQ (p = 0.26). The daily calcium intake from the questionnaire was correlated with the calcium intake from the DR by linear regression analysis (p <0.0001). Bland and Altman graphs did not show any difference in variability between the DR method and the FFQ (p = 0.567). Intra-class correlation coefficient of reliability (ICC) for 20 patients was 0.66 (95% confidence interval: 0.04–0.87).
Conclusion: Based on these preliminary results, this FFQ could be a reliable tool for the evaluation of dietary calcium intake in hemodialysis patients.

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Prognostic usefulness of nutritional assessment in maintenance hemodialysis (HD) patients

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Purpose: Impairment of nutritional status is frequent in HD patients and is associated with worse prognosis both for mortality and intercurrent illness. However, nutritional assessment is cumbersome and its predictive value has not systematically been tested in a Swiss HD population.
Methods and Materials: Clinical, anthropometrical and biochemical factors associated with nutritional status were analyzed in several multivariate regression models to predict death, hospitalization and quality of live (QoL) in a Swiss maintenance HD population derived from the *monitor!* cohort. A total of 157 patients were studied with a mean follow-up of 828 days.
Results: The observed yearly mortality rate was 16% and the average length of hospital stay (LOS) 7.5 days per patient year. Survivors and non-survivors differed significantly with regard to body mass index (BMI), midarm muscular circumference (MAMC), nPCR and serum cupper concentration. In combination with serum albumin, vitamin D, C-reactive protein and patient age predictive models for mortality and LOS could be developed with some accuracy using both continuous and dichotomous variables. Similarly, QoL could be predicted for its physical but not mental composite.
Conclusion: Variables associated with nutritional status can be helpful to quantitatively predict mortality, hospitalization and QoL in a Swiss maintenance HD population. Nevertheless, the predictive accuracy is limited. This is explained by the complex pathophysiological interrelations of malnutrition and disease states. Moreover, the usefulness of nutritional assessment may be limited in a population with fairly satisfactory and stable nutritional status such as the one examined in this study.

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Spontaneous retroperitoneal hematoma during the treatment of peritonitis in a patient on peritoneal dialysis

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Purpose: Peritonitis is a common complication of peritoneal dialysis (PD). Initial treatment commonly includes the combination of cephalosporins.
Methods and Materials: not applicable
Results: A 46 years old caucasian man presented with sudden unilateral flank pain. Symptoms started on the 14th day of antibiotic therapy with cefazolin for a PD peritonitis. The treatment consisted of the combination of ceftazidime and cefazolin during the first 4 days and was switched to cefazolin monotherapy after the microbial evaluation demonstrated coagulase-negative staphylococci. The

abdominal computertomography showed a hyperdense mass next to the right kidney consistent with a retroperitoneal hemorrhage. Both kidneys contained multiple complicated cysts. At the time of presentation his international normalized ratio (INR) was 4.4. Previous analyses were within normal ranges and the patient did not take anticoagulant drugs. After administration of 10 mg vitamin K the INR normalized. The pain resolved with conservative therapy. The MRI of the kidney cysts showed a strong suspicion for bilateral renal tumors.
Conclusion: Cephalosporines are known to be able to cause hypoprothrombinemia most likely as a result of an N-methyl-thiotetrazole (MTT) side chain, which interferes with the Vitamin K metabolism. Both of the administred drugs have no MTT side chain which suggests a different mechanism. Cefazolin is more likely to be the cause for the bleeding diasthesis. This is the first documented case of a intraabdominal administred cefazolin induced hypoprothrombinemia. This is a rare, but serious complication of peritonitis treatment.

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Assisted peritoneal dialysis (PD) in a handicapped nursery home patient with a "Witzel fistula"

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Purpose: Renal replacement therapy by PD has theoretical benefits over hospital based hemodialysis (HD) in handicapped patients. However, implementation of PD is limited in these patients due to their inability to perform renal replacement therapy independently.
Methods and Materials: We report on a 47y/o male living in a nursery home with history of congenital cerebral palsy, residual chronic spastic tetraparesis and dysphagia after cerebral bleeding. HD treatment due to ESRD from hypertensive nephropathy was performed for 2 years previously. Adequate enteral nutrition depends on percutaneous endoscopic gastrostomy (PEG). Transfers between nursery home and hospital posed a great burden on both the patient and the involved health care team. Therefore, it was decided to switch treatment to assisted PD.
Results: A Tenckhoff catheter was inserted after surgical installation of a gastrostomy for percutaneous gastric tube placement ("Witzel fistula"). PD is performed successfully by trained nursery home staff. Both PD and enteral nutrition can be administered transperitoneally without evidence of intercompartmental leakage of either dialysate fluids or nutrients, respectively. Dialysis efficacy is excellent both for volume control and solute transport. No episodes of peritonitis have occurred so far over a treatment period of 5 months. The patients qualitiy of life has improved considerably under these measures.
Conclusion: This case report illustrates that assisted PD can be a feasible and attractive alternative to hospital based hemodialysis treatment even under challenging medical conditions. Surgical placement of a Witzel fistula is a safe technique to ensure both peritoneal dialysis and nutrition.

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Erythropoiesis, erythrocyte survival and hemoglobin cycling in hemodialysis patients treated with monthly Darbepoietin alfa or C.E.R.A.

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Purpose: Hemoglobin cycling in hemodialysis patients treated with rHuEPO is a well described phenomenon. However, we still lack knowledge about the etiologic factors. Purpose: to analyse the correlations between hemoglobin variability, the dynamics of the reticulocyte population and the red blood cell life span, comparing two rHuEPO, Darbepoietin alfa and CERA.
Methods and Materials: This study was conceived as an open label, 3-period cross-over study. 30 hemodialysed patients receiving rHuEPO were randomly assigned to monthly Darbepoietin alfa or CERA. Patients were monitored weekly with hemoglobin values (Hb), reticulocyte counts (RET) and measurements of exhaled CO as parameter to estimate the RBC lifespan
Results: Results of the first study period (24 weeks) before cross-over are available. The mean Hb level for patients receiving Darbepoietin alfa was 11.40 ± 0.97 g/dl, compared to 11.06 ± 1.16 g/dl for patients receiving CERA; P = 0.4. The "monthly delta Hb" emerged as the parameter that best translates intra-patient Hb variability. Hb cycling depended on the variability in reticulocytes, assessed as "monthly delta RET count" (P = 0.0039). There were no differences between reticulocyte count in the 4 weeks following rHuEPO administration when comparing the 2 groups.
Conclusion: These preliminary findings results in new insights into RBC kinetics under rHuEPO stimulation. First, the difference between Hb values performed at monthly intervals emerged as the best indicator of Hb variability. The reticulocytary dynamic was identified as an etiologic factor of Hb cycling. Surprisingly, we didn't identify significant pharmacodynamic differences between the two rHuEPOs based on reticulocytary behavior.

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Clinical and biochemical factors associated with hemoglobin levels below target range: First interim analysis of the Swiss MOTION survey at 6 months

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Purpose: Anemia treatment recommendations advise a hemoglobin (Hb) range of between 100–120 g/L. Maintaining patients' Hb within target is challenging due to events that influence Hb levels. The objective of this survey is to describe factors associated with Hb levels below 100 g/L and anemia management in patients experiencing such episodes.
Methods and Materials: Non-interventional, practice-based survey in patients on dialysis documenting potential factors associated with Hb drops below 100 g/L, corresponding Hb levels and darbepoetin alfa (DA) dosing regimens.
Results: 49 (16.5%) patients had Hb values below 100 g/L with at least one Hb drop of ≥10 g/L in relation to the preceding Hb value. The two leading factors associated with Hb levels below target were classified as disease related (39.3%) and bleeding episodes (15.9%). Hb levels and dosing regimens are shown below:

	Total Population (n = 298)	Patients without Hb drop below 100 g/L (n = 214)	Patients with Hb drop(s) below 100 g/L and ≥10 g/L (n = 49)
Dosing regimens, %			
Baseline			
QW	41.6	40.2	44.9
Q2W&QM	58.4	59.8	55.1
6 month			
QW	35.2	31.8	44.9
Q2W&QM	57.8	61.2	44.9
Off-therapy	7	7	10.2
Hb level, g/L Mean (SD)			
Baseline	116.3 (13.9)	120.1 (11.2)	113.5 (14.3)
6 month	115.1 (12.8)	117.2 (10.4)	105.9 (15.8)
Weekly DA dose, µg Mean (SD)			
Baseline	43.4 (39.5)	39.3 (38.0)	48.1 (42.1)
6 month	42.5 (43.1)	36.4 (38.3)	56.2 (56.5)

Conclusion: Events leading to Hb drops occur frequently in routine clinical practice and require adjustments of ESA therapy. The distribution tended towards shorter dosing intervals in the patients who experienced events affecting Hb level.

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A single center audit comparing the switch from darbepoetin alfa to an epoetin alfa biosimilar and backwards in hemodialysis patients

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Purpose: In order to investigate the effectiveness and cost saving potential of biosimilars in a private dialysis center, we switched patients on darbepoetin alfa to a biosimilar epoetin.
Methods and Materials: In 2010 we converted our hemodialysis patients (n = 22) to biosimilar therapy. Before and afterwards patients received DA therapy. In the first DA phase they were recorded for three months on DA. Then they were switched to biosimilars (conversion: 200 IU biosimilar = 1 µg DA). After 3 months on biosimilars all patients were reconverted to DA and recorded for another 3 months. Reasons for switching back to DA were: adverse events with biosimilar, corresponding expenditure, low effectiveness.
Results: Mean (SD) age was 68.9 (14.0) years, mean weight 86.1 (16.1) kg. Hb target level achievement (≥110 g/L) was 100% during first DA phase, then decreased during biosimilar phase to 50% and increased to 100% during second DA phase. During DA administration phases patients were on extended dosing interval, during biosimilar phase on weekly/3-weekly administration. Median weekly dose remained stable after a 9% dose increase from DA to biosimilars. On biosimilar 5 patients had serious adverse events: dyspnoea (2), aggression (2), fatigue (1), inactivity (1), lack of concentration (1) feeling of oppression in the throat (1) and in the chest (1). After stopping biosimilars all symptoms disappeared.

Conclusion: Our audit demonstrated for biosimilar administration a trend towards lower Hb levels and target achievement compared to DA and an increase in adverse events and subsequent additional visits.

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Folic acid supplements and CRP levels in dialysis patients with metabolic syndrome

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Purpose: The prevalence of metabolic syndrome in dialysis patients is high. Circulating C-reactive protein is associated with metabolic syndrome and might be causally linked to it. Recently, folic acid supplements have been reported to lower plasma total homocysteine (tHcy) levels and according to some studies, they are proposed as a treatment for metabolic syndrome. The aim of the study was to investigate the effect of folic acid treatment on CRP levels.
Methods and Materials: We studied for 6 months, 28 dialysis patients with metabolic syndrome according to NCEP ATP III (19 male, 9 female). They were divided into two groups according to if they received folic acid supplements (5 mg/day) or not. Results were analyzed using Student's paired t-tests.
Results: Group A comprised of 15 patients (9 male, 6 female) who did not receive folic acid. Mean age was 67.67 ± 9.6 years and duration of dialysis 33.07 ± 15.48 months. Mean CRP value in this group was 3.56 ± 2.36 mg/dl. Group B included 13 patients (10 male, 3 female), who were treated with folic acid (5 mg/day) for at least one year. Mean age was 62.15 ± 18.92 years and duration of dialysis 38.46 ± 43.48 months. Mean CRP value was 1.6 ± 1.39 mg/dl. According to statistical analysis the difference was quite significant.
Conclusion: Our data suggest that dialysis patients with metabolic syndrome receiving folic acid supplements, have lower CRP levels. However further studies with larger sample size are needed to confirm this and to investigate the pathogenetic mechanism.

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Positive impact on hypertension during haemodialysis with a 37 °C temperature dialysate

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Purpose: Cool dialysate temperature improves tolerance for dialysis in hypotensive patients and helps increase ultrafiltration while maintaining haemodynamic stability during dialysis. In an other hand, the utilization of a warm 37 °C dialysate temperature to decreased blood pressure has not been completely studied.
Methods and Materials: We decided to analyze the variation of the blood pressure during 6 sessions of dialysis: three times with a 36 °C dialysate temperature, three times with a 37 °C dialysate temperature in a single case control patient, a 73 years old diabetic type 2 woman with a long history of resistant hypertension. Medical past: metabolic syndrome, diabetic type 2, hypertension, ischemic nephropathy. Antihypertensive drugs: furosemide, inhibitor of the renin-angiotensin system, amlodipine, metoprolol. The compliance and the physical status were unchanged during the 6 evaluations. The volume of ultrafiltration/dialysis was the same for all the sessions (1.2–1.3 l).
Results: The figure represents the average of the 6 evaluations. We observed a better control of hypertension during the dialysis and especially at the end of the session with a 37 °C warm dialysate (∗ p <0.05).

	0 mn	30 mn	1h	1h30	2h	2h30	3h	3h30	4h
Cold syst BP mm Hg	195	180	175	160	163	158	171	175	178
Warm syst BP mm Hg	198	182	177	170	167	162	165	160	157
Cold diat BP mm Hg	109	101	100	98	99	83	87	89	103
Warm diast BP mm Hg	107	103	99	96	100	85	82	79	75

Conclusion: A dialysis solution at 37 °C could be an interesting vasodilatator stimulus and could be an additive antihypertensive option.

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Peritonitis after minor interventions in patients on peritoneal dialysis

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Purpose: Peritonitis is a major cause of morbidity and hospitalization among PD patients. Common infectious organisms isolated are Staphylococcus epidermidis, Staphylococcus aureus and Pseudomonas species.
Methods and Materials: We describe two episodes of peritonitis with atypical organisms, i.e. Streptococcus mitis and Moraxella sp.
Results: A 75-year old female caucasian presented with typical symptoms of chills, fever and diffuse abdominal pain. She was on PD for 37 months and had no previous episodes of peritonitis. Streptococcus mitis was isolated from the dialysate. She was initially treated with cefazolin and ceftazidim, later with cefazolin alone for 14 days. Complete recovery was achieved. A workup including echocardiography revealed no specific source. She had received an intravitreal injection with Bevacizumab to treat an age-related *macular degeneration* 2 days before the start of the peritonitis, which may be a potential source. A 56 year old female patient was admitted to the hospital with abdominal pain and chills. She was on PD for 15 months and had one previous episodes of peritonitis. A Moraxella sp. Was isolated from the peritoneal fluid and the blood culture. The patient reported a dental extraction one day before. She was treated with ceftazidim and ciprofloxacin for two weeks and acchieved complete recovery
Conclusion: We conclude that peritonitis may occur in PD patients after minor interventions. The relationship with the intervention is sometimes difficult to establish, and the value of antibiotic prophylaxis is poorly evaluated. The peritonitis workup should include a detailed history of recent medical or dental interventions.

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Hemoglobin and ESA dose in hemodialysis patients after conversion to C.E.R.A. A multicenter observational study

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Purpose: C.E.R.A. allows to treat patients on hemodialysis in a monthly interval. In the EIRA survey we analyzed data of dialysis patients treated with erythropoesis stimulating agents (ESA) over a period of 12 months.
Methods and Materials: Multicentre, prospective survey performed in 25 Swiss dialysis centers. Hemoglobin values,ESA dose, iron parameters, and CRP were collected at Baseline, month 6 and 12.
Results: Over 6 months 208 patients were included. Mean hemoglobin value was stable throughout the observation period (11.8 ± 1.22 at BL vs. 11.9 ± 1.09 month 12; p = 0.95). Before conversion mean doses of epoetin alfa/beta were 39663 ± 6442 IU/month and darbepoetin 239 ± 42 µg/month. The mean C.E.R.A. dose decreased from 169 ± 92 µg/month at BL to 137 ± 95 µg/month at month 12. Cost of treatment declined from CHF 775 to CHF 569. In 107 patients complete data on iron status was available. Ferritin 404 ± 300 µg/l vs. 411 ± 262 µg/l, p = 0.97) and Transferrinsaturation (25.4 ± 11.7% vs. 27.7 ± 12.7%, p = 0.25) were not different between BL and month 12. 42 patients (39%) at BL and 45 patients (42%) at month 12 did not fulfill one of the goals of ferritin >200 µg/l or transferrin saturation >20%.
Conclusion: Patients switched to C.E.R.A. from other ESA maintained stable hemoglobin values in 12 months after conversion. After the switch cost of ESA treatment decreased significantly in this Swiss dialysis population. Analysis of iron parameters revealed room for improvement in iron replacement therapy that might further decrease cost of treatment.

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Course of hemoglobin and iron metabolism under treatment with C.E.R.A. A single center experience

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Purpose: Erythropoiesis stimulating agents (ESA) and Iron are the basis of anemia management in patients on hemodialysis. We present 12 month data from 33 patients at a single center treated with Mircera.
Methods and Materials: Excerpt from a multicentre, prospective survey performed at 22 centers. Hemoglobin, iron parameters, ESA dose and CRP were collected at baseline (BL), month 6 and 12.
Results: Average ESA before BL was 128 µg/month and remained stable until month 12 (129 µg/month). Hemoglobin was 11.6 (± 2.12) g/dl at BL and 11.3 (±1.39) g/dl at month 12. Ferritin (392 ± 247 µg/l vs. 573 ± 334 µg/l; p = 0.02) and TSAT (20.2 ± 15.4% vs. 27.2 ± 15.1 %; p = 0.03) were significantly higher at month 12 vs. BL. At BL 10 patients had Fer values below 200 µg/l. For TSAT 18, 4 and 9 values below 20% could be found at BL, month 6 and 12. 61%, 75% and 78% of the low TSAT values were associated with CRP above normal range.
Conclusion: We show that the 33 patients remaind stable for dose and hemoglobin values over a period of 12 month. While 30% of patients showed Fer values below 200 mg/l at BL this was corrected in all patients within the first 6 months of the survey. TSAT values of below 20% were found in 55% of the patients at BL. While 50% of these patients returned to values >20% over 12 month, the rest remained below. In the majority of these patients the decreased values for TSAT were associated with elevated CRP values, suggesting functional iron deficiency associated with inflammation.

The numbers refer to the pages of this supplement.