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Phone +41 61 467 85 55
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Pioglitazone Improves Insulin Sensitivity, Reduces Visceral Fat and Stimulates Lipolysis in Non Diabetic Dialyzed Patients

A. Zanchi[1], L. Tappy[1], N. Theumann[1], G. Halabi[1], C. Mathieu[1], T. Gauthier[2], S. Tremblay[1], P. Coti[1], M. Burnier[1], D. Teta[1]
[1]Lausanne, [2]Vevey

Purpose: Dialyzed patients have insulin resistance, increased visceral adipose tissue (VAT), reduced lean mass and increased lipolysis, all associated with poor prognosis. This study investigates the effect of pioglitazone (PIO), a powerful insulin sensitizer, on carbohydrate and lipid metabolism, and body composition, in dialyzed non-diabetic patients.
Methods and Materials: A double blind randomized cross-over study was performed in 8 hemodialysis (age: 59.6 ± 4.4y) and 4 peritoneal dialysis patients (43.5 ± 3.6y). Each treatment phase lasted 16 weeks, starting with either oral PIO 45 mg/d or placebo, then switching to the other phase. At the end of each phase, patients underwent hyperinsulinemic euglycemic clamps, dual energy X-ray absorptiometry, abdominal CT (abdominal fat distribution), anthropometric measurements and plasma biochemical analysis.
Results: Nine of 12 patients completed both phases. Three patients dropped out (renal transplantation/2 HD and peritonitis/1 PD). Under PIO, insulin sensitivity improved at clamp baseline, as assessed by increased total glucose disposal rate (GDR) (1.98 ± 0.24 vs 1.58 ± 0.12 µmol/kg/min, p <0.05), and reduced endogenous hepatic production. PIO further magnified GDR under insulin clamps. PIO did not affect post-HD body weight, fat and lean mass, but significantly reduced abdominal VAT/SAT (subcutaneous adipose tissue) areas. Subscapular skinfold was increased (19.1 ± 1.5 vs 16.0 ± 1.2 mm, p <0.05). Glycerol turnover was paradoxically increased (3.20 ± 0.38 vs 1.99 ± 0.30 µmol/kg/min, p <0.05) by PIO, at clamp baseline, as well as circulating glycerol and non esterified fatty acids. PIO significantly reduced CRP and significantly improved plasma leptin/adiponectin ratio.
Conclusion: PIO has favorable metabolic effects in non-diabetic dialyzed patients, with improvement in insulin sensitivity, body fat redistribution, reduction in inflammation and improvement in adipokine plasma profile. The paradoxical stimulation of systemic lipolysis by PIO may reflect adipose tissue remodeling.

Serum Ionized Calcium Levels Determine Arterial Stiffness in Dialysis with Regional Citrate Anticoagulation

M. B. Moor, A. Kruse, D. E. Uehlinger, U. Eisenberger
Berne

Purpose: Hemodynamic effects of changes in serum ionized calcium (iS_{Ca}) are difficult to determine during conventional hemodialysis (HD) using a fixed dialysate concentration of calcium. The model of regional citrate anticoagulation (RCA) using continuous calcium infusion allows to study the effects of predefined iS_{Ca} changes on arterial stiffness and blood pressure during HD.
Methods and Materials: In a cross-over study, 15 patients with chronic kidney failure underwent two HD sessions with RCA. Each session was divided into 2 study phases in which iS_{Ca} was titrated either to 0.8–1.0 mmol/L or to 1.1–1.4 mmol/L. Sequence of phases was randomly chosen and alternated for the second session. 30 minutes after reaching a stable iS_{Ca} level, pulse wave velocity (Pulse Trace PWV, Micro Medical Ltd, UK), arterial blood pressure and heart rate were measured. Statistical analysis was performed with SAS 9.2 for Windows on an X64_VSPRO platform.
Results: IS_{Ca} levels were modified during sequence 1 (iS_{Ca} low-high) from a predialysis baseline value of 1.15 ± 0.09 mmol/L, first to 0.92 ± 0.05 mmol/L (time point 1; *p <0.001 vs baseline) and then to 1.18 ± 0.05 (time point 2; ns). During sequence 2 (iS_{Ca} high-low), iS_{Ca} levels were modified from 1.15 ± 0.12 mmol/L first to 1.20 ± 0.05 mmol/L (time point 1; ns vs baseline) and then to 0.93 ± 0.03 (time point 2; *p <0.001). Assuming a basic linear repeated measures model, PWV was positively related to iS_{Ca} levels (p <0.03) independent of systolic or diastolic blood pressure, heart rate or ultrafiltration rate.
Conclusion: PWV, an indirect measure of arterial stiffness known to impact on long-term survival in chronic hemodialysis patients, is closely related to serum ionized calcium levels in HD patients using RCA as a study model.

Is Urinary Calcium and Magnesium Excretion Related to Mineralocorticoid-Activating Steroid Hormones in Renal Stone Formers?

M. Mohaupt, C. Gennari, N. Eisele, B. Dick, S. Arampatzis, A. Pasch
Berne

Purpose: Hypercalciuria has been observed in arterial hypertension with high aldosterone levels. If mineralocorticoid receptors are involved, activation via aldosterone or alternatively via increased cortisol (F) availability might be implicated. The latter can be diagnosed by a decreased 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) activity In patients presenting clinically affected by a history of renal stone formation we hypothesized that enhanced distal tubular Na^+ reabsorption via the mineralocorticoid receptor would reduce Na-transport dependent Ca^{++} and Mg^{++} reabsorption such as in the loop of Henle.
Methods and Materials: We measured spontaneous 24-h urinary Ca++ and Mg++ excretion corrected for urinary creatinine and determined urinary steroid hormone metabolites by gas chromatography-mass spectrometry in 141 renal stone formers. The major F metabolites were combined as total cortisol metabolites. Tetrahydro (TH)-aldosterone was measured as the major urinary aldosterone metabolite. Apparent activity of the enzyme 11β-HSD2 was assessed by calculating F/cortisone (E) and (THF+5aTHF)/THE.
Results: Calciuria and magnesiuria correlated with urinary TH-aldosterone excretion (p = 0.03 and 0.005). In contrast to our hypothesis, a reduced apparent 11β-HSD2 enzyme activity was associated with a lower calciuria (F/E: p = 0.0059; and (THF+5aTHF)/THE: p = 0.0213) without effect on magnesiuria.
Conclusion: We conclude that enhanced F availability as indicated by a reduced 11β-HSD2 activity does lower calciuria and does not affect magnesiuria contrasting the effect of aldosterone. Aldosterone was associated with an enhanced excretion of both cations suggesting divergent mechanisms influenced by aldosterone and F, respectively, on the regulation of Ca^{++} and Mg^{++} balance in renal stone formers.

Renal Ultrasound Findings in the Swiss Population

M. Pruijm[1], B. Ponte[2], D. Ackermann[3], S. Rodriguez[1], U. Eisenberger[3], M. Burnier[1], P.-Y. Martin[2], F. Frey[3]
[1]Lausanne, [2]Geneva, [3]Berne

Purpose: Kidney dimensions and the prevalence of simple renal cysts, stones and other abnormalities in the Swiss population are largely unknown. The aim of this study was to assess renal characteristics in a non-selected, asymptomatic sample of the Swiss population using renal ultrasound.
Methods and Materials: The SKIPOGH study (Swiss Kidney Project on Genes in Hypertension) is a multicenter (Bern, Geneva, Lausanne) family-based cross-sectional examination survey exploring the role of genes and kidney hemodynamics in blood pressure regulation and hypertension. Anthropometric parameters and renal ultrasound measurements were assessed in index subjects and at least one first degree relative. In each center, renal Gray-scale ultrasounds were performed by the same physician according to a standardized protocol.
Results: Baseline characteristics of all participants are shown in the table. Kidney volume was higher in men than women, and this difference persisted after correction for body surface area (BSA). The majority of kidney masses were angiomyolipoma's (n = 11); the remaining two turned out to be malignant tumors. Three persons had congenital agenesis of one kidney, one person an accessory kidney. In total, 19.8% presented at least one renal anatomical abnormality (11.3% of participants aged <60 years, versus 35.2% aged ≥60 years).

	Overall (n = 558)	Men (n = 264)	Women (n = 294)
Age (years)	50.8 (18–89)	51.2 (18–89)	50.2 (19–86)
Body Mass Index (kg/m²)	25.4 ± 5.1	26.3 ± 4.2*	24.6 ± 5.6
eGFR (ml/min/1.73 m²	92.3 ± 16.9	93.6 ± 17.3	91.3 ± 16.5
Kidney length (cm)	110.4 ± 8.8	113.9 ± 8.1*	107.3 ± 8.2
Kidney volume (cm³)	138 ± 36	154 ± 35*	123 ± 31
Nephrolithiasis (%)	4.8	5.7	4.1
Simple renal cyst (%)	12.4	17.1*	8.1
Renal mass (%)	2.3	1.9	2.7

Values are shown as mean ± SD, median (min-max), or percentage;*p <0.05 men versus women.

Conclusion: The prevalence of renal anatomical abnormalities was relatively high in the Swiss general population, especially in persons aged ≥60 years. These data suggest that the usefulness of renal ultrasound screening in persons >60 years merits further study.

Assessment of Glomerular Filtration Rate in Children: From the New Revised Schwartz Formula to a New Generalized Formula

H. Chehade, A. Gao, F. Cachat, M. Faouzi, D. Bardy, D. Mosig, E. Girardin
Lausanne

Purpose: Bedside Glomerular Filtration Rate (GFR) is a primordial parameter to evaluate infants' renal function, by using formulas developed for mild and moderate chronic renal failure (CRF). The new revised Schwartz formula (0.413 x height [cm]/Serum creatinine [mg/dl]) for estimating GFR (eGFR) demonstrates good agreement with iothalamate renal clearance in infants' GFR ranging between 15 and 75 ml/mn per 1.73 m^2. Our objective was first, to provide additional data that assess the accuracy of the revised Schwartz formula by using another gold standard method of GFR determination (inulin clearance); and second, to examine the possibility of applying this formula in children with less or no renal impairment.
Methods and Materials: We retrospectively analyzed 551 inulin clearances (mGFR) of patients aged between 2 and 18 years. Serum creatinine was measured using the compensated Jaffe method which is adjusted to the enzymatic measurement of creatinine. The correlation between mGFR and eGFR was assessed using the Lin's concordance correlation coefficient. As a complementary approach, the Bland and Altman's limits of agreement were calculated as well as an F test of equality of means and variance. Moreover, a regression analysis was performed to fit the best relationship between mGFR and eGFR.
Results: We found a good correlation between mGFR and eGFR. The relationship between mGFR and eGFR was linear in children with mGFR between 15 and 75 ml/mn per 1.73 m^2 (concordance correlation coefficient 0.82). However, the relationship was quadratic for patients presenting less renal impairment or normal renal function. When applying this quadratic formula to all patients, we could accurately calculate the eGFR (concordance correlation coefficient 0.81).
Conclusion: The new Schwartz formula is applicable for children with mild to moderate CRF but not for those presenting less renal impairment or normal renal function. Our data yielded a new simple bedside quadratic formula applicable for children in all renal function groups.

Low Klotho Levels in Autosomal Dominant Polycystic Kidney Disease: Potential Mechanism of Resistance to FGF23

I. Pavik[1], P. Jaeger[2], A. Kistler[1], D. Poster[1], K. Rentsch[1], R. Wüthrich[1], C. Schmid[1], A. L. Serra[1]
[1]Zurich, [2]London/UK

Purpose: Fibroblast growth factor 23 (FGF23) levels are elevated in both, patients affected by autosomal dominant polycystic kidney disease (ADPKD) and X-linked hypophosphatemia (XLH). The latter condition is characterized by renal phosphate wasting whereas in ADPKD the close to normal phosphate excretion suggests resistance to FGF23, although the underlying mechanisms are not known. The activation of the FGF receptor by FGF23 requires Klotho which is expressed along the nephron, where also cysts evolve. To elucidate the cause of relative FGF23 resistance in ADPKD, we studied the relationship between FGF23/Klotho and renal phosphate handling.
Methods and Materials: Our study was conducted in in 99 patients with ADPKD, 32 non-cystic chronic kidney disease (CKD) patients, 12 patients with XLH, and 20 healthy volunteers; all with a GFR greater than 60 ml/min per 1.73 m^2.
Results: FGF23 levels were higher in ADPKD than in CKD and XLH patients, whereas the TmP/GFR was similar to that in CKD and even higher than that in XLH. Serum Klotho levels were lowest in ADPKD, whereas CKD and XLH patients and volunteers had similar levels. Within the ADPKD patient group, those with an apparent renal phosphate leak had a two-fold higher Klotho level than those without renal phosphate leak. Serum Klotho values correlated negatively with cyst volume and kidney growth.
Conclusion: We conclude that the loss of Klotho related to cyst growth constrained the FGF23 activity in the majority of ADPKD patients and prevented phosphate wasting whereas normal serum Klotho levels were associated with presumably normal FGF23 biological activity in all XLH and in a minority of ADPKD patients. Loss of Klotho and the concomitant increase in FGF23 appear to exceed and precede changes which can be explained by loss of GFR in patients with ADPKD.

The Impact of Central Obesity, Hypertension and Related Risk Factors on All-Cause Mortality Evolves with Age

F. Thomas[1], B. Pannier[1], A. Benetos[2], U. Vischer[3]
[1]Paris/FR, [2]Nancy/FR, [3]Thônex

Purpose: Obesity is a strong risk factor for diabetes, CV diseases and death in the general population. However, its prognostic significance and its interaction with other risk factors may evolve with age. We aimed to determine the relative impact of obesity, hypertension and related risk factors on all-cause mortality according to age.
Methods and Materials: After excluding subjects with a BMI <20 kg/m^2 or <2 years follow-up, we studied 79325 men and 39765 women undergoing a standard health check-up at the Investigations Préventives et Cliniques Center (Paris, France). Mean follow-up was 5.6 ± 2.4 years. All-cause mortality was calculated according to BMI and waist circumference (WC) categories. The impact of WC and BMI, alone or combined, was further analyzed in age groups (<55, 55–65, >65 years old) using Cox regression models, adjusted for related risk factors and previous CV events.
Results: The prevalence of elevated WC (≥102/88 cm in men/women) increased with age, more strongly than elevated BMI (≥30 kg/m^2). All-cause mortality was higher in patients with an elevated WC, but was inversely associated with the BMI within WC categories. WC adjusted for the BMI, an index of central obesity, was strongly associated with mortality in multiple Cox models (HR = 1.025 per cm unit, p <0.0001). This association was observed in subjects <55 and 55–65 years old (HR = 1.030, p <0.0001 and 1.023, p <0.05), but not in subjects >65 years old (HR = 1.010, p = NS). In contrast hypertension (HR = 1.31, p <0.05), previous CV events (HR = 1.98, p <0.05) and smoking (HR = 1.33, p <0.05) remained associated with mortality even after age 65.
Conclusion: Central obesity was not associated with all-cause mortality in subjects >65 years old, in contrast to hypertension, smoking and previous CV events. Our data are important in determining the hierarchy of risk factors according to age, and suggest that hypertension treatment, smoking cessation and secondary prevention after a CV event are of greater potential benefit than weight reduction in older persons.

Prevalence of Microalbuminuria in the Swiss Survey on Salt

P. Meier[1], T. Schoen[2], V. Forni[3], A. Chappuis[3], I. Binet[4], A. Péchère-Bertschi
[1]Sion, [2]Basel, [3]Lausanne, [4]St. Gallen

Purpose: Microalbuminuria (MA) is a marker of cardiovascular risk and chronic kidney disease (CKD). Population-based data across multiple linguistic regions are lacking in Switzerland. We estimated the prevalence and determinants of MA in the Swiss Survey on Salt.
Methods and Materials: Cross-sectional population-based survey in 11 Swiss centers (2010–2011). Participants (N = 1377) aged 15 years and older were recruited using a 2-stage sampling strategy. Urine albumin and creatinine were measured after a 24-hour urine collection by immunonephelometry and Jaffe kinetic compensated method, respectively. Microalbuminuria 1 (MA1) was defined as present if the urinary-albumin-to-creatinine ratio was >30 mg/g and <300 mg/g (>0.265 and <2.65 mg/mol) and MA2 if MA was 30 to 300 mg/24-hour. We used multiple logistic regression to analyze the determinant of MA1, or MA2, including age, sex, body mass index, smoking and creatinine clearance as covariates. We also explored regional differences.
Results: The 431 men and 453 women with MA data had mean (SD) age 49(18) and 47(17) years. Twenty-six percent of MA2 were missed by the MA1 definition. The prevalence of MA1 and MA2 were 3.1% and 4.0% overall, 2.6% and 4.2% in men, 3.5% and 3.8% in women and similar across linguistic regions. In multiple logistic regression analysis, hypertension was significantly associated with MA1 (OR [95%CI] = 6.6 [2.0–21.9], P = 0.002) and MA2 (OR = 3.1 [1.1–8.6], P = 0.03), whereas diabetes medication use only tended to be positively associated with MA1 (OR = 3.9 [0.7-21.0], P = 0.11) and MA2 (OR = 2.5 [0.6–10.6], P = 0.22).
Conclusion: The prevalence of MA is low and homogenous across linguistic regions in Switzerland. Hypertension is a major independent determinant of MA. MA defined based on urinary albumin-to-creatinine ratio in 24-hour urine underestimates MA defined on absolute albumin excretion (30 to 300 mg/24h). These data will be useful to explore the potential for population-based CKD screening in Switzerland.

Normative Oscillometric Blood Pressure Values for Pre-School Children

G. D. Simonetti[1, 2], N. Jeck[3], G. Klaus[3], R. Schwertz[2], M. Klett[2], A. Schroer[3], C. Kuhnen[3], F. Schaefer[2], E. Wühl[2]
[1]Bern, [2]Heidelberg/DE, [3]Marburg/DE

Purpose: Commercially available oscillometric blood pressure (BP) devices are increasingly used in children. Due to technical differences and device specific algorithms validated for measurements in adults, oscillometric BP readings in children often deviate from auscultatory measured BP values. Thus, normative auscultatory BP standards cannot simply be conferred and device specific normative data sets for children may be required.
Methods and Materials: Standardized BP measurements were performed in German pre-school children aged 5 to 7 years by 2 different oscillometric devices (Boso medicus prestige™ and Omron M5 professional™). In a subgroup also auscultatory BP measurements were performed. The median of 3 consecutive measurements was used for analysis and calculation of BP percentile curves.
Results: BP measurements were performed in 7417 children with a mean age of 5.8 ± 0.5 years. BP was correlated to height, weight and BMI (all p <0.0001). The 5th, 50th, 90th and 95th systolic blood pressure percentiles were 89, 102, 113, 117 mm Hg (for both oscillometric devices). The 5th, 50th, 90th and 95th diastolic oscillometric BP percentiles were 54, 65, 74, and 77 mm Hg for the Boso and 49, 60, 69, and 73 mm Hg for the Omron device, respectively. Oscillometric measurements were 2.1 mm Hg higher for systolic (both devices, p <0.0001), and 1.6 mm Hg higher (Boso, p <0.0001) or 1.9 mm Hg lower (Omron, p <0.0001) for diastolic BP when compared to auscultatory BP.
Conclusion: Oscillometric devices facilitate BP measurements in children, however oscillometric BP assessment requires device specific reference values or correction factors.

Association Between Obesity and High Glomerular Filtration Rate in the Population-Based Swiss Survey on Salt

A. Ogna[1, 2], V. Forni[2], P. Vuistiner[2], D. Hayoz[3], P. Suter[4]
[1]Locarno, [2]Lausanne, [3]Fribourg, [4]Zurich

Purpose: Overweight and obesity are independent risk factors for chronic kidney disease (CKD), although underlying mechanisms remain unclear. Glomerular hyperfiltration (GHF) might be one of the mechanisms of renal function deterioration in obesity. We explored the association of overweight and obesity and GHF in the general Swiss resident population.
Methods and Materials: Cross-sectional population-based survey in the 3 linguistic regions of Switzerland (01.2010 – 7.2011). Data of 1241 out of 1377 participants aged 15–95 years (602 men, 639 women) were available for the analysis. GFR was estimated using creatinine clearance (CrCl) determined from a 24-hour urine collection. We used a CrCl ≥140 ml/min as cutoff for GHF. BMI was categorized in 3 groups: lean (<25 kg/m^2), overweight (25–30 kg/m^2) and obese (≥30 kg/m^2).
Results: The prevalences of overweight and obesity were 32.8% and 14.0%, respectively. Median CrCl [95%CI] was 100 ml/min [97-103] in lean, 107 ml/min [104-112] in overweight and 125 ml/min [120-132] in obese participants. The prevalence of GHF increased across lean, overweight and obese participants (10.2%, 19.6% and 34.7% respectively; p <0.001). The association between GHF and BMI category remained significant after adjusting for age, sex, blood pressure and diabetes medication use, with an OR [95%CI] = 3.42 [2.26–5.21] (p <0.001) for overweight and an OR [95%CI] = 10.32 [6.20–17.19] (p <0.001) for obesity.
Conclusion: Overweight and obesity affect nearly half of the Swiss population aged >15 years. We found a positive association between BMI and GHF, independent of other known CKD risk factors. Longitudinal studies will be needed to confirm the association of GHF with the deterioration of renal kidney function. If GHF represents an early sign of kidney damage and a risk factor for CKD, the implementation of a systematic screening of GHF in the overweight and obese Swiss populations should be considered.

A Novel Mechanism Explaining Salt Sensitivity: Post-Transcriptional Regulation of 11-Hydroxysteroid Dehydrogenase Type 2 by Mirna

F. J. Frey, B. Frey, T. Andrieu, B. Dick, M. Rezaei
Berne

Purpose: A decreased activity of 11b-hydroxysteroid dehydrogenase (11β-HSD2), the enzyme protecting the mineralocorticoid receptor from cortisol, induces salt sensitivity in humans and rodents. The mechanism(s) for tissue specific and inter-personal differential expression of 11β-HSD2 in humans and animals are unknown. We hypothesized for the first time that miRNAs determine 11β-HSD2 activity.
Methods and Materials: The 11β-HSD2 activity in salt sensitive Sprague Dawley (SD) and salt insensitive Wistar (W) rats was investigated, the differences between the target sequence of miRNAs in the 3'UTR of HSD11B2 were analyzed,and the role of dicer, the main actor for miRNA maturation, to regulate 11β-HSD2, was studied. The urinary ratio of corticosterone/dehydrocorticosterone (B/A) and their metabolites were assessed by gas chromatography/mass spectrometry.
Results: The B/A ratio was increased in SD when compared to W rats (0.8 ± 0.2 vs 0.5 ± 0.1, p <0.05) while (tetrahydrocorticosterone+5α-tetrahydrocorticosterone)/tetradehydrocorticosterone was decreased (0.5 ± 0.1 vs. 1.3 ± 0.3, p <0.001), indicating diminished 11β-HSD2 activity in SD rats.To demonstrate whether miRNAs are involved in the diminished 11β-HSD2 activity observed *in vivo,* the 3'UTR of HSD11B2 of SD and W rats were sequenced and cloned downstream of a reporter gene. Different cell lines (SW620, HT29, HCT116) were transfected with these constructs. The SD 3'UTR construct showed a lower reporter activity than W 3'UTR construct, an effect continuously reversed by cloning various mutated sequences progressively restoring the sequence of the 3'UTR of HSD11B2 found in W rats. These data indicate that the 3'UTR regulates 11β-HSD2 activity.
Conclusion: These data indicate for the first time that the 3'UTR and miRNAs determine 11β-HSD2 expression and activity and are of potential relevance for glucocorticoid-mediated increased salt sensitivity.

Prevalence of Hypertension in the Swiss Survey on Salt Intake (Sss)

N. Glatz[1], D. Conen[2], F. Muggli[3], A. Pechère[4], P. Suter[5], M. Burnier[1]
[1]Lausanne, [2]Basel, [3]Lugano, [4]Geneva, [5]Zurich

Purpose: Arterial hypertension (HT) prevalence in the general Swiss population has not been investigated so far. The purpose of this analysis was to assess HT prevalence and treatment in an unselected group of subjects of the Swiss population.
Methods and Materials: Preliminary results of the SSS, a population based, cross sectional study including 1377 subjects from the 3 main linguistic regions of Switzerland were used to assess HT prevalence. HT was defined as current antihypertensive treatment, mean systolic blood pressure (BP) ≥140 mm Hg and/or mean diastolic BP ≥90mm Hg, based on 8 BP measures performed at 2 visits (2x4). BP measurement was performed with oscillometric BP devices. The 1° BP measure of each visit was excluded to reduce white coat effect. We compared HT prevalence across regions using a Chi square test, and multiple logistic regression to explore the determinants of HT.
Results: 1371 subjects (668 men, 703 women) were included in the present analysis. HT prevalence was 27% overall, 20% in women and 33% in men. In the 15–29, 30–44, 45–59 and ≥60 year old groups, HT prevalence was 2.0%, 3.4%, 16.1% and 52.5% in women and 2.9%, 11.6%, 36.7% and 64.5% in men. Compared to the French and Italian speaking regions, HT prevalence was higher in the German-speaking region with respectively 23.1%, 17.7% and 31.2% (P <.05). Among hypertensive subjects, 28.9% were unaware of their HT, 85% of those who were aware, were currently treated and 60.3% were controlled. In multiple logistic regression analysis, sex (OR[95%CI] = 0.6 [0.4–0.8], p<.001), age (OR[95%CI] = 1.09 [1.08–1.10], p <.001), body mass index (OR[95%CI] = 1.1 [1.08–1.16], p <.001), and German speaking region (OR[95%CI] = 1.5 [1.03–2.05], p<.001), but not urinary salt excretion were significantly associated with HT.
Conclusion: Overall HT prevalence in Switzerland is similar to other Western countries, although regional heterogeneity was found. As expected HT prevalence is higher in men and older age categories. BP control remains an important but difficult task.

Targeting the Apoptosis Pathway to Prevent the Anti-Tolerogenic Effect of Calcineurin Inhibitors

P. E. Cippà[1], J. Chen[1], A. K. Kraus[1], P. D. Bardwell[2], R. P. Wüthrich[1], T. Fehr[1]
[1]Zurich, [2]Worcester/US

Purpose: Transplantation tolerance, a state in which the immune system does not reject an allograft, but normally responds to foreign antigens, would solve most problems currently encountered after solid organ transplantation. In experimental models, induction of mixed chimerism by non-myeloablative bone marrow transplantation results in donor-specific tolerance without any immunosuppressive therapy. In contrast, for a clinical translation of this approach, administration of immunosuppressive drugs in the initial phase after transplantation has to be considered to minimize the risk of acute rejection. However, in previous studies the most important class of immunosuppressants – calcineurin inhibitors (CNIs) – inhibited tolerance induction due to unknown mechanisms.
Methods and Materials: The impact of CNIs on apoptosis regulation in alloreactive T cells during tolerance induction was investigated using a mixed chimerism induction protocol in the mouse, consisting of non-myeloablative total body irradiation, CD154-blockade and bone marrow transplantation. Chimerism was assessed in blood by FACS, donor-specific tolerance by skin transplantation. NFAT-KO, BIM-KO, and TCR transgenic mice were used for mechanistic studies.
Results: Activation of the calcineurin–NFAT pathway was intrinsically required in recipient CD8 T cells to achieve complete peripheral deletion of alloreactive T cells and tolerance. This effect was related to the regulation of apoptosis after T cell activation and particularly to the up-regulation of the pro-apoptotic BH3-only protein Bim. As a result, mice treated with cyclosporine A – similarly to mice deficient of BIM – were more resistant to tolerance induction, and in the former setting this effect was prevented by combination with the pro-apoptotic BH3-mimetic small molecule ABT-737.
Conclusion: CNIs impair tolerance induction via a dysregulation of the intrinsic apoptosis pathway. This effect is reversed by combination treatment with pro-apoptotic ABT-737.

Angiotensinergic Innervation of the Kidney: Localization and Relationship with Catecholaminergic Postganglionic and Sensory Nerve Fibers

J. Bohlender[1], B. Pfarrer[2], J. Patil[2], J. Nussberger[1], G. Thalmann[3], H. Imboden[2]
[1]Lausanne, [2]Berne

Purpose: The kidney function is under comprehensive control of the sympathetic nervous system which releases norepinephrine (NE) as its principal neurotransmitter and neuropeptide Y as a co-transmitter. The presence of an angiotensinergic innervation of the kidney, however, has not yet been reported.
Methods and Materials: Rat, pig and human kidney specimens were formaldehyde-fixed. Cryosections were investigated by immunocytochemically with a sensitive mouse monoclonal antibody against angiotensin (Ang) II using a free-floating incubation protocol. Co-staining was with antibodies against tyrosine 3- or dopamine beta-hydroxylase to identify catecholaminergic, and calcitonin gene related peptide (CGRP) to identify sensory nerve fibers. Additional staining was with anti-synpatophysin and anti-renin antibodies. Immunofluorescence detection was by fluorescent light or laser scanning microscopy.
Results: A dense angiotensinergic innervation of the kidney was detected with the same pattern as for the sympathetic innervation. Ang II-containing nerve fibers were abundantly present in the renal pelvis, adjacent to the urothelium, within the arterial nerve plexus including the periglomerular arterioles, and in the cortex and outer medulla. Angiotensinergic fibers innervated JG cells, larger veins and the renal capsule but not glomerula or the papilla. Three distinct fiber types with an angiotensinergic, catecholaminergic or a combined phenotype were identified. Intrarenal microganglia contained neurons with the same three phenotypes. Angiotensinergic fibers co-staining for CGRP but not for synaptophysin or catecholaminergic markers were identified as sensory-afferent with a mainly pelvic distribution.
Conclusion: The kidney harbors an important angiotensinergic postganglionic and sensory-afferent innervation. Ang II as a peptide co-transmitter may modulate sympathetic neurotransmission and kidney function independently from humoral Ang II including natriuresis, renin secretion, and renal adaptation of blood pressure.

Comparison of Renal Gene Expression Between Control and Cirrhotic Mice with Ascites

D. Mordasini, M. Maillard, E. Hummler, M. Burnier, B. Vogt
Lausanne

Purpose: Cirrhosis, most of it related to alcohol abuse or viral hepatitis, is a frequent and severe disease complicated by abnormal renal Na^+ retention, promoting edema and ascites formation. Although many aspects of the abnormal renal Na^+ retention in patients with cirrhosis are understood, the precise mechanisms that initiate and maintain renal Na^+ retention remain a matter of debate. Which ion transporters are deregulated? Is an aldosterone dependent or independent mechanism involved in such a deregulation?
Methods and Materials: In order to shed some light on the topic, we performed microarray and compare renal transcriptomes of control (sham-operated) and mice with decompensate cirrhosis (bile duct ligated).
Results: The transcriptomes analysis revealed that the abundance of 283 transcripts was significantly altered between 1.3 to 32.4 times, 121 transcripts were upregulated and 162 were downregulated. Surprisingly, we observed no alteration regarding the mRNA abundance of Na^+ or water transporters between control and ascitic mice. Moreover, despite high aldosterone plasma level in ascitic mice, there was no alteration in the mRNA level of aldosterone or vasopressin induced/repressed genes, described by Robert-Nicoud et al. in 2001.
Conclusion: In summary, these data bring a new sight on the renal side of decompensate cirrhosis. They suggest that the renal deregulation of Na^+ and water balance is not directly linked to mRNA level but more likely to protein activity or abundance involved in Na^+ and water transport. They also participate to the debate about the role of aldosterone in Na^+ retention observed in decompensate cirrhosis since, despite high aldosterone plasma level observed in ascitic mice, the expression level of most of the known aldosterone regulated gene is not altered.
References: Robert-Nicoud M, et al. Transcriptome of a mouse kidney cortical collecting duct cell line: effects of aldosterone and vasopressin. Proc Natl Acad Sci U S A. 2001;98(5):2712–6.

Nadph-Oxidase 4 Knock-Out Mice Display Increased Tubular Apoptosis and Interstitial Fibrosis in the Unilateral Obstruction Model

S. Nlandlu Khodo, E. Dizin, E. Feraille, K. H. Krause, P.-Y. Martin, S. De Seigneux
Geneva

Purpose: Kidney interstitial fibrosis is correlated with chronic kidney disease (CKD) progression. NOX4 is the major kidney NADPH-oxidase expressed mostly in the tubular compartment. NOX isoforms are involved in apoptosis and prosurvival pathways as well as in hypoxia signaling and may therefore play a role in fibrosis progression.
Methods and Materials: We studied unilateral urinary obstruction (UUO) in wild type and NOX4 knock-out (KO) mice as well as in NOX2/4 double-KO mice to decipher the role of these enzymes in kidney fibrosis progression in a tubular stress model. mCCDcl1 cells were used to examine their role in apoptosis.
Results: NOX4 was expressed in the proximal tubule and collecting duct whereas NOX2 was expressed at low levels along the nephron. Interstitial fibrosis assessed by quantification of Sirius red staining and collagen-I Western blot after 7 and 14 days UUO was two times higher in NOX4 KO compared to wild type mice. Tubular apoptosis was significantly enhanced in NOX4 mice compared to wild type. Peritubular capillary density and VEGF expression assessed by Western blot were significantly lower in UUO kidneys of NOX4 and NOX2/NOX4 KO mice compared to wild type. Oxidative stress was paradoxically increased in the interstitium of obstructed kidneys of NOX4 KO. Apoptosis, interstitial fibrosis and oxidative stress were attenuated in NOX2/NOX4 KO compared to NOX4 KO animals. In mCCDcl1 cells NOX4 si-RNA silencing led to apoptosis in the presence of TGF-[beta]1.
Conclusion: We demonstrate that complete NOX4 deficiency is deleterious in the UUO model and increases tubular cell apoptosis under conditions of tubular cell stress in vitro and in vivo. NOX4 deletion also decreases kidney peritubular vascularisation via decreased tubular VEGF production in the UUO model. NOX2 has a different role from NOX4 in this model and participates to the oxidative stress. These effects of NOX4 on tubular apoptosis, vascularisation and NOX2 activation may explain enhanced kidney fibrosis in UUO NOX4 KO mice.

Glut9 and Uric Acid Handling by the Kidney

M. Auberson, B. Thorens, O. Bonny
Lausanne

Purpose: Uric acid is a metabolite of purine degradation and hyperuricemia is strongly associated with gout and kidney stones, and has been linked to several other pathological conditions such as hypertension, the metabolic syndrome and inflammation. GLUT9 (SLC2A9) is a newly identified urate transporter, initially cloned by homology with the glucose transporter family. GLUT9 mutations in humans have been shown to be causative for the familial renal hypouricemia, a condition in which affected patients present hypouricemia, renal uric acid wasting, kidney stone and a propensity to acute renal failure during strenuous exercise. The in vivo role of GLUT9 has been recently unravelled in the mouse. Mice with whole

body deletion of Glut9 are hyperuricemic and display severe nephropathy that results from intratubular uric acid precipitation. Mice in which GLUT9 has been deleted only in the liver present with hyperuricemia, due to the role of GLUT9 in facilitating the entry of uric acid in the hepatocyte for its degradation by the enzyme uricase. By contrast, the role of GLUT9 in the kidney remains largely unknown. In particular, the exact localization of GLUT9 (proximal vs. distal tubules, apical vs. basolateral side of the epithelium), and the precise mode of urate transport have not been solved yet.
Methods and Materials: In order to address these points, we generated mouse models carrying kidney-specific disruption in different parts of the tubules.
Results: We showed that GLUT9 is essential for proper urate reabsorption in the mouse kidney. Indeed, tetracycline-inducible whole nephron deletion of GLUT9 led to hyperuricosuria.
Conclusion: These results point out GLUT9 as a crucial partner in the renal handling of uric acid and designate it as a new target for uricosuric agent.

Dnam-1 – a New Player in Renal Allograft Rejection

A. K. Kraus[1], P. E. Cippa[1], J. Chen[1], A. Gaspert[1], R. P. Wüthrich[1], G. Bernhardt[2], T. Fehr[1]
[1]Zurich, [2]Hannover/DE

Purpose: Despite effective treatment protocols to prevent rejection many renal allografts are lost due to the toxicity of immunosuppressants. Thus, more specific and less toxic immunosuppression is needed. DNAM-1 (CD226) on T cells has been shown to play an important role for allogeneic graft-versus-host responses. DNAM-1 has two ligands: the adhesion molecules CD155 and CD112. The role of DNAM-1 during renal allograft rejection is unknown.
Methods and Materials: Primary cultures of murine renal tubular epithelial cells (rTECs) were prestimulated with IFN-β and IFN-γ to induce high surface expression of MHC. Surface expression of CD 155 and CD112 was tested by FACS. Responder T cells were restimulated in vitro with allogeneic fully MHC-mismatched splenocytes. From these restimulation cocultures we measured proliferation (thymidine incorporation), cytokine production (ELISA) and cytotoxicity against IFN-stimulated rTECs from WT or $CD155^{-/-}$ mice (^{51}Cr-release-assay). To test for a role of this pathway in vivo, we performed fully MHC-mismatched skin and kidney grafts.
Results: CD155 and CD112 were both highly expressed on rTECs and could be further increased by IFN-stimulation. However, when CD155 was missing on targets in an allospecific chromium-release-assay, no difference in cytotoxicity was measured compared to WT targets. Also, allospecific T cell proliferation and IFN-γ secretion were not altered, when stimulator cells lacked CD155. In contrast, when adding a blocking antibody against DNAM-1, allospecific T cell proliferation and cytotoxicity against rTECs were reduced. When testing for the role of this pathway for allograft rejection in vivo, no difference between skin graft survival of WT and $CD155^{-/-}$ was observed.
Conclusion: DNAM-1 is an important costimulatory receptor for alloreactive T cells as its blockade reduces alloreactivityof T cells against rTECs in vitro. However, CD155 does not seem to be the crucial ligand in this context. The role of the second ligand CD112 is currently under investigation.

Oral Presentations – Transplantation

A Multicentric Protocol Using Glycosorb® Immunadsorption for Ab0-Incompatible Kidney Transplantation: The Swiss Experience

M. Schiesser[1], T. Fehr[1], I. Binet[2], U. Eisenberger[3], K. Hadaya[4], M. Dickenmann[5]
[1]Zurich, [2]St. Gallen, [3]Berne, [4]Geneva, [5]Basel

Purpose: In order to expand the kidney donor pool we have developed a national protocol for AB0-incompatible kidney transplantation in Switzerland. The protocol consists of a standardized immunosuppression and perioperative Glycosorb® immunoadsorption to reduce circulating anti-A/-B antibodies.
Methods and Materials: Patients qualifying for AB0-incompatible kidney transplantation received Rituximab® one month before transplant and standard immunosuppression with tacrolimus, mycophenolate mofetil and steroids. Perioperative immunoadsorption was performed using Glycosorb® columns. Graft survival, patient survival, kidney function, rejections and anti-A/-B antibody titers were assessed.
Results: A total of 59 patients (12 females and 47 males) were transplanted within a period of 5 years in 5 Swiss transplant centers. The mean follow up was 22 months and the mean recipient age was 52 years. The median number of immunoadsorptions performed prior to transplantation was 5 (range 3–16), and the antibody titer at the time of transplantation was less than 1:8. Only 8 (13.5%) patients needed immunoadsorption after transplantation (median number of immunoadsorptions after transplantation: 0; range 0-11). All centers successfully performed regular column reuse (1–3 columns per patient). The patient survival rate was 98.3% and the overall graft survival rate was 96.6%. One graft had to be removed due to emphysematous pyelonephritis two months after transplantation, and one patient died due to E. coli sepsis. Kidney graft function was excellent with a mean serum creatinine level of 126 µmol/l (SD 36.2) one year after transplantation. We observed 11 biopsy proven rejections (18.6%) at mean interval of 7.4 months after transplantation.
Conclusion: We have established a national protocol using Glycosorb® immunoadsorption in AB0-incompatible kidney transplantation, which is efficient and safe. Only a minority of patients needed postoperative immunoadsorption. Column reuse proved to be efficient.

Diffusion-Weighted Mri-Imaging Reveals Longitudinal Functional Changes in the Remaining Kidney During the First Year After Living Donor Nephrectomy

U. Eisenberger, T. Binser, H. Thöny, C. Boesch, F. J. Frey, P. Vermathen
Berne

Purpose: Diffusion weighted imaging (DWI) is a new functional MRI imaging method. We performed a prospective longitudinal diffusion in living kidney donors and recipients before and after transplantation we hypothesized that diffusion parameters will change after nephron loss due to uninephrectomy.
Methods and Materials: 13 healthy kidney donors and their recipients were randomly enrolled. They underwent MR examinations at 7 days (D07), 3 months (M03) and 12 months (M12) after living donation and pre transplant only in donors. Clinical and laboratory parameters were obtained at each time point. Coronal single shot EP-DWI was performed on a 3T MR scanner (Trio, Siemens) with 10 diffusion gradient b-values using respiratory triggering. DWI processing was performed I) without separating diffusion and perfusion contributions, yielding a "total" apparent diffusion coefficient (ADC_T), and II) separating diffusion and perfusion, yielding ADC_D (mostly determined by diffusion), and the perfusion fraction, F_P.
Results: Most importantly, ADC_D (and similarly ADC_T) rose in the remaining kidney at D07 after explantation and remained high at M03. At M12, ADC_D declined again in cortex, while it remained significantly elevated in medulla, demonstrating only a trend towards lower values. The corticomedullary difference of ADC_D ($DADC_D$), which is present pre-transplantation, persisted until M03 and then vanished at M12. F_P values showed a trend towards higher values, primarily in cortex. ADC values in medulla and the corticomedullary difference $DADC_T$ and $DADCT_D$ correlated significantly with eGFR ($p < 0.002$). In the transplanted kidney all parameter remained remarkably stable during follow-up.
Conclusion: Increased diffusion parameters showed post-explantation compensatory changes of the remaining kidney, which might be induced by hyperfiltration. DWI measurements appear valuable to study pathophysiologic changes after renal transplantation.
References: Acknowledgment: Supported by SNF 320000-111959.

Non-Invasive Detection of Subclinical Tubulo-Interstitial Inflammation by the Urinary Cxcl10 Chemokine: Validation in a Real-Life Setting

P. Hirt-Minkowski[1], P. Amico[1], J. Ho[2], G. Ang[2], H. Hopfer[1], J. Steiger[1], D. Rush[2], P. Nickerson[2], S. Schaub[1]
[1]Basel, [2]Winnipeg/CA

Purpose: Urinary CXCL10 has been proposed as a non-invasive biomarker for subclinical tubulo-interstitial inflammation. The aim of this study was to validate these results in an independent and unselected patient population.
Methods and Materials: 208/228 consecutive patients (91%) contributed 362 urine samples at the time of their surveillance biopsies at three (n = 176) and six months (n = 186) post-transplant. Allograft histology was graded by Banff criteria. Urine CXCL10 was measured by ELISA.
Results: 255/362 surveillance biopsies (70%) had a t-score of 0, 107/362 biopsies (30%) a t-score ≥1 (t1: 86/362 (25%), t2: 16/362 (4%), t3: 5/362 (1%)). t0-biopsies and t≥1-biopsies had similar serum creatinine levels (135 vs 134 µmol/l; p = 0.64), total urine protein/creatinine ratios (13 vs 14 mg/mmol; p = 0.18), and urine α1-microglobulin/creatinine ratios (4.5 vs 4.9 mg/mmol; p = 0.28). By contrast, urine CXCL10/creatinine ratios were significantly higher in t≥1-biopsies than in t0-biopsies (median 2.24 ng/mmol (IQR: 0.7–8.4 ng/mmol) vs median 0.7 ng/mmol (IQR: 0.4–1.8 ng/mmol); p <0.0001). ROC-analysis revealed an AUC of 0.69 (p <0.0001). At a urine CXCL10/creatinine ratio cut-off of 1.82 ng/mmol, sensitivity and specificity for detection of a t≥1-biopsy were 57% and 75%, respectively. A urinary CXCL10-guided strategy would have reduced the number of performed surveillance biopsies from 362 to 125. 191/255 t0-biopsies (75%) would have been correctly omitted, while 46/107 t≥1-biopsies (43%) would have been missed (t1: 40; t2: 6). Similar results were obtained if surveillance biopsies were grouped according to the combined Banff t- and i-score, or the total Banff acute score.
Conclusion: In a real-life setting, urinary CXCL10 correlated with subclinical tubulo-interstitial inflammation. A urinary CXCL10-guided surveillance biopsy strategy should be evaluated in a prospective study.

BK Viremia is Independently Associated with Hla-Mismatches and Acute Rejection Episodes, but not with Type of Immunosuppression

A. Hässig, M. Roos, A. Etter , W. Bossart, N. Müller, M. Schiesser, R. Wüthrich, T. Fehr
Zurich

Purpose: BK viremia and polyomavirus-associated nephropathy represent a significant problem after kidney transplantation. Both are associated with intensified immunosuppression, but other risk factors and the impact of a screening program on outcome are incompletely understood.
Methods and Materials: Here we report on the short- and long-term outcome of a cohort of patients who were transplanted in 2006/2007 and included in a newly introduced systematic 3-monthly screening for BK viremia at the University Hospital Zurich. In patients testing positive for BK viremia, screening frequency was intensified and immunosuppression reduced. Patients with suspicion for PVN got a transplant biopsy.
Results: Among 152 included patients, 49 (32%) tested positive for BK viremia, but only 8 developed biopsy-proven polyomavirus-associated nephropathy. BK viremia had a significant impact on GFR and proteinuria in the first two years. Acute rejection episodes and the number of HLA-mismatches were the strongest predictors of BK viremia in a multiple logistic model. In contrast no particular immunosuppressive agent or regimen was associated with enhanced risk.
Conclusion: With adaption of immunosuppression an excellent outcome is achieved. The independent association of HLA-mismatches with BK viremia suggests impaired polyomavirus immunosurveillance in highly mismatched allografts.

Pre-Transplant Hla-Dsa that Persist Post-Transplant Predict Increased Risk of Antibody-Mediated Rejection and Graft Loss in Renal Transplantation

P. Amico[1], N. Banuelos[2], G. Hönger[1], H. Hopfer[1], P. I. Terasaki[2], S. Schaub[1]
[1]Basel, [2]Los Angeles/US

Purpose: Since not all recipients with pre-transplant HLA-DSA exhibit antibody-mediated rejection (AMR) and poor allograft survival, the aim was to identify predictors of allograft outcome by studying longitudinally post-transplant profile of HLA-DSA.
Methods and Materials: In this retrospective study, pre-transplant HLA-DSA of 51 patients were analyzed by single antigen flow beads (SAFB), IgG subclasses, and C1q assay at time of clinical and protocol biopsy (at 3 and 6 months). The results were correlated with incidence of clinical/subclinical AMR and allograft survival.
Results: In 14 of 51 recipients (27%), HLA-DSA were not detectable by SAFB (MFI <500) in post-transplant sera (noDSA group) at a median of 93 days (7–138), whereas in 37/51 recipients (73%) HLA-DSA were still detectable at 6 months (DSA group). Cumulative incidence of AMR at 12 months was significantly higher in DSA group than in noDSA group (78% vs. 22%, p = 0.0009). At 5 years, death-censored graft survival was significantly lower in the DSA group (DSA group: 67% versus noDSA group: 92%; p = 0.01). IgG subclasses and complement-activating capability were then analyzed in DSA group to evaluate their predictive value. Post-transplant complement-activating capability was neither predictive for AMR (p = 0.21) nor for allograft failure (p = 0.15). No single subclass was significantly
Conclusion: In recipients with pre-transplant HLA-DSA, a relevant predictor of low risk of AMR and superior allograft survival was early disappearance of HLA-DSA. Assessment of complement-activating capability and analysis of IgG subclasses post-transplant were not helpful in predicting clinical outcome.

Delayed Graft Function Is not Associated with an Increased Incidence of Renal Allograft Rejection

P. Hirt-Minkowski, P. Amico, G. Hönger, C. Praehauser, J. Steiger, M. Mayr, S. Schaub
Basel

Purpose: Delayed graft function (DGF) is a risk factor for inferior renal allograft function, but its association with allograft rejection is not well studied.
Methods and Materials: In this retrospective study we analyzed all deceased donor transplantations performed between 1999 and 2009 (n = 345). DGF was defined as the need for dialysis during the first week post-transplant due to inadequate allograft function. Investigated outcomes were rejection episodes and allograft function.
Results: Sixteen of 345 recipients experiencing primary-non-function (5%) were excluded from the analysis. DGF occurred in 93/329 patients (28%), immediate graft function (IGF) in 236/329 recipients (72%). 89/93 patients with DGF (96%), and 221/236 patients with IGF (94%) had at least one allograft biopsy within the first year post-transplant (p = 0.6). Among the DGF and IGF group, the cumulative incidence of patients with clinical (35% vs 34%; p = 0.62) and combined (sub)clinical rejection (58% vs 60%; p = 0.79) within the first year was not different. Furthermore, there was no difference regarding rejection phenotypes and the time frame of occurrence. Patients with donor-specific HLA-antibodies had a higher incidence of clinical rejection than patients without (48% vs 30%; p = 0.001). In both groups, however, rejection episodes were not different in patients with DGF and IGF (54% vs 45%; p = 0.45, 28% vs 31%; p = 0.77). Median GFR one year post-transplant was lower in the DGF than the IGF group (45 ml/min vs 50 ml/min; p = 0.007).
Conclusion: DGF is not associated with an increased incidence of allograft rejection, but an inferior allograft function likely due to non-immunological factors of ischemia/reperfusion injury.

01

A Label-Free Serum Test Measuring Overall Calcification Inhibition

A. Pasch[1], S. Farese[1,2], J. Flöge[3], W. Jahnen-Dechent[3]
[1]Berne, [2]Solothurn, [3]Aachen

Purpose: Accelerated vascular and soft tissue calcification is a major problem in patients with chronic kidney disease (CKD). As serum is supersaturated with regard to calcium and phosphate, inhibitors of calcification critically determine pathological calcification. Therefore, an assay measuring the overall calcification inhibitory capacity in blood would be helpful to make informed therapy decisions.
Methods and Materials: We developed a label-free assay to quantify calcification-inhibitory properties contained in serum. The assay measures the formation of protein-mineral aggregates in real time.
Results: Using this assay, we demonstrate that in the presence of high amounts of calcium and phosphate, primary calciprotein particles (CPPs) are formed in serum. Primary CPPs are spherical colloidal particles of 50–100 nm diameter. Subsequently, these primary CPPs undergo spontaneous transition to spindle shaped secondary CPPs. Primary CPPs are mainly comprised of fetuin-A and albumin, as demonstrated by protein gel and Western blot analyses. The size of the resulting secondary CPPs is regulated mainly by two serum-inherent proteins: fetuin-A and albumin, with albumin synergistically substituting low fetuin-A concentrations. We furthermore demonstrate that the transition step is delayed in the presence of magnesium, and accelerated in the presence of phosphate.
Conclusion: We have developed a novel test to assess the overall calcification inhibitory capacity of serum. This test may have an important role in the identification and specific treatment of calcification-prone CKD patients.

02

Paricalcitol Lowers Plasma Renin Activity and Improve Blood Pressure Control in the 2-Kidney, 1-Clip Hypertensive Rat Model

O. Phan, M. Maillard, C. Perregaux, M. Burnier
Lausanne

Purpose: Vitamin D has been shown to regulate renin expression in juxtaglomerular cells. The aim of the study was to compare the effects of two vitamine D analogs, paricalcitol and calcitriol on plasma renin activity (PRA), blood pressure (BP) and heart weight (HW) in a high-renin model of hypertension i.e the 2-kidney one-clip rat model.
Methods and Materials: Male wistar rats were used at 150 gr. Hypertension was induced by clipping the left renal artery. After 10 days, rats were randomly assigned (based on the normal distribution of baseline body weights) into 3 groups with a standard diet: calcitriol (80 ng/kg), paricalcitol (240 ng/kg), and control (vehicle) with an intraperitoneal injection every 3 days for a total of 4 injections (N = 11/group). A sham group was also created as sham control. 24 h before sacrifice, a catheter was inserted into the right femoral artery to measure BP. The rats were placed in large Plexiglas tubes without noise or visual stimulation for two hours. The catheter was attached to a combination pressure transducer, and arterial blood pressure (BP) was collected using computerized data acquisition software.
Results:

	Heart Rate (/mn)	Systolic BP (mm Hg)	Diastolic BP (mm Hg)	Mean BP (mm Hg)	Heart weight (gr)	PRA (ng/ml/h)
Sham control	361 ± 13	142 ± 8*	96 ± 8*	113 ± 9*	1.03 ± 0.1*	1.53 ± 0.38*
Clip control	366 ± 7	193 ± 9	141 ± 7	166 ± 8	1.36 ± 0.06	4.81 ± 1.27
Clip calcitriol	365 ± 8	182 ± 10	129 ± 7	154 ± 8	1.07 ± 0.07*	3.28 ± 0.48
Clip paricalcitol	354 ± 9	163 ± 7*	119 ± 6*	139 ± 7*	1.02 ± 0.06*	1.62 ± 0.3*

* p <0.01 vs clip control

Conclusion: In this model, only paricalcitol is associated with a significant decrease in BP and plasma renin activity. However, both paricalcitol and calcitriol reduce cardiac hypertrophy suggesting a BP-independent effect on cardiac mass.

03

Characterization of the Renal CD4+ T Cell-Response in Experimental Autoimmune Glomerulonephritis

H. Hopfer[1], J. Holzer[2], S. Hünemörder[2], H.-J. Paust[2], M. Sachs[2], J.-E. Turner[2], U. Panzer[2], H.-W. Mittrücker[2]
[1]Basel, [2]Hamburg/DE

Purpose: Autoimmunity against the Goodpasture antigen α3IV-NC1 results in antiglomerular basement membrane (GBM) glomerulonephritis (GN). Little is known about the role of autoreactive T lymphocytes in induction and progression of the disease.
Methods and Materials: We used the mouse model of experimental autoimmune GN (EAG) to characterize the renal $CD4^+$ T cell response.
Results: Immunization of DBA/1 mice with α3IV-NC1 resulted in proteinuria and finally a loss of kidney function. Kidney disease displayed a biphasic course. In the "preclinical" phase, mice mounted α3IV-NC1-specific IgG responses and showed IgG depostion along the GBM. Despite IgG deposition and steadily increasing proteinuria, kidneys demonstrated only marginal signs of inflammation with limited leukocyte infiltration. After 9-13 weeks, mice proceeded to a "clinical" stage with crescentic GN, extensive tubulointerstitial damage and massive macrophage infiltration. T cell infiltration was less pronounced and confined to the interstitium. Renal T cells had an activated phenotype and a significant fraction of $CD4^+$ T cells were Th1 or Th17 cells. Closer examination revealed the presence of autoreactive T cells producing IFNγ upon restimulation with α3IV-NC1.
Conclusion: In summary, our results suggest that accumulation of effector T cells, including autoreactive T cells, represents a critical step in the progression from mild GN with limited kidney damage to severe GN with tubulointestinal inflammation and loss of kidney function.

04

Periostin – A Matricellular Protein Involved in Peritoneal Injury During Peritoneal Dialysis

N. Braun[1], K. Sen[2], D. M. Alscher[1], P. Fritz[1], M. Kimmel[1], A. Jörres[3], I. Edenhofer[2], R. P. Wüthrich[2], C. Cohen[2], S. Segerer[2]
[1]Stuttgart/DE, [2]Zurich, [3]Berlin/DE

Purpose: Periostin is a matricellular protein involved in tissue remodelling through the promotion of adhesion, cell survival, cellular dedifferentiation, and fibrogenesis. It can be induced by transforming growth factor beta and high glucose concentrations. We hypothesized that this protein might be expressed in the peritoneal cavity of patients on peritoneal dialysis (PD) and patients with signs of encapsulating peritoneal sclerosis (EPS).
Methods and Materials: In this retrospective study we included peritoneal biopsies from patients on PD with EPS (n = 7), on PD without signs of EPS (n = 10), and compared them with biopsies taken during hernia repair from patients not on PD as controls (n = 11). Periostin was localized by immunohistochemistry and double immunofluorescence (in combination with smooth muscle actin). Periostin staining was quantified by morphometry and scored semiquantitatively by an observer blinded to the diagnosis. Expression of periostin mRNA was also quantified in peritoneal fibroblasts in-vitro.
Results: Periostin was present in the wall of larger arteries and focally in the extracellular matrix in the submesothelial zone in control biopsies. Patients on PD demonstrated interstitial periostin in variable amounts depending on the severity of submesothelial fibrosis. In EPS there was a very prominent and diffuse accumulation of periostin in the sclerosis layer. The area of periostin was significantly larger in EPS as compared
to control biopsies. The percentage of periostin positive area and the semiquantitative scores were prominently associated with the thickness of the submesothelial fibrosis zone. A strong periostin mRNA expression was found
in peritoneal fibroblasts in-vitro.
Conclusion: Periostin is strongly expressed in the peritonael cavity in patients with EPS and with simple peritoneal sclerosis on PD. It might play a role in the progression of peritoneal injury.

05

Prevalence pf Reduced Renal Function in Switzerland – Results of a Multicenter, Cross-Sectional Study

Y. Tomonaga[1], T. Szucs[2], L. Risch[3]
[1]Zurich, [2]Basel, [3]Schaan/FL

Purpose: To estimate the prevalence of reduced renal function (RF) and chronic kidney disease (CKD) in Switzerland.
Methods and Materials: A multicenter, cross-sectional study in seven Swiss cantons was performed. Adult patients visiting the randomly selected general practices during defined periods were asked to participate. Emergency patients were excluded. Demographic and social variables, clinical status and co-morbidities were reported on a questionnaire. Urine and blood samples were sent to a central laboratory for analysis. Reduced RF was assessed by creatinine-based estimates of the glomerular filtration rate (eGFR), calculated with the CKD-EPI equation:
– Normal RF: eGFR ≥90 ml/min/1.73 m^2
– Mildly reduced RF: eGFR 60-89 ml/min/1.73 m^2
– Moderately reduced RF/ CKD Stage 3: eGFR 30–59 ml/min/1.73 m^2
– Severely reduced RF/ CKD Stage 4-5: eGFR <30 ml/min/1.73 m^2
Results: 1001 patients were included. 57% were women and the mean age was 57 ± 17 years. Normal RF was reported by 47.1% of the patients, whereas 42.5% showed a mildly and 9.6% a moderately decreased RF. About 0.8% of the patients reported a severely decreased RF. At national level, after age and gender adjustment, we have estimated that about 425 000 (6.5%) and 35 000 (0.5%) individuals may have a moderately and severely reduced RF respectively. These results are very similar to those of the US National Health and Nutrition Examination Survey (NHANES), which reported prevalence of 7.69% for CKD stage 3 and 0.35% for CKD stage 4.
Conclusion: These results emphasise the high prevalence of reduced renal function in Switzerland. Whereas severe renal dysfunctions are usually known, mildly to moderately reduced RFs are probably under-diagnosed and therefore at high risk for progression. Screening and prevention programs may become a basic necessity.

06

Comparison Between PA21, a New Iron-Based Non-Calcium Phosphate Binder and Lanthanum and Sevelamer Carbonate in Uremic Rats

O. Phan[1], M. Maillard[1], F. Funk[2], M. Burnier[1]
[1]Lausanne, [2]St. Gallen

Purpose: In a previous study, we demonstrated that PA21, a new calcium-free, iron based phosphate binder effectively controlled hyperphosphatemia and iPTH levels, and was superior to calcium carbonate in preventing the development of vascular calcifications in rats with chronic renal failure (CRF). This ongoing study expands on our previous findings and compares the efficacy of PA21 with lanthanum (La) and sevelamer carbonate (Se) on hyperphosphatemia, and secondary hyperparathyroidism.
Methods and Materials: CRF was induced in rats using 0.75% adenine-enriched high phosphorus 1.3% diet for 4 weeks. Then, rats were randomized to receive the same % of active ingredient of each binder in the diet without adenine for another 4 week period. The concentration (%) of each binder was chosen to deliver the same amount of active pharmaceutical ingredient to each rat: PA21 5%, La 2%, Se 1.5%. N = 6/group.
Results:

	Body weight g	Creatinine mol/l	P mmol/l	Ca mmol/l	iPTH pg/ml	U. P/creat
CRF placebo	311 ± 8.6	157 ± 14	4.2 ± 0.6	2.4 ± 0.5	3704 ± 868	21 ± 4.6
CRF PA21	300 ± 6.3	136 ± 14	2.1 ± 0.1***	2.5 ± 0.03*	1277 ± 411**	4.6 ± 1.0**
CRF La	306 ± 5.8	144 ± 21	2.5 ± 0.1***	2.5 ± 0.5 *	1109 ± 355**	10 ± 1.1***
CRF Se	305 ± 5.7	130 ± 8	2.4 ± 0.1***	2.6 ± 0.01 *	1000 ± 212**	7.3 ± 1.1*

***p <0.001, **p <0.01, *p <0.05 vs CRF placebo

Conclusion: These experimental data show that the iron based, calcium-free phosphate binder PA21, is at least as effective as La and Se in controlling P and iPTH in rats with CRF.

07

Selective Production of Hyaluronan by Epithelial Cells is Necessary but not Sufficient to Induce Tubulogenesis

P. Soulie, A. Chassot, R. Montesano, P.-Y. Martin, E. Féraille
Geneva

Purpose: Branching morphogenesis is a fundamental process in the development of many organs, including mammary gland and kidney. Extracellular matrix composition plays an important role in tubulogenesis. We hypothesized that epithelial cells can modify their own pericellular matrix to drive branching tubulogenesis.
Methods and Materials: To test the role of hyaluronic acid (HA), in epithelial branching tubulogenesis, we used three different *in vitro* models of epithelial tubulogenesis: 1) hepatocyte growth factor (HGF)-induced tubulogenesis by renal MDCK cells; 2) spontaneous tube formation by kidney mCCD-N21 cells and 3) tube formation by mammary gland-derived J3B1A cells, in response to transforming growth factor β1 (TGF-β1).
Results: Induction of tubulogenesis by either HGF or TGF-β1 strongly induced hyaluronan synthase 2 (HAS2) expression. Immunostaining revealed that HA is preferentially produced at the tips of growing tubes. Reduced HA production, either by pharmacological inhibition (4-MU) or by shRNA-mediated knockdown of HAS2, completely abrogated tube formation in all three cell lines. By contrast, overexpression of HAS2 did not promote tubulogenesis but led to the formation of giant cysts or enlarged disorganized structures when cells are grown in absence or presence of HGF, respectively. We then analyzed the role of HA major receptor, CD44. Addition of CD44 blocking antibody had no effect in mammary cells and did not recapitulate the selective suppression of tubulogenesis observed in response to either 4-MU or *HAS2* silencing in renal cells.
Conclusion: These results indicate that the localized production of HA by epithelial cells is necessary but not sufficient for tubulogenesis and that CD44 is not mandatory in this process.

08

Multiscale Hemodynamic Modeling of the Intrarenal Circulation

K. M'Rabet Bensalah, J. Czerwinska, R. M. Kalicki, D. E. Uehlinger
Berne

Purpose: In silico research is gaining interest in the medical field. Simulation of the renal circulation is a challenging task due to the high morphological and functional complexity of this system. Using the COMSOL multiphysics software, the geometry and hemodynamics of the intrarenal circulation were simulated.
Methods and Materials: The complex arterial branching geometry of a renal lobule was built and meshed with the geometry and mesh tools of COMSOL. The dimensional parameters were taken from Nordsletten et al.'s measures on the rat kidney[1], based on Trueta et al.'s statement that the minute vascular pattern of the unilobar kidney, as the rat's, has no fundamental difference to the individual lobules of the multilobar kidney, as the human's[2].
Results: In the stationary study, pressure follows a proximal to distal gradient, while velocity follows a center to periphery gradient, and shear rate is elevated in constriction and bifurcation regions. In the time dependent study, velocity, shear rate and the Reynolds number vary proportionally to the pulsatile variation of pressure. Pressure, velocity and shear rate are markedly altered by pathologic constriction compared to the physiologic condition.
Conclusion: The pressure and velocity values are in the range of physiologic condition described in the literature[1,2]. Using these flow parameters, the Reynolds number are calculated. The values match those based on literal data at the proximal sites and the flow regime is predicted to be laminar in physiologic condition. Future studies will relate the results of these simulations to renal doppler ultrasound flow measurements.

09

Evaluation of a Renal Risk Score in the Swiss Population: Consolidated Results from a Screening Project in Pharmacies in the Years 2008–2011

S. Favre[1], S. Liniger[1], A. Bock[2], P.-Y. Martin[3], A. Fischer[4], I. Binet[5], F. Frey[1], P. Meier[6], M. Magnin[7], M. Burnier[8]
[1]Berne, [2]Aarau, [3]Geneva, [4]Lucerne, [5]St. Gallen, [6]Sion, [7]Zug, [8]Lausanne

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.
Methods and Materials: 86 pharmacies in the cantons SG, VD, LU, ZG, GE, AG, BE and VS participated from 2008 to 2011 in this screening activity. 1350 people were screened and their scores analysed. The score included the 12 items. The responsible pharmacists were specifically trained for screening activities and consulting. 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 and renal risk scores n (N = 1323)
Age >50 years 923 70%
Sex: female 927 70%
Family history: Chronic kidney disease 125 9% / Diabetes 270 20% / Cardiovascular disease: myocardial infarction 280 21% / Cardiovascular disease: vascular diseases 407 31%
Personal history: Chronic kidney disease 204 15% / Diabetes (treated) 62 5% / Cardiovascular disease (treated) 327 25%
Systolic BP >140 365 28%
Diastolic BP >90 218 16%
Microalbuminuria >2 mg/mmol 287 22%
Results n (N = 1323)
Low risk (<2) 313 24%
Moderate risk (2-4) 499 38%
High risk (>4) 511 39%
Conclusion: 76% of the participants showed a moderate or high renal risk score. They were mostly women >50 years old and persons with known risk factors for kidney disease. 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. For 4 years, this successful chronic kidney disease screening activity in pharmacies has allowed acquisition of useful epidemiological data in Switzerland.

10

Neutrophil-Gelatinase-Associated Lipocalin and Cystatin C vs. Creatinine-Based Estimates of the Glomerular Filtration Rate (EGFR)

Y. Tomonaga[1], T. Szucs[2], L. Risch[3]
[1]Berne, [2]Basel, [3]Schaan/FL

Purpose: To analyse the levels of neutrophil-gelatinase-associated lipocalin (NGAL) and cystatin C (CysC) for different stages of renal functions.
Methods and Materials: A multicenter, cross-sectional study in seven Swiss cantons was performed. Adult patients visiting the randomly selected general practices during defined periods were asked to participate. Emergency patients were excluded. Demographic and social variables, clinical status and co-morbidities were reported on a questionnaire. Urine and blood samples were analysed in a central laboratory. Renal function (RF) was assessed by creatinine-based estimates of the glomerular filtration rate (eGFR), calculated with the CKD-EPI equation:
– Normal RF: eGFR ≥90 ml/min/1.73 m^2
– Mildly reduced RF: eGFR 60–89 ml/min/1.73 m^2
– Moderately reduced RF/ CKD Stage 3: eGFR 30–59 ml/min/1.73 m^2
– Severely reduced RF/ CKD Stage 4–5: eGFR <30 ml/min/1.73 m^2
Results: 1001 patients were included. 57% were women and the mean age was 57 ± 17 years. Both NGAL and CysC were significantly associated with the eGFR (both p <0.001). The mean NGAL values were 35.30 ng/ml for normal RF, 49.17 ng/ml for mildly decreased RF, 116.10 ng/ml for moderately decreased RF and 95.81 for severely decreased RF. Concerning CysC, the mean values were 0.71 mg/l for normal RF, 0.84 mg/l for mildly reduced RF, 1.24 mg/l for moderately reduced RF and 2.52 mg/l for severely reduced RF.
Conclusion: Impairments in renal function was good characterised by elevated NGAL and CysC values. Being less affected by age, race, or muscle mass, and being better predictors of death and cardiovascular events if compared to creatinine, the analysis of these biomarkers may improve the early detection and treatment of renal diseases.

Posters – Transplantation

11

Mycoplasma and Ureaplasma in Kidney Allograft Recipients: Innocent Bystanders or a Cause for Concern?

L. Gerber[1], A. Gaspert[1], N. Müller[1], H. Zwahlen[2], T. Fehr[1]
[1]Zurich, [2]Bellinzona

Purpose: *Mycoplasma hominis* and *Ureaplasma urealyticum* belong to the family of purely intracellular bacteria called *Mycoplasmataceae.* Although a potential pathogenicity of these bacteria is well known (mainly non-gonococcal urethritis), the clinical relevance of positive urine samples in immunocompetent hosts is unclear. In kidney allograft recipients *Mycoplasma hominis* and *Ureaplasma urealyticum* are occasionally found in urine samples, but there are only few reported cases of severe infections, and the pathogenic role in patients after kidney transplantation is debated.
Methods and Materials: In our transplant outpatient clinic, kidney allograft recipients with clinical symptoms of urinary tract infection and/ or leucocyturia first receive a work-up with standard urinary cultures. If negative Mycoplasma/Ureaplasma, Chlamydia, Gonococci and Mycobacteria are assessed. Here we report eight cases tested positive for either Mycoplasma or Ureaplasma in the years 2010 and 2011.
Results: We detected eight patients (four females) with positive urine samples for *Mycoplasma hominis (1 patient)* or *Ureaplasma urealyticum (7 patients)*. Four of these patients were asymptomatic, showed no systemic inflammation and maintained a stable graft function. The remaining four patients (three females) developed pyelonephritis of the allograft. Three of them presented with a deterioration of graft function, one developed multiple cortical abscesses in the transplanted kidney, as shown by MRI. In all four patients Ureaplasma or Mycoplasma were considered the sole causative agents and were successfully treated with tetracyclines. The patient with the abscesses showed a considerable contraction of the lesions after antibiotic treatment but her GFR remained reduced.
Conclusion: In kidney allograft recipients Ureaplasma and Mycoplasma potentially cause invasive allograft infections and should be searched in transplant patients with signs of urinary tract infection and sterile leucocyturia.

12

Is There an Association Between HES Administration to Organ Donors and Delayed Kidney Graft Function?

C. Bucher, J. Neuweiler, I. Binet; St. Gallen

Purpose: Delayed graft function is increasing with the number of transplanted organs of extended criteria donors. Hydroxyethyl starch (HES) is often used in hemodynamic instable donors and is known to cause osmotic nephrosis.
Methods and Materials: We report a case of osmotic nephrosis in a recipient from a deceased donor kidney exposed to HES before donation. Furthermore we reviewed all time-zero biopsies from deceased donor kidneys since 2007 (n = 61) and analyzed delayed graft function (DGF) in the group with versus without osmotic nephrosis.
Results: A donor had been resuscitated with adrenaline and volume, in total 4,5L HES 6% (Voluven®). After initial cardiac arrest, spontaneous circulation had returned and brain death was diagnosed by cerebral angiography. The recipient received an induction with Thymoglobuline, IVIG, Tacrolimus, Mycophenolate and Steroids. DGF occurred and dialysis was required until day 6. Baseline creatinine was reached after day 30 (88 umol/l, eGFR 90 ml/min). Time-zero biopsy showed osmotic nephrosis, it persisted in the day 7 biopsy without signs of tubular necrosis but resolved in the day 60 biopsy. Osmotic nephrosis was diagnosed in 20% (12/61) of the time zero biopsies after deceased donor kidney transplantation. DGF occurred in 67%

(8/12) with osmotic nephrosis vs. 42% without (20/49), RR 1.56 (0.93–2.6), p = 0.13. If DGF was present the median duration of post-transplant dialysis was similar in both groups (11 (IQR 4–16) days with vs. 11 (5-16) without osmotic nephrosis). eGFR at day 15 was 32 ± 23 ml/min, at day 30 40 ± 18 and at 1 year 42 ± 15, not differing between groups.
Conclusion: Delayed graft function trends to happen more in cases with biopsy proven osmotic nephrosis and administration of HES prior to donation may be the cause. However graft function did not differ significantly at 15 days and after 1 year. As HES is not routinely reported in the donor sheet it remains unclear if all cases of osmotic nephrosis are due to HES administration to the donor.

13

Preserved Circannual Rhythm of Vitamin D in Kidney Transplant Patients

F. Burkhalter, M. Dickenmann
Basel

Purpose: The aim of this study was to examine whether circannual rhythm of vitamin D is totally reversed in kidney transplant patients due to avoidance of solar ultraviolet B (UVB) exposure.
Methods and Materials: In 31 kidney transplant patients at our center serum concentration of 25-hydroxvitamin D (25(OH)D were measured during winter (January/February) and during summer (July/August). In addition there was a questionnaire regarding avoidance of solar ultraviolet B exposure.
Results: We found in 93.5% (29/31) of patients a vitamin D insufficiency (25(OH)D <50 nmol/l) during winter and in 64.5% (20/31) during summer. There was a rise of 25(OH)D in 90% (28/31) of the patient from winter to summer. The median rise of 25(OH)D during this periode was 18 nmol/l (range 3–35 nmol/l). Result of the questionnaire showed very good sun protection in all of the patients.
Conclusion: Vitamin D insufficiency during winter is very common in kidney transplant patients at our center. Despite very good avoidance of exposure to UVB there is still a circannual rhythm of vitamin D in these patients. One third of the patients showed normal vitamin D status during summer.

14

A Phase III, Investigator-Initiated, Randomized, Open-Label Single-Center Study on the Effect of Denosumab on the Prevention of Bone Mineral Density Loss after Renal Transplantation (Postop Study; NCT01377467)

M. Bonani, J. Brockmann, C. D. Cohen, T. Fehr, D. Frey, A. Nocito, M. Schiesser, A. Serra, M. Blum, M. Struker, R. P. Wüthrich
Zurich

Purpose: Renal allograft recipients are at high risk for substantial loss of bone mineral density (BMD) within the first year after transplantation. Receptor Activator of Nuclear factor-Kappa-B Ligand (RANKL) is a key molecule regulating activity and survival of osteoclasts. Denosumab (Prolia®) is a humanized monoclonal antibody against RANKL, recently approved for the treatment of osteoporosis. Whether denosumab is effective to prevent BMD loss after renal transplantation has not been evaluated.
Methods and Materials: POSTOP is a randomised 1-year trial on the efficacy and safety of denosumab to prevent BMD loss in kidney allograft recipients. The study started in June 2011 at the University Hospital Zurich. It is planned to recruit 100 patients who have been transplanted with a kidney graft, have a functioning graft within 14 days after transplantation and are on standard triple immunosuppression including steroids. After bone density measurement, study patients will be randomized 1:1 to receive either 60 mg denosumab within 14 days and 6 months after transplantation in addition to standard treatment with calcium/vitamin D or standard treatment alone. Patients with severe osteoporosis (T score < -4) are excluded. The primary endpoint is the change in total hip BMD after one year. Secondary endpoints include changes in bone mineral metabolism parameters, incidence of fractures, and allograft function at one year.
Results: At time of abstract submission, 9 patients have been randomized (4 denosumab vs. 5 control). Their mean age was 47.75 ± 6.16 vs. 52.2 ± 8.7 years, eGFR 56.4 ± 19.3 vs. 57.8 ± 19.4 ml/min at baseline, DEXA BMD total hip –0.8 ± 0.8 vs. –0.9 ± 0.6 and lumbar spine –0.86 ± 0.85 vs. –1 ± 0.85, 25OH vit D 17.9 ± 3.68 vs. 14.9 ± 4.98 ug/l, PTH 233 ± 236.4 vs. 277.6 ± 284.7 ng/l, mean dose of steroids until randomization 1055 ± 163 mg vs. 1069 ± 180 mg.
Conclusion: The POSTOP trial represents the first study to investigate whether denosumab prevents BMD loss within the first year after kidney transplantation.

15

Oxalate Nephropathy in Kidney Allografts

A. Schleich, T. Fehr, A. Gaspert, R. P. Wüthrich, N. Mohebbi
Zurich

Purpose: Oxalate nephropathy is a common cause of crystal induced kidney disease and potentially leads to chronic renal failure. Apart from primary hyperoxaluria caused by genetic defects, various etiologies for secondary hyperoxaluria have been described. Hyperoxalosis can be triggered by gastrointestinal hyperabsorption, metabolic overproduction and finally by diminished renal excretion. Although this feature is well documented in native kidneys, little is known about oxalate nephropathy in kidney transplant patients.
Methods and Materials: We report two cases of oxalate nephropathy in kidney allografts due to enteric hyperoxaluria. Both patients had chronic renal failure due to diabetic nephropathy and underwent simultaneous kidney and pancreas transplantation. After transplantation both developed intestinal complications and underwent resection of ileum and colon. Subsequently both developed short bowel syndrome.
Results: In the first patient, 14 years after kidney transplantation and 7 years after intestinal surgery his creatinine started to rise significantly and the diagnosis of oxalate nephropathy was made by kidney biopsy. One year later he developed end-stage renal failure and started hemodialysis. Similarly in the second patient, 7 years after transplantation und 5 years after enteric resection transplant biopsy was performed and the diagnosis of oxalate nephropathy was made. Subsequently her estimated glomerular filtration rate (eGFR) remained stable at 25 ml/min to date.
Conclusion: Prevention of secondary hyperoxaluria in kidney transplant patients is not different than in native kidneys and is dependent on the underlying cause of oxalate accumulation. Our cases demonstrate an atypical cause of graft failure. Optimal management of secondary hyperoxaluria could potentially avoid or delay chronic graft failure due to oxalate nephropathy. We report underlying causes, histologic findings and prevention strategies of secondary hyperoxaluria.

16

Pharmacokinetic of Tacrolimus after Gastric Bypass Surgery

S. Riethmüller, D. Tsinalis, I. Binet
St. Gallen

Purpose: Obesity is an increasing problem in kidney transplant recipients. Surgical treatment such as gastric bypass (GBP) may be a strategy for improving post-transplant outcome. However little data exist about pharmacokinetics (PK) of immunosuppressive drugs after GBP surgery and the available data show a wide variability. At least three mechanisms can alter PK after GBP: shortening of the small intestine, increasing density of the efflux pump P-glycoprotein and decreasing density of cytochrome P450 3A4/5 along the intestine. Following GBP, the bioavailability of Tacrolimus (TAC) should be decreased by the first 2 mechanisms and increased through the 3rd mechanism.
Methods and Materials: A 43 year-old man with BMI 38.2 on haemodialysis and on the waiting-list for a kidney transplant underwent proximal gastric bypass surgery one year ago (biliopancreatic limb 60 cm, alimentary limb 150 cm). His weight reduced from a maximum of 113 to 72 kg within one year. To test the PK of TAC in this patient, a standard dose of TAC was administered according to our protocol. Starting with 0.05 mg/kg bid the dose was adjusted for a trough level of 10–12 µg/l. After achieving a stable trough level a 12-hour AUC was calculated using the trapezoidal method.
Results: Using a dose of 6 mg bid in steady-state (0.167 mg/kg/d) our patient showed a normal shaped curve of TAC-levels over time with a maximal whole blood level of 43 µg/l after 2 hours and a trough level of 12 µg/l after 12 hours. The 12-hour AUC was 242 µg x h/l.
Conclusion: The relation between TAC trough level and AUC in our patient after GBP was within the expected range for subjects without GBP. Still we suggest evaluating pre-transplant pharmacokinetics in GBP patients the PK of TAC shows a wide inter-patient variability which might be more pronounced in GBP patients.

17

Heart Failure and Mitral Insufficiency in a Renal Allograft Recipient

A. Schleich[1], C. Kocher[1], S. Segerer[1], R. Caduff[1], L. G. Wyler[1], V. Müller[1], B. Beck[2], J. Blum[2], J. Kamarchev[1], N. Müller[1]
[1]Zurich, [2]Basel

Purpose: The incidence of opportunistic infections during the first year after kidney transplantation is high due to the level of immunosuppression.
Methods and Materials: We report the course of a 73 year old Caucasian patient who had been treated with hemodialysis for 2 years, when he received a renal allograft from a diseased donor. About two months after transplantation he developed acute dyspnea due to a newly documented mitral insufficiency. Coronary angiography and transesophageal echocardiography did not provide a cause for valvulopathy. Percutaneous mitral valve repair did not improve the symptoms. Two months later he was admitted due to cardiac decompensation. A bronchoscopy with broncho-alveolar lavage was performed for evaluation of fever and a small pulmonary infiltrate on a CT scan.
Results: In the lavage Trypanosoma species were noted in special staining. Parasitemia was seen in blood smear and reactivation of the disease rather than transmission with the organ transplant was established by performing PCR and serology in donor and recipient. Despite the combined treatment with benznidazole and allopurinol and adequate decrease of the parasitemia, the condition of the patient deteriorated. Four months after transplantation and seven days after the start of antiparasitic treatment he died as consequence of cardiogenic shock. The autopsy confirmed disseminated trypanosomiasis with myocarditis.
Conclusion: *Trypanosoma cruzi i*s the pathogen of Chagas' disease, a zoonosis mainly prevalent in Latin America. Case reports in allograft recipients described either reactivation of previously infected recipients or infection via graft of a donor with a subclinical Chagas' disease. Our patient had never lived in an endemic area, but had traveled in South America. Given the rising number of transplantations in patients with a migration background and the mobility of our population reactivation of tropical diseases will likely become more common and specific screening procedures have to be considered.

18

Eculizumab Therapy in Acute Recurrence of Thrombotic Micro Angiopathy Associated with Anti-Phospholipid Antibodies after Renal Transplantation

K. Hadaya, S. Ferrari-Lacraz, D. Fumeaux, F. Boehlen, C. Toso, S. Moll, P.-Y. Martin, J. Villard
Geneva

Purpose: Renal thrombotic micro angiopathy (TMA) in systemic lupus erythematosus (SLE) is associated with the presence of anti-phospholipid antibodies (aPL). In his most fulminant form, TMA can rapidly lead to irreversible end stage renal disease. Recently, Eculizumab, anti-C5 monoclonal antibody, was successful to prevent recurrence of catastrophic anti-phospholipid antibody syndrome in a patient after renal transplantation.
Methods and Materials: We report the case of a 27-year-old woman with past history of one abortion that was referred for evaluation of end stage renal disease. Kidney biopsy showed severe TMA, complete glomerular scarring and diffuse tubule-interstitial fibrosis. The presence of aPL antibodies (lupus anticoagulant, IgG anti cardiolipine and IgG anti B2 glycoprotein type I), anti-nuclear and anti-nucleosome antibodies and a reduce level of C3 level was compatible with the diagnosis of fulminant TMA in a SLE patient in presence of aPL.
Results: After 10 months of dialysis, the patient underwent living related kidney transplantation. Immunosuppression was based on thymoglobulin induction, mycophenolate mofetil and methyl-prednisolone, without calcineurin inhibitors. The graft produced urine immediately. As serum creatinine remained at 172 µmol/L at day 6, a graft biopsy was performed. Isolated diffuse glomerular and arteriolar TMA was seen leading to daily plasma exchange, from day 7 to 10. The patient developed oligoanuria and weekly Eculizumab perfusion was administered under penicillin prophylaxis. Renal function improved after the third perfusion. Three months post transplant, serum creatinine is 100 µmol/L, without proteinuria. C3 level is within the normal range and aPL antibodies are undetectable. Graft biopsy revealed complete resolution of TMA without sequel.
Conclusion: This case report illustrates for the first time the effectiveness of Eculizumab therapy in a severe and early TMA recurrence, in the presence of aPL antibodies, after kidney transplantation.

Posters – Dialysis

19

Effect of Blockers of the Renin-Angiotensin System on Renal Tissue Oxygenation in Type 2 Diabetics as Measured by Bold-MRI

M. Pruijm, L. Hofmann, A. Zanchi, M. Maillard, V. Forni, M. Cassat, G. Wuerzner, B. Vogt, M. Burnier
Lausanne

Purpose: Previous studies have shown that acute intake of certain drugs alters renal tissue oxygenation, and animal studies suggest that blockers of the renin-angiotensin system might exert their renoprotective effect by correcting diabetes-induced renal hypoxia. The aim of this study was to investigate the chronic effect of the ATII- type 1 receptor blocker (ARB) candesartan, compared to the ACE-inhibitor (ACEI) enalapril on renal tissue oxygenation in type 2 diabetics with microalbuminuria and/or hypertension, using blood oxygenation level dependent magnetic resonance imaging (BOLD-MRI).
Methods and Materials: Ten patients (aged 63.8 ± 8.4 y, BMI 35.0 ± 3.0, 30% women) underwent BOLD-MRI at baseline, after one month of enalapril (20 mg/day), and after one month of candesartan (16 mg/day). BOLD-MRI was performed before and after intravenous administration of furosemide. Four coronal slices were selected in each kidney, and combination sequence was used to acquire T2* weighted images. The mean R2* values (= 1/T2*) were calculated, a low R2* indicating a high tissue oxygenation.

Results: Baseline characteristics and their changes are shown in the table. The mean cortical and medullary R2* did not differ significantly between groups (p trend = 0.88 and 0.24). Furosemide did not change cortical R2*, and decreased medullary R2* with 7.84 ± 2.6 s^{-1} at baseline, 7.45 ± 1.2 s^{-1} after candesartan, and 7.23 ± 2.6 s^{-1} after enalapril administration (p trend = 0.83).

	Baseline	Candesartan	Enalapril
SBP (mm Hg)	135.4 (10.2)	132.4 (12.2)	132.4 (10.5)
DBP (mm Hg)	74.4 (14.6)	72.4 (9.2)	73.0 (10.3)
Creatinine (µmol/l)	86 (67-186)	89 (58-210)	89 (64-202)
Clearance (ml/min)	105.4 (48.7)	99.8 (30.8)	99.6 (36.2)
Urinary sodium (mmol/24h)	198.6 (23.6)	185.0 (51.7)	174.0 (46.9)
HbA1c (%)	7.60 (0.9)	7.47 (1.07)	7.45 (0.8)
Medullary R2* (1/s)	28.5 (1.3)	27.9 (1.6)	29.1 (1.6)
Cortical R2* (1/s)	17.8 (1.5)	17.8 (1.4)	18.1 (1.7)

Conclusion: At the current stage, chronic intake of ACEI or ARB does not seem to alter renal tissue oxygenation in type 2 diabetics.

20

Epidemiological Trends in Maintenance Dialysis Treatment: 40 Years of Single Center Experience

P. Rhyn, M. Ambühl, D. Corleto, P. M. Ambühl
Zurich

Purpose: To analyze time trends in maintenance HD treatment with regard to epidemiology and mortality, and possible modifiers such as age, gender, treatment modality and transplantation.
Methods and Materials: Epidemiological data have been collected prospectively from all patients initiating dialysis treatment (HD: 795, PD: 160) at the Waidspital Zurich since its start of operation in 1970. A total of 964 patients were stratified into quartiles according to date of dialysis start ("decades": 1st: 1970–1979; 2nd: 1980–1990; 3rd: 1991–1999; 4th: 2000–2008). Follow-up was censored per December 31 2010.
Results:

	Patient characteristics according to decade of dialysis start (mean ± SD)				
	1970–1979	1980–1990	1991–1999	2000–2008	P (ANOVA)
Age at initiation, yr	48.0 ± 14	49.7 ± 16	55.1 ± 15	63.9 ± 16	0.000
Time to TPL, mo	27.2 ± 42	29.0 ± 33	29.2 ± 28	29.8 ± 34	0.934
Time to death, yr	8.3 ± 8	7.6 ± 7	5.8 ± 4	2.9 ± 3	0.000
3-/5-yr survival, %	62.5 / 38.8	65.8 / 44.4	64.8 / 43.1	46.0 / 25.3	ND

Overall 10-yr survival adjusted for age at time of initiation of dialysis was not significantly different when stratified for gender or therapy modality (HD versus PD). However, survival was significantly improved in patients being transplanted with a renal allograft.
Conclusion: Patient characteristics have significantly changed over four decades of maintenance dialysis therapy in a single Swiss center cohort. Advances in dialysis technology have not necessarily resulted in better patient survival. Although being an independent modifier older age at onset of treatment is not attributable solely for the worse outcome in more recent times. Survival is most likely influenced by increasing polymorbidity in patients with endstage renal disease.

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Effect of One Week Naproxcinod Treatment on Sodium Balance and Acute Natriuretic Effect of Furosemide: A Randomized Double-Blind Placebo and Naproxen-Controlled Trial in Healthy Volunteers

N. Glatz[1], G. Wuerzner[1], M. Maillard[1], B. Vogt[1], C. Roger[2], M. Burnier[1]
[1]Lausanne, [2]Sophia Antipolis/FR

Purpose: To evaluate the effects of Naproxcinod (CIN), a cyclooxygenase inhibiting nitric oxide (NO) donor on sodium (Na) balance and response to furosemide (FUR).
Methods and Materials: 31 healthy male volunteers were randomized into three parallel groups: CIN 750 mg *bid*, naproxen (NAP) 500 mg *bid* or placebo (PLA) *bid* during 8 days (D1-D8). 24h-Na and aldosterone excretions were measured from D-1 to D4. On D8, natriuresis, plasma renin activity (PRA), and glomerular filtration rate (GFR), using inulin clearances, were measured before and after 40 mg of intravenous FUR.
Results: On D-1 24h Na and aldosterone excretions were respectively 193 ± 34 mmol/24h and 5.2 ± 0.9 µg/24h for PLA , 174 ± 40 mmol/24h and 5.4 ± 0.7 µg/24h for CIN, 196 ± 54 mmol/24h and 6.5 ± 0.8 µg/24h for NAP. On D1 24h Na excretion was 182 ± 49 mmol/24h for PLA, 147 ± 34 mmol/24h for CIN, 140 ± 45 mmol/24h for NAP. On D4 aldosterone excretion was 6.2 ± 1.0 µg/24h for PLA, 2.9 ± 0.5 µg/24h for CIN, 2.7 ± 0.4 µg/24h. The table shows Na excretion, GFR and PRA before and after FUR on D8 (values are means ± SD).

Day 8		FUR (Baseline)	FUR + 60'	FUR + 120'
Natriuresis (mmol/h)	PLA	**38.2** ± 12.1	**136.5** ± 34.7	**53.5** ± 10.8
	CIN	**32.7** ± 5.2	**129.9** ± 17.5	**54.7** ± 21.3
	NAP	**27.2** ± 9.9	**131.2** ± 19.1	**54.8** ± 14.3
GFR (ml/min)	PLA	**117** ± 36	**105** ± 13	**108** ± 55
	CIN	**94** ± 22	**94** ± 20	**79** ± 24
	NAP	**103** ± 21	**96** ± 28	**79** ± 22
PRA (ng/ml/h)	PLA	**0.82** ± 0.52	**1.79** ± 0.91	**2.72** ± 0.81
	CIN	**0.32** ± 0.21	**0.84** ± 0.36	**1,37** ± 0.63
	NAP	**0.35** ± 0.19	**1.01** ± 0.49	**1.91** ± 0.89

Conclusion: CIN and NAP had some degree of Na retention (progressive decrease in 24h urinary aldosterone excretion) compared to PLA. After 8 days of treatment, no difference in Na excretions after FUR was detected between groups, but PRA response to FUR were slightly blunted in the CIN and NAP groups. Addition of NO moiety to naproxen does not seem to influence the Na balance or natriuretic response to FUR compared to naproxen alone in healthy volunteers.

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Renal Function Follow-Up Evaluation Measuring Cystatin C in Patients Prenatally Diagnosed for Congenital Kidney Malformation

P. Parvex, C. Combescure, J. Birraux, M. Rodriguez, A. Whilelm-Bals, E. Girardin
Geneva

Purpose: Congenital abnormalities of the kidney and urinary tract (CAKUT) account for 20% of all significant anomalies detected on prenatal ultrasound. Despite this frequent occurrence, no reliable method to measure renal function (RF) is validated in neonates. Cystatin C (CysC) has been proposed to be an accurate renal marker for the neonatal period. The aim of the study was to assess long term RF, using Cystatin C, prospectively from birth in neonates prenatally diagnosed with CAKUT
Methods and Materials: 21 patients (pts) with severe kidney malformation (KM) had renal function follow-up with the measure of CysC. Median follow-up was 235 (IQR: 137; 739) days. Gender ratio was 17 boys: 3 girls. KM were distributed as follow: 8 pts present unilateral KM, 12 bilateral KM. Among those 2 pts were diagnosed with TCF2 mutation and 3 with post urethral valves. 5 pts underwent interventions. One pt was started on dialyses and excluded from analyses. Factors influencing CysC were analyzed performing a linear mixed model to take into account the repeated measures.
Results: In our 20 pts, CysC decreased rapidly in the first month (M) (16.2%) p <0.001), slower between 1 M and 1 year (y) (3.9% per month, p <0.001) and stabilized after 1 y (0.2% per month, p = 0.83). CysC was significantly increased in pts with bilateral KM compared to pts with unilateral KM (p = 0.02) and in TCF2 pts (p = 0.002). The decrease of the CysC over time was less pronounced in pts with bilateral KM (p = 0.04) and in TCF2 pts (p <0.001), highlighting in these pts a worse prognosis in RF. Regression analyses for the other variables (gender, interventions, valves) were not significant.
Conclusion: Cystatin C was able to discriminate among neonates with congenital renal anomalies, those who were susceptible to present a worse prognosis in renal function.

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Ceftriaxone in Chronic Haemodialysis: Experience Fribourg Switzerland

O. M. Hemett, E. Descombes, V. Erard, C. Chuard
Fribourg

Purpose: Study objective.
Ceftriaxone is a third-generation cephalosporin with a broad spectrum activity against Gram Positive and Gram negative bacteria. The drug exhibits a long half-life and a concentration-dependent protein binding. No consensus exists on the dosing of the drug in hemodialysed patients. Demonstrate that the administration of 2 g of ceftriaxone /48 hours and 2.5 g/72 hours covers efficiently the time during which serum concentration are above the MIC90 of susceptible organisms in hemodialysed patient with infection.
Methods and Materials: Between 02. 2009 and 05 2011 all cases of hemodialysed patients with proven or probable infection and for whom ceftriaxone was considered as reasonable treatment were empirically treated with ceftriaxone 2 g/48H or 2.5 g/72H, according to the protocol in use in our center. For susceptible organisms, dosing of ceftriaxone was adapted according to the trough rate and/or MIC 90, when applicable. The determination of the residual rate of ceftriaxone was performed by using a high performance fluid chromatography.
Results: Twenty patients were treated with ceftriaxone, 10 presented with lung infection, 4 with skin infection, 4 with urinary tract i or gastrointestinal infection, 2 with vascular access or sinusitis Seven patients had microbiologically documented infection. The median MIC90 of organisms isolated was 0.25 mg/l (0,12–4) Of 20 patients 32 through rate of ceftriaxone was performed (median 1, range1–4). The median (range) through rate was 0.25mg/l (1,5–78). Large variability was observed in the same patient. The 32 through rates cover 100% of time of useful antibiotic of 50% of germs with MIC90 to the median and less than 4 mg/l (resistant to ceftriaxone).

Conclusion: To avoid hospitalization in chronic infected haemodialysis patients, ceftriaxone outpatient treatment can be instituted at rate of 2 g/48H and 2.5 g/72H.
References: 1 Nicolas Simon, et al. Population pharmacokinetics of ceftriaxone and pharmacodynamic consideration in haemodiallysed patients.

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Intracranial Arachnoid Cysts in Adpkd Patients

D. B. Poster, F. Krauer, U. Ahmadli, J. Bleisch, S. Kollias, A. L. Serra
Zurich

Purpose: Autosomal dominant polycystic kidney disease is the most common inherited renal affection and the most frequent cause of endstage renal disease at all. Showing a multisystemic feature ADPKD is widely known to appear with manifold cystic organ involvement. Furthermore there is a known intracranial manifestation with aneurysms and arachnoid cysts. Here we report on a case series of 15 patients of our ADPKD cohort affected with arachnoid cysts of the brain.
Methods and Materials: In our ADPKD cohort, patients who underwent cranial imaging were investigated for the existence of arachnoid cysts. A total number of 122 MRIs (11 follow-up included) and 3 CTs were conducted in 111 patients. The volumes of the arachnoid cysts were calculated by multiplication of the three measured diameters. Medical records of all patients were reviewed.
Results: Among 111 ADPKD Patients with brain imaging arachnoid cysts were identified in 15 cases (13.5%, 9 male, 6 female, mean age 39 y). Of ten patients with follow up imaging two women showed a volume increase after 2 and 1 year, respectively.Two male patients showed extreme dimensions of the lesions with cystic expansion nearly over the whole hemicranium. Most of the total 20 cystic lesions were localized in the posterior fossa (8 of 20) followed by middle (7 of 20) and anterior configuration (5 of 20). No patient showed clinical symptoms of arachnoid cysts.Three patients were diagnosed with intracranial aneurysms in addition, causing a subarachnoidal hemorrhage in one female.
Conclusion: We found a similiar incidence of arachnoid cysts in ADPKD patients as reported in literature. Lesions appeared anterior, middle and posterior in the brain. The absence of clinical symptoms seems to implicate a more benign behaviour of archanoid cysts compared to cysts in kidney or liver. However the cystic lesions can extent to bizarre dimensions.
References: Schievink (1995) “Intracranial cysts in ADPKD” J Neurosurg **83.**
Leung (2005) “Chronic subdural haematoma and arachnoid cyst in ADPKD” J Clin Neurosci **12.**

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Functional and Social Status, Actual and Perceived Social Support in a Population of Swiss Maintenance Haemodialysis (HD) Patients

G. Herfs[1], P. M. Ambühl[2], H. R. Räz[1]
[1]Baden, [2]Zurich

Purpose: To analyze a Swiss cohort of dialysis patients regarding functional and social status.
Methods and Materials: Established questionnaires were used in 157 maintenance HD patients to determine general and instrumental activities of daily life (ADL/IADL), social status (SAI: employment, education, subjective income, substance abuse, marital status, job position, insurance status), and current/desired (SSL-I/-D) social support. Asymptomatic depression was assessed to reduce confounding (GDS).
Results: Mean age was 69.7 years, participation 80%. IADL revealed dependencies mainly in performing laundry (54%), cooking (51%), shopping (45%) and other domestic work (33%). Dependencies in ADL were found in activities of personal hygiene (27%), stair climbing (23%) and bowel control (22%). SSL-I mean total score was 47 ± 2 out of 92. Conversely, perceived desired social support was high (SSL-D score 58 ± 9 out of 69). Depression (GDS) was slight or severe in 32 and 9%, respectively. SAI was low, comparable with US data, influenced mainly by the high percentage of retirement and patients with below average income. No significant correlation between level of social support and social status was detectable.
Conclusion: Swiss maintenance HD patients have a high level of instrumental and non-instrumental activities of daily life. Social status of our population is low, mainly due to retirement and perceived low income. Surprisingly, clear deficits of social support and signs of depression contrast with an unexpectedly high level of satisfaction. Clinical relevance of these data will be investigated prospectively.

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A Comparison between Pediatric Renal Biopsy Findings in Zurich and Armenia

A. Sarkissian[1], G. Laube[2], H. Nazaryan[1], A. Sanamyan[1], A. Babloyan[1], E. Leumann[2], A. Gaspert[1]
[1]Yerevan/AR, [2]Zurich

Purpose: The spectrum of renal biopsy findings varies considerably between different countries. However, criteria for performing biopsies and biopsy evaluation are not uniform and render interpretation of data difficult. We therefore compared biopsy data of native kidneys of children in Armenia and Switzerland, based on similar biopsy policy and joint work-up.
Methods and Materials: During the last 18 years (1993–2010) sufficient material for biopsy was obtained in 238 patients in Yerevan (EVN; age 1–18 years (11.1 ± 4.6); 56% males) and in 207 in Zurich (ZRH, age 0.1–17.9 years (8.7 ± 4.8); 63% males). Evaluation of biopsies from Armenia was done in EVN by light microscopy (LM). If amyloidosis was excluded by Congo red stain, the material was further examined in ZRH by LM, electron microscopy (EM) and immunohistochemistry (last 58 samples). Biopsies from ZRH were evaluated by LM, EM and immunofluorescence (IF).
Results: The most striking difference between both countries concerns the high frequency of amyloidosis due to familial Mediterranean fever (FMF) in Armenia (22% vs 0%) and of IgA-nephropathy/HSP in Switzerland (26 vs 7%). Certain forms of glomerulonephritis (GN) tended to be more frequent in Armenia than in Zurich: Membranoproliferative GN I (6 vs 4%), Membranous GN (5 vs 2%) and SLE (7 vs 4%). In contrast, the percentage of minimal change nephrotic syndrome (10%) and primary FSGS (10.5%) was identical at both places.
Conclusion: 1) The large number of amyloid nephropathy due to FMF in Armenia is alarming, 2) The far higher frequency of IgA-nephropathy in the Swiss as compared to the Armenian series was unexpected; it may partially be related to earlier referral and the availability of IF in ZRH and the heterogeneous population in Switzerland, 3) Certain forms of primary GN and SLE were observed more often in Armenia, 4) Long-term close collaboration allowed true comparison.

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Nutritional Counselling of Stone Patients by the Physician – Is it Worth the Hassle?

K. Günther, D. Tsinalis, I. Koneth, S. Schultes, I. Binet
St. Gallen

Purpose: Urine volume, salt and protein intake are modifiable risk factors for urolithiasis, and changing nutritional habits represents a crucial secondary prevention. We evaluated to which extent kidney stone patients modify these parameters after counselling by a nephrologist.
Methods and Materials: At our center kidney stone patients are evaluated by a 24-h urine collection and a nutrition protocol. Based on the findings they receive counselling by a nephrologist and written recommendations. After 6–12 months the urine collection is repeated. Between 2002 and 2011, 121 kidney stones patients were evaluated. 13 were excluded because of prior counselling elsewhere, 64 because the second urine collection was lacking and further 16 due to inconsistency of urine collections (>20% difference in daily urine creatinine excretion). Thus 28 patients were analyzed before and after counselling regarding urine volume, natriuresis for salt intake and urea excretion for protein intake.
Results: The 28 patients consisted in 20 males and 8 females; mean age was 42 (18–74) years. The second urine collection occurred after a mean of 7.6 ± 3.5 months after counselling. The mean urine volume increased non-significantly of 265 ± 738 ml/d. The mean natriuresis decreased from 210 ± 75 mmol/d to 183 ± 66 mmol/d ($p < 0.05$) representing about 10.7 g/d salt. Urea excretion did not change (406 ± 94 vs. 439 ± 153 mmol/d, p = NS) representing about 1.2 g/kg/d protein intake. The changes in all 3 parameters were independent of initial values, age, weight, gender and native language.
Conclusion: In conclusion a 3 to 4 hours counselling spent per patient by a nephrologist had no relevant impact on the fluid and protein intake in the small group of patients which could be analysed. There was a slight benefit regarding salt intake which remained however above the aim. The question is if a more rigorous and intensive follow-up with periodical assessments would be more successful.

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A Prospective Analysis of Falls in Patients on Maintenance Haemodialysis (MHD)

A. Rossier, R. Bullani, M. Silva Pereira, S. Dubrit, P. Viot, A. Van Ranst, M. Burnier, D. Teta
Lausanne

Purpose: We previously demonstrated that the incidence of severe falls in MHD patients was 0.22 per patient-year and that fractures complicated 54.8% of them (Rossier A et al. Nephrol Dial Transplant 2011;0:1–6). In order to implement a strategy to prevent falls, this new study aimed to characterize all falls, severe and not severe, and to establish possible relationships between HD sessions and the occurrence of falls.
Methods and Materials: The timing, location, cause, consequence and direct cost of each fall, which occurred in 2010 in our total MHD population, were collected prospectively through a weekly questionnaire. A fall was defined as an event resulting in a person coming to rest inadvertently on the ground; a severe fall as one requiring presentation to an emergency department.
Results: During a mean follow-up of 260 days, 35 of 88 patients (mean age 64.9 y) underwent 65 falls. Incidence of falls and severe falls were 1.04 and 0.22 per patient-year, respectively. Thirty falls occurred at home, 22 outside, 12 in the dialysis center and 1 at workplace. On dialysis days, 36.7% of falls (n = 30) occurred before, 3.3% during and 60.0% after the session. Among 18 falls which occurred within12 hours after a session, 9 took place in the center, 4 outside and 5 at home. Severe falls (n = 14) caused 4 fractures and 8 hospitalizations, which generated 66 hospitalization-days, reaching a total direct cost of CHF 47 545, and ultimately leading to 3 deaths.
Conclusion: The incidence of falls was >2 times higher in this MHD population than in a non-dialyzed geriatric population (Tinetti ME et al. N Engl J Med 1988;319:1701–7) and this generated adverse consequences and costs. The high incidence of falls occurring within 12 hours after the session suggests that the MHD treatment *per se* promotes them. Adjustments in the treatment prescription, together with appropriate management of high risk patients, after the session, may be required. Interventional studies aimed to reduce the incidence of falls are underway in our center.

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Immediate Peritoneal Dialysis (PD) After PD Catheter Placement and/or Abdominal Hernia Operation: Is There Still a Need for Temporary Haemodialysis

R. Chautems, V. Reinmann
Solothurn

Purpose: To avoid a temporary haemodialysis after a PD catheter placement and / or an abdominal wall hernia repair, we achieved a primary sealing of the peritoneum and began directly with a adapted PD (lower volume, frequent PD).
Methods and Materials: Between Mai 2003 and April 2010, 30 patients with kidney failure have had a PD catheter placement and / or an abdominal wall hernia repair. Among them 13 patients (11 men, 2 women, mean age 64.4 [39–81]) needed en emergency dialysis which had been started during the 48 hours after the operation. For 5 patients, the PD began after a catheter placement, for 7 after the hernia repair and for 1 after a synchronous PD catheter placement and hernia repair. The watertightness was tested during the operation.
Results: The PD could be started during the first 48 hours after the operation for the 13 patients. There was no leak for 12 patients. For 1 patient there was a suspected leak which was not confirmed after the surgical revision on post operative day 5. There was a local bleeding at the skin level around the catheter. There was an obstruction of the catheter by the great omentum which fixed by laparoscopy and the PD could be again started after 1 day.
Conclusion: Thanks to a concept which combines a primary peroperative watertightness and adapted PD volumes and frequency, we could avoid a temporary haemodialysis and hence the potential related morbidity by patients with kidney failure needing an emergency PD after PD catheter placement and / or a abdominal wall hernia repair.

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Small Solute and Ultrafiltration Kinetic Modelling in Capd Patients Using the Three-Pore Membrane Model – A Population Approach

R. M. Kalicki, D. E. Uehlinger
Berne

Purpose: Available computer-assisted support systems correctly describe the clearance of small solutes but fail to predict ultrafiltration (UF) with sufficient accuracy in CAPD patients. The aim of this work was to overcome this issue by implementing the more mechanistic three-pore membrane model, using a population approach.
Methods and Materials: Data from the 2nd and 3rd consecutive dwell of 242 CAPD patients (data on file, Fresenius Medical Care, Bad Homburg, GER) were analyzed by a non-linear mixed-effect approach using NONMEM. Observed UF, glucose and urea concentrations in the outlet were fitted to the three-pore membrane model using self-supplied differential equations and first-order estimation method. The ultrafiltration coefficient (LpS), the permeability surface area of small pores (PS) for urea and glucose respectively (PSSU, PSSG) were estimated. The peritoneal residual volume (VR), the intraperitoneal hydrostatic pressure (IP), the lymphatic flow (L), the less relevant permeability surface area of large pores for the urea and glucose (PSLU, PSLG) and the size and repartition of transcellular, small and large pores were fixed to values previously described in the literature. Interindividual variability (IIV) of estimated parameters and the residual error were best described by a proportional model.
Results: LpS, PSSU and PSSG were estimated to 0.12, 13.6 and 7.4 ml/min respectively. Their respective IIV variability was 19%, 48% and 25%. The correlation between PSSU and PSSG IVV was 0.28. The accuracy of the individual predictions decreased across observed compartments as follows: urea > glucose > UF. The high interoccasion variability (IOV) limited the convergence of the model to only two consecutive dwells when using parametric estimation methods.
Conclusion: The obtained estimates vary substantially from those described in the literature, indicating either their high variability across patient subpopulations or more probably their limited validity due to model complexity and overparameterization.

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Determinants of Bone Specific Alkaline Phosphatase, an Alternative Marker of Bone Turnover in Hemodialysis Patients

M. Tufail Hanel, A. Bock
Aarau

Purpose: Bone specific alkaline phosphatase (BSAP) has been suggested to be an excellent indicator of bone turnover with values <12.9 ng/ml predicting low turnover osteodystrophy.
Methods and Materials: To characterize the interdependence of BSAP and iPTH, we measured these parameters as well as ionized calcium and serum phosphate in a cross-sectional sample of our hemodialysis patients (n = 85), cross-correlated BSAP turnover categories (low: <12.9 ng/ml; "normal": 12.9–21 ng/ml; high: >21 ng/ml) with K/DOQI iPTH categories (<150 ng/ml: low; 150–300 ng/ml: normal; >300 ng/ml: high) and sought to identify factors affecting BSAP levels.
Results: BSAP and iPTH were correlated to some degree, but the BSAP and iPTH based bone turnover categories were hardly congruent. Of 31 patients in the BSAP-based "low turnover" group, only 3 were in the "low", 15 in the "normal" and 13 in the "high" PTH group. Of 30 patients in the BSAP-based "high turnover" group, 2 were in the "low", and 5 in the "normal" PTH group. Significant univariate correlations for BSAP were found with pre-dialysis phosphate ($r = -0.25$, $p = 0.023$), iPTH ($r = +0.32$, $p = 0.003$) and cinacalcet treatment ($r = +0.32$, $p = 0.005$). BSAP levels were higher in females (22.8 ± 2.4 [SEM] vs. 17.0 ± 1.3 ng/ml, $p = 0.023$). Multivariate analysis confirmed that iPTH ($p = 0.003$), serum phosphate ($p = 0.008$), gender ($p = 0.02$), and cinacalcet treatment ($p = 0.03$) were independently associated with BSAP. There was no association with age, ionized calcium, predialysis urea, nPCR or spKt/V. iPTH was negatively correlated with serum ionized calcium, but not with phosphate.
Conclusion: BSAP based and iPTH based classifications of uremic bone turnover show poor concordance. While the significant association of BSAP with iPTH is expected and the higher values in female dialysis patients have previously been described, the association of low serum phosphate with high BSAP and the relatively high BSAP values in cinacalcet treated patients have not been reported.

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Cardiac Function during Hemodialysis

S. A. Kalbermatter, D. Kiss
Liestal

Purpose: The assessment of dry weight is usually based on clinical signs like changes in blood pressure (BP) and history of dyspnoea, edema and orthostatic symptoms. Monitoring of body impedance (BIA) and changes in blood volume during hemodialysis (HD) has become popular. To evaluate cardiac function in different clinical situations we performed serial measurements of cardiac output (CO) during HD by an ultrasound dilution technique (transonic) in view of dry weight assessment
Methods and Materials: In 34 chronic HD patients (mean age 66.9y) we measured CO by transonic at the start after 120 and 240 min. of HD. BP, heart rate (HR), ultrafiltration rate and total ultrafiltration (UF) were recorded. Mean arterial pressure (MAP), stroke volume (SV),

cardiac index (CI) and total peripheral resistance (TPR) were calculated
Results: In relation to the UF – BP and MAP dropped continuously during HD. The interindividual fall in BP and MAP was sign. In spite of reduction of BP and MAP the HR remained unchanged. There was a wide range of SV at the start of treatment (32.1–129.4). During HD with UF – SV (71.9 to 57) and CI (2.9 to 2.1) fell significantly. The reduction of SV correlated with the amount of total UF. TPR increased from 17.4 mm Hg/L/min to 21.4. The increase in TPR correlated sign. with the reduction of the SV and total UF. The comparison of different age (<70y/>70y) groups revealed sign. differences in SV (81.3 and 67.3) at the start of HD. There was a tendency of smaller reduction of SV during HD in the pts. >70 y. The change of SV correlated with the amount of UF
Conclusion: In chron. HD pts. measurement of cardiac function by the transonic device during HD reveals impressive differences of SV at the start and during HD. In comparison with younger pts. older pts. have a sign. lower SV. Due to higher UF in younger pts. the fall of SV is more pronounced. According to the course of BD/MAP there is an adequate increase of TPR. The results give rise to the suspicion that common dry weight assessment should be improved

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Enhanced Suppressive Function of Tregs from Eskd Patients Using a New a High Cutoff HD Technique

P. Meier
Sion

Purpose: Considering the effect of oxLDL accumulation on Tregs viability and function in chronic HD patients, a new generation of protein-leaking dialyzers, with very large pores (i.e. HCO 1100 Gambro), could be useful to clear oxLDL and thus improve Tregs survival and function in this population. The aim of this study was to make *in vivo* assessments of several hemodialyzers (i.e. Polyflux 21 L – Polyflux 210 H [regular membranes: RM] *vs.* HCO [high cutoff] 1100) in plasma oxLDL clearing, and to analyze the Tregs suppressive function to restore the proper balance of immunity in ESKD patients.
Methods and Materials: Thirty ESKD patients on chronic HD (3 x 4 hours weekly) were studied in three equal groups during three months. Plasma and dialysate oxLDL concentrations were measured using a mAb-4E6–based ELISA. To determine the frequencies and phenotypes of $CD4^+/CD25^+/CD127^-$ Tregs, multicolor flow cytometry was performed. Apoptosis was indirectly assessed by Fas staining and flow cytometry.
Results: The RM exhibited elevated plasma level of oxLDL compared with HCO 1100 at three months (P = 0.002, ANOVA). In parallel, Tregs from patients on RM represented 1.34 to 1.73% of $CD4^+$ T cells whereas the frequency of Tregs in patients on HCO 1100 was 3.42 ± 0.19%; P <0.01. After PHA stimulation, increment in Tregs response was much more substantial in patients on HCO 1100 than in patients on RM. The apoptotic DNA fragmentation significantly increased in FAS-sorted Tregs from patients on RM compared with those on HCO 1100 (P = 0.005), in accordance with the decline in cell viability. Finally, Tregs from patients on RM did not efficiently suppress the proliferation of the co-cultured $CD4^+/CD25^-$ T cells (1:1; 21153 ± 2045 cpm) compared with Tregs from patients on HCO 1100 (1:1; 4172 ± 382 cpm; P <0.001).
Conclusion: In ESKD patients on chronic HD using HCO 1100, Tregs number, viability and suppression capacity were significantly improved compared with RM without significant side effects.

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Estimation of Dehydration with the Bioimpedance Technique in Children with Gastroenteritis

L. Dunkelmann, S. Tschumi, I. Pegiazoglu, A. Duppenthaler, G. D. Simonetti
Berne

Purpose: The estimation of the degree of dehydration is essential for the correct management of acute gastroenteritis. According to the clinical score of the American Academy of Pediatrics (AAP), patients are classified into three subgroups: mild dehydration (3–5% of body weight reduction), moderate dehydration (6–9%), and severe dehydration (>10%). The aim of the present study was to compare the clinical score of the AAP with the measurement of the body water content with a bioimpedance device.
Methods and Materials: Children aged between 0.5 and 10 with acute gastroenteritis were included in the study. Prior to fluid resuscitation, the clinical score of the AAP and the bioimpedance measurement (BCM-Monitor, FMC) were assessed.
Results: 26 children aged between 0.6 and 9.2 years (median 3.1 years, 14 females) were included. According to the clinical score of the AAP, 13 children had mild, 11 moderate and 1child severe dehydration. The bioimpedance measurement was not possible in one child. The median relative dehydration measured with the bioimpedance device was –5% of body weight (interquartile range –9.8 – 0.3%), which did not correlate with the clinical score. The impedance values (Ω), measured at 50 kHz, showed a linear correlation with the clinical score of the AAP ($r^2 = 0.30$, p = 0.004). The group of children with mild dehydration had significantly lower impedance values at 50 kHz compared to the group of children with moderate dehydration (p = 0.008). A cutoff set by 810 Ω is able to discriminate mild to moderate dehydration with a sensitivity of 91% and a specificity of 85%.
Conclusion: The results of this study demonstrate that the relative dehydration given by the device do not correlate with the clinical evaluation, however the impedance measured at a frequency of 50 kHz is able to discriminate the degree of dehydration. Further studies are needed to assess the clinical usefulness of these devices in the clinical practice.

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An Integrated Care Approach Using Electronic Compilation of Cinacalcet Adherence Data to Reach IPTH Targets in Hemodialysis Patients: A Multicenter, Randomized Trial

V. Forni[1], M. Pruijm[1], E. Tousset[2], G. Wuerzner[1], C. Zweiacker[1], I. Menetrey[1], L. Berwert[3], R. Bullani[1], A. Cherpillod[4], G. Halabi[5], L. Gabutti[6], C. Mathieu[4], T. Gauthier[7], P. Meier[8], O. Phan[9], S. Pianca[10], C. Schoenholzer[10], D. Teta[1], E. Violetti[10], B. von Albertini[4], B. Vrijens[2], H. Zwahlen[3], M. Burnier[1]
[1]Lausanne, [2]Visé/BE, [3]Bellinzona, [4]Lausanne, [5]Yverdon, [6]Locarno, [7]Vevey, [8]Sion, [9]Payerne, [10]Lugano

Purpose: Controlling secondary hyperparathyroidism (sHPT) in hemodialysis patients is cumbersome, partly due to patient's non-adherence to prescribed drugs. Medication Event Monitoring System (MEMS™) is a reliable approach to estimate drug adherence, but it is actually unknown whether it might be a way to improve the control of sHPT. The aim of this study was to assess whether an integrated care approach (IC) using cinacalcet adherence data leads to lower iPTH values and/or higher percentage of patients on pre-defined iPTH target, as compared to a usual care approach (UC).
Methods and Materials: This is a multi-center prospective randomized study including patients on chronic hemodialysis receiving a stable dose of cinacalcet for at least 1 month. Patients were randomized either to the UC approach in which adherence data were blinded or to an IC approach in which adherence data were used in the therapeutic decision process. iPTH, phosphate, and calcium targets, as well as the prescription of additional drugs were left to the discretion of the physician.
Results: 50 patients were enrolled and 41 were analyzed for the 6 months data. iPTH significantly decreased in the IC group: from median [iqr] 417 ng/l [352–622] to 339 ng/l [236–529] (p = 0.02) as compared to the UC group: from 419 ng/l [275–548] to 436 ng/l [288–682] (p = ns). In the IC group, mean adherence significantly improved (+10% IC vs. –5% UC; p = 0.008), and a higher percentage of patients achieved the nephrologists pre-defined iPTH targets (59% UC vs. 84% IC; p = 0.08). There were no significant differences in phosphate, total calcium, mean cinacalcet dose, vitamin D and phosphate binder between the groups at baseline and after 6 months.
Conclusion: An integrated care approach in which detailed electronically-compiled cinacalcet dosing history data are used to provide feedback to the hemodialysis patients led to improved adherence to cinacalcet and increased percentage of patients reaching iPTH targets. No significant reduction in cinacalcet dose was observed.

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High Prevalence of Anti-Apolipoprotein A-1 Autoantibodies in Maintenance Haemodialysis and Associations with Dialysis Vintage

M. Pruijm[1], J. Schmidtko[1], A. Aho[1], S. Pagano[2], P. Roux-Lombard[3], D. Teta[1], M. Burnier[1], N. Vuilleumier[2]
[1]Lausanne, [2]Geneva

Purpose: To establish the prevalence of anti-Apolipoprotein (Apo) A-1 IgG in patients with end stage kidney disease on maintenance haemodialysis (MHD), and to examine its correlation with inflammatory biomarkers related to atherosclerotic plaque vulnerability and vintage dialysis, a major determinant of arterial calcification and prognosis in MHD patients.
Methods and Materials: Single-centre, cross sectional study. Anti-ApoA-1 IgG levels and the concentrations of Interleukin-6 (IL-6), Interleukin-8 (IL-8), monocyte chemoattractant protein-1 (MCP-1), metalloproteinase-9 (MMP-9), Tumor Necrosis Factor-alpha (TNF-α), and C-reactive protein (CRP) were assessed in the sera of 66 MHD patients.
Results: In this MHD-population (mean age: 67.5 ± 14.5 years, 36% women, 32% diabetics), anti-ApoA-1 IgG positivity was 20%. Circulating levels of anti-ApoA-1 IgG correlated positively with dialysis

vintage, and iPTH levels, but not with cardiovascular risk factors or previous cardiovascular events; no significant correlations were found with circulating levels of IL-6 (r = 0.12, p = 0.36), IL-8 (r = –0.04, p = 0.76), MCP-1 (r = –0.01, p = 0.93), and MMP-9 (r = –0.006, p = 0.96). TNF-α (r = 0.24, p = 0.06), CRP (r = 0.23, p = 0.07), or LDL.cholesterol (r = 0.21, p = 0.10). In multivariable linear regression, adjusted for age, sex, and iPTH, only dialysis vintage remained positively and independently associated with anti-ApoA-1 titers (β 0.05, 95%CI 0.006;0.28, p=0.049).
Conclusion: Prevalence of anti-ApoA-1 IgG is raised in the MHD-population, and was positively associated with dialysis vintage, a major determinant of cardiovascular outcome, suggesting that antiApoA-1 antibodies may play a role in the pathophysiology of accelerated atherosclerosis in this population.

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Impact of Systemic Inflammation on Anemia Status and Management in Hemodialysis Patients – A 12 Months Interim Analysis of the Swiss "Motion" Survey

P. M. Ambühl[1], P. Meier[2], Z. Fumeaux[3], L. Gabutti[4]
[1]Zurich, [2]Sion, [3]Nyon, [4]Locarno

Purpose: A frequent complication in patients with kidney diseases, chronic anemia is commonly treated with erythropoietin stimulating agents (ESA). At present, the target for hemoglobin (Hb) concentration is 100–120 g/L. The objective of this analysis is to document factors that affect Hb control over time in hemodialysis (HD) patients in a clinical setting.
Methods and Materials: Multicenter, observational, non-interventional survey in HD patients. We present an analysis of pooled measurements of 378 patients. Each patient contributes 3 data points (baseline, 6, 12 months) to the analysis (n = 1134 data points) to assess the relationship between C-reactive protein (CRP) as an inflammation parameter and other anemia related parameters. Data are provided as mean (SD).
Results: Baseline mean age was 66 (14) years and mean weight was 73 (16) kg. Biochemical parameters were pooled: mean CRP of 15 (27) mg/L and serum ferritin of 475 (287) µg/L. For an arithmetic mean Hb concentration of 115 (13) g/L, darbepoetin alfa was administered at a dose of 41 (39) µg/week.

Table
Anemia treatment parameters according to CRP tertiles (mean ± SD):

	CRP <4 mg/L n = 282	4 ≤ CRP ≥11 mg/L n = 281	CRP >11 mg/L n = 271
CRP (mg/L)	2 ± 1	7 ± 2	38 ± 37
Serum ferritin (µg/L)	502 ± 281	476 ± 262	526 ± 338
Hb (g/L)	115 ± 12	116 ± 13	112 ± 14
ESA dose/ week (µg)	30 ± 27	36 ± 34	53 ± 47

Conclusion: For an Hb concentration in the recommended target range, a trend to higher ESA doses has been observed from the 1st to the 3rd CRP tertile. Therefore, monitoring CRP levels may support clinicians in their treatment of anemia in HD patients.
References: This study and abstract were sponsored by Amgen.

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Migraine Induced Kidney Stones?

L. Gerber, R. P. Wüthrich, N. Mohebbi
Zurich

Purpose: A 42-year-old woman was referred to our stone clinic for metabolic evaluation after two episodes of kidney stones with a composition of 90% apatite and 10% calcium oxalate.
Methods and Materials: She was suffering from migraine that was diagnosed four years ago, currently treated with topiramate. She had no family history of kidney stones. The physical examination showed no abnormalities. Her laboratory results revealed a hyperchloremic non-anion-gap metabolic acidosis, a marked hypocitraturia as measured by 24-hour urine collection (0.6 mmol/24h; norm 1.6–4.5) and a urinary pH of 7.0 with a positive urinary anion gap. All other laboratory parameters were normal and no hyperoxaluria or hypercalciuria could be detected. Thus, the diagnosis of nephrolithiasis due to renal tubular acidosis was made.
Results: To evaluate the cause of renal tubular acidosis we could exclude autoimmune diseases, other kidney diseases affecting tubular function such as medullary sponge kidneys or obstructive nephropathy and diseases associated with hypercalcemia or hypercalciuria. However, our patient had been taking 400 mg topiramate daily, a drug that has been shown to induce renal tubular acidosis and kidney stones. Since it is an excellent migraine drug, our patient refused to switch to a different regimen. Therefore our treatment consisted of citrate supplementation and dietary modifications, e.g. increasing the daily fluid intake to (at least) 2–3 liters and recommending a greater consumption of fruits and vegetables.
Conclusion: Topiramate acts as a carboanhydrase inhibitor in the proximal and distal tubules, leads to an increased bicarbonate excretion, a higher urinary pH and a RTA of a mixed (proximal and distal) type. Prescribing physicians should be aware of topiramate´s potential side effect and should monitor the patient´s plasma bicarbonate and potassium while on treatment. Patients on topiramate should be informed about the risks and should be advised of dietary modifications, e.g. increasing the fluid intake.

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A Curious Case of Acute Renal Failure (ARF) After Enteroclysis

T. Perrin, O. M. Hemett, M. Menth, E. Descombes
Fribourg

Purpose: A 57 y.o. woman was admitted to the ICU because of an acute rise of creatinine (67 to 134 µmol/l in 24h) with oliguria and drowsiness. She had a long history of intestinal resections and 2 stomies were made 4 months before. Since then, the patient had several episodes of severe infection, without any decrease in renal function (baseline creatinine: 45–50 µmol/l). 3 days before ICU admission, she developed fever with CRP elevation attributed to digestive translocation, and was treated with Imipenem 500 mg t.i.d. On the same day, an enteroclysis through the jejunostomy was performed with 300 ml of Iopamiro300 (= 90 g of iodine) and showed no intestino-peritoneal fistula. On ICU admission temperature was 37.3 °C, BP 110/70 mm Hg and HR 80 bpm. In the following hours, she remained hemodynamically stable and after rehydratation a normal diuresis resumed. However, creatinine continued to increase rapidly up to 481 µmol/l on day 6, with normalization within a month. To note, at ICU admission the urine sediment was normal while the urinary βNAG and lysozyme were markedly increased. Looking for a cause for ARF, it turned out that the radiologist noticed the presence of radiocontrast in the urinary tract during the enteroclysis. For this reason, 1 hour later, he performed a native abdominal CT which confirmed the presence of radiocontrast in both renal pelvis, ureters and bladder, without evidence of peritoneal resorption.
Methods and Materials: Case report.
Results: NA.
Conclusion: Although no iv-radiocontrast had been administrated, we diagnosed a *contrast-induced nephropathy*, based on the presence of radiocontrast in both urinary tracts, associated with a typical clinical and laboratory presentation and evolution. As no peritoneal resorption of radiocontrast was detected on CT, we assumed that its rapid absorption occurred through the intestinal mucosa, due to increased permeability presumedly caused by the local inflammatory state. This mechanism seems to be quite rare, as we have found no similar report in the literature.

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Hyponatremia and Hyperkalemia in a Newborn Boy as First Manifestation of a Complex Syndromal Disease

B. S. Bucher, G. Simonetti, B. Goeggel Simonetti, J.-M. Nuoffer, J. Lemke, C. Flück, S. Tschumi
Berne

Purpose: Muscular dystrophy, primary hypoaldosteronism, pseudohypertriglyceridemia and mental retardation may be associated as a contiguous gene syndrome in Xp21. It is characterized by congenital adrenal hypoplasia (CAH), Duchenne muscular dystrophy (DMD), glycerol kinase deficiency (GKD), psychomotor retardation and characteristic facies.
Methods and Materials: case report
Results: A newborn boy born at term, was referred to hospital for a weight loss of >10% after the first week of life. He presented in reduced general condition with severe hyponatremia (116 mmol/l) and hyperkalemia (6.5 mmol/l) without acidosis. Newborn screening was normal, aldosterone within normal range and renin extremely elevated supporting the diagnosis of primary hypoaldosteronism. Creatine kinase (CK) and triglycerides (TG) were massively elevated. Baseline plasma ACTH and cortisol were within normal range but cortisol did not respond appropriately to ACTH stimulation. The combination of CK elevation, primary hypoaldosteronism and hypertriglyceridemia (in fact a pseudohypertriglyceridemia) was suspicious for contiguous gene deletion syndrome in Xp21. Family history disclosed mental retardation in the patient's sister and mother. An array comparative genomic hybridization confirmed the diagnosis with a microdeletion Xp21 concerning the Duchenne muscular dystrophy –, glycerolkinase –, congenital adrenal hypoplasia – and x – linked mental retardation – gene. (DMD-, GK, NROB1-, IL1RAPL1- genes). A therapy with hydrocortisone, fludrocortisone and low fat diet was started successfully.

Conclusion: The combination of adrenal insufficiency and elevated CK as well as TG is highly suspicious for a contiguous gene deletion syndrome in Xp21. Even though it is a rare disease, the diagnosis is crucial for affected individuals because of potentially life threatening adrenal crisis early on and long-term consequences of DMD. Measurement of TG and CK in patients with adrenal insufficiency are simple screening tests that may facilitate early diagnosis.

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Iron Substitution in Absolute and Functional Iron Deficiency: Effect on Erythropoietin Resistance and Iron Parameters

J. Trachsler, S. Dimitrijevic, P. Koch, P. M. Ambühl
Zurich

Purpose: Reticuloyte hemoglobin content (CHr), percentage of hypochromic red blood cells (%HRC), soluble transferrin receptor (sTfR) and erythrocyte zinc protoporphyrin (ZPP) may better reflect iron availability than ferritin and transferrin saturation (TSAT).
Methods and Materials: We measured ferritin, TSAT, CHr, %HRC, sTfR, ZPP and erythropoietin resistance index (ERI) over six months in hemodialysis patients with absolute (ferritin <200 µg/L; A) or functional (ferritin >200 µg/L and TSAT <20%; B) iron deficiency receiving i/v iron saccharate (Venofer®).
Results: In 23 patients (A: n = 8, B: n = 15) receiving iron (mean: 1143 g; A: 1537 g, B: 913 g), ferritin rose from 282 to 573 µg/L (p = 0.000), and TSAT from 17.0 to 27.9% (p = 0.002). ERI (10.1 to 5.4; p = 0.049) and sTfR (4.6 to 3.1; p 0.008) decreased significantly in group A, but not in the whole population and group B. Surprisingly, %HRC rose in all pts. and group A, as well as ZPP in group B. Correlation was better for ERI with CHr, %HRC, sTfR and ZPP than with Ferritin and TSAT, most distinctively in group B (table).

		Ferritin	TSAT	CHr	%HRC	sTfR	ZPP
All pts.	ERI	–0.140*	–0.209**	–0.509**	0.464**	0.436**	0.520**
A	ERI	–0.373**	–0.316**	–0.632**	0.149	0.206	0.580**
B	ERI	–0.002	–0.110	–0.465**	0.587**	0.580**	0.517**

p <0.05; **p <0.01

Conclusion: Iron substitution therapy improved erythropoiesis in patients with absolute, but not functional iron deficiency. In functional iron deficiency CHr, %HRC, sTfR and ZPP may be valuable parameters in guiding iron therapy.

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Course of Hemoglobin and Iron Metabolism under Treatment with C.E.R.A. Once-Monthly. Twelve-Month Observational Analysis (RICH) of 22 Swiss Dialysis Centers

A. Komarek[1], D. Tsinalis[2], C. Schönholzer[3], O. Maurer[4]
[1]Reinach, [2]St. Gallen, [3]Lugano, [4]Interlaken

Purpose: In the RICH survey we analyzed dialysis patients (pts), treated with erythropoiesis stimulating agents (ESA) in dosing intervals of at least four weeks over a period of 12 months. The goal was to analyze the relationship between hemoglobin (Hb) and ESA dosing on one hand, and iron substitution and iron parameters on the other.
Methods and Materials: Multicenter, prospective analysis performed in 22 Swiss dialysis centers. Hb, iron parameters, ESA dose and CRP were collected at baseline (BL), month 6 and 12.
Results: A total of 242 pts participated in the analysis. For 209 pts complete data was available. Mean age was 70.4 (29-90) years; with 58.3% male and 41.7% female. Before BL 148 pts were treated with C.E.R.A., 39, 11, and 7 pts with Epoetin beta, Epoetin alfa and Darbepoetin alfa, respectively, and 4 pts were naïve. Hb remained stable over the course of treatment with 11.6 (± 1.1) g/dl at BL and 11.5 (± 1.1) g/dl at month 12. Average ESA dose at BL was 147 ± 91 µg/month and decreased to 125 ± 71 µg/month at month 12 (p = 0.14). In 131 pts complete data on iron status was available at BL. Transferrin saturation (TSAT; 26.0 ± 14.0% BL vs. 28.8 ± 12.6% M12; p = 0.09) and Ferritin (462 ± 340 µg/l BL vs. 520 ± 370 µg/l M12; p = 0.13) changed marginally. No significant change was seen in the iron substitution over the 12-month period (monthly dose 184 mg at BL vs 172 mg at M12; p = 0.13). The number of pts with insufficient iron status (Ferritin <200 µg/l or TSAT<20%) improved from 53% at BL to 20% at month 12. Low TSAT values were associated with high CRP (>5 mg/l) in 65% of these pts at BL and 78% at month 12.

Conclusion: Our analysis shows that Hb and C.E.R.A. dose remained stable over the course of treatment. Although iron status improved in pts with insufficient BL parameters, 20% remained with at least one value below K-DOQI criteria at month 12. In the majority of pts with low TSAT, these decreased values were associated with elevated CRP, suggesting functional iron deficiency associated with inflammation.

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Heterogeneity of Target Values for IPTH and Phosphate in Hemodialysis Clinical Practice in Italian- and French-Speaking Switzerland

V. Forni, M. Pruijm, I. Menetrey, C. Zweiacker, M. Burnier
Lausanne

Purpose: In the last decade two successive guidelines (KDOQI 2003, KDIGO 2009) have been published to assist nephrologists in decision making in the management of bone metabolism in CKD patients. We asked 9 Swiss dialysis centres to define their iPTH, phosphate and calcium target values, and assessed the influence of the guidelines on clinical practice.
Methods and Materials: Data were collected from a Swiss multicentre randomized trial comparing an integrated care approach using electronic pillbox monitoring of cinacalcet to a usual care approach to reach iPTH targets in hemodialysis patients. 9 dialysis centers (6 in French-, 3 in Italian-speaking Switzerland) agreed to participate. At the beginning of the trial, the investigators of each center were asked in a questionnaire to define their iPTH, total calcium and phosphate target values.
Results: For each center, target values are shown in the table. For iPTH, 3 centers followed KDOQI, 2 centers applied KDIGO guidelines, and 4 centers used personalized target values. For phosphate, 4 centers followed KDOQI, the others KDIGO propositions. No significant difference was observed for total calcium targets.

Center	Region	Target iPTH (ng/l)	Target iPTH (pmol/l)	Target iPTH nx ULN	Phosphate (mmol/l)	Calcium (tot) (mmol/l)
1	I	175–789 DIGO	18.6–83.7 DIGO	2.0–9.0	<1.60 DIGO	2.10–2.65
2	F	140–630 DIGO	15–67 DIGO	2.0–9.0	<1.80 DOQI	2.00–2.40
3	F	300–500	32–53	4.6–7.7	<1.50 DIGO	2.20–2.55
4	I	189–569	20–60	2.2–6.5	<1.80 DOQI	1.80–2.50
5	F	283–472	30–50	3.7–6.1	<1.50 DIGO	2.00–2.60
6	F	236–330	25–35	4.1–5.7	<1.40 DIGO	2.15–2.50
7	F	150–350 DOQI	16–37 DOQI	2.2–5.1	<1.80 DOQI	2.20–2.50
8	F	189–377 DOQI	20–40 DOQI	2.4–4.9	<1.45 DIGO	2.10–2.60
9	I	113–330 DOQI	12–35 DOQI	1.3–2.7	<1.70 DOQI	2.00–2.50

F/I = French/Italian-speaking; ULN = Upper Limit of the Norm

Conclusion: A lack of consensus exists among clinicians on bone disease targets. This heterogeneity reflects perhaps the lack of confidence and clinical evidence on which guidelines are based.

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Hemoglobin and ESA Dose Values in CKD Patients not on Dialysis after Switching to C.E.R.A.: Results from the Multicenter Observational Last Study

S. Franz[1], A. Corsenca[2], P. Meier[3], O. Phan[4], A. Komarek[1,], G. Meffert[5]*
[1]Reinach , [2]Zurich, [3]Sion, [4]Payerne, [5]Aarau

Purpose: C.E.R.A. allows treating renal anemia patients (pts) with a once monthly interval. In the LAST survey we analyzed data of CKD patients (pts) not on dialysis, treated with erythropoiesis stimulating agents (ESA) over 12 months.
Methods and Materials: Multicenter, prospective survey in 20 Swiss nephrology centers. Hemoglobin (Hb), ESA dose, iron parameters, and CRP were collected at Baseline (BL), month (mth) 6 and12.
Results: Out of 120 included pts, 103 had complete data. Before BL, 14 pts received epoetin beta, 32 darbepoetin alfa and 14 C.E.R.A. At BL 43 pts were ESA naive. At mth 12 all pts received C.E.R.A. Mean Hb value increased significantly from 10.8 g/dl to 11.3 g/dl (p = 0.0001) over 12 mths. Mean C.E.R.A. dose was stable (91.7 mcg at BL vs. 98.6 mcg at mth 12, p = 0.4). The estimated creatinine clearance (CrCl) decreased from 24.4 ml/min at BL to 20.9 ml/min

at mth 12 (p = 0.08). Ferritin was significantly higher at mth 12 vs. BL (331 ng/ml vs. 250 ng/ml, p = 0.01) while CRP lacked significant difference (11.7 mg/l vs. 7.3 mg/l, p = 0.1), suggesting a connection between ferritin increase and conscious iron management. CrCl and Hb levels correlated at BL (p = 0.01) but not at mth 12, likely due to treatment start in 40% naïve pts. 11 pts received C.E.R.A. in extended intervals up to 8 weeks. All pts reached stable Hb levels. Of 43 naïve pts, 38 had C.E.R.A. once monthly from start. Here, mean Hb increased from 10.0 g/dl (BL) to 11.8 g/dl (mth 12) (p <0.001) and mean C.E.R.A. dose increased slightly (81.8 mcg at BL vs. 95.0 mcg at mth 12, p = 0.2), with a mean of 2.85 dose changes.
Conclusion: Patients in Switzerland with CKD stages II-V and renal anemia had stable Hb levels and ESA dose under C.E.R.A. In nearly 90% of all ESA-naïve pts Hb levels were smoothly corrected to target levels with a once-monthly dosing interval. During maintenance, the frequency of C.E.R.A. was extended up to 8 weeks, providing stable Hb values. This allows physicians to adjust administration of C.E.R.A. to an individual patient schedule.

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A Very Atypical Pneumonia

S. A. Kalbermatter[1], G. Mansella[1], W. Zimmerli[1], F. Jüngling[2], D. Kiss[1]
[1]Liestal, [2]Basel

Purpose: A 46- year-old woman had a history of fever, cough and abdominal pain. She had been diagnosed with autosomal dominant polycystic kidney disease (ADPKD) in 1996. Physical examination showed tachypnea and a pulse rate of 98 bpm with a RR of 119/69. Her temperature was 38.7 °C. Percussion was dull in the basal region of the chest on both sides without any crackles in the auscultation. Abdominal examination showed palpable masses in the right and left upper quadrant with an epigastric tenderness.The chest X-ray (fig. 1) showed a consolidation at the right lower lobe. C-reactive protein (CRP) was 344 mg/L.
Methods and Materials: After diagnosing pneumonia an antibiotic treatment with amoxicillin-clavulanate was started. Five hours later the patient complained of increasing abdominal pain with strong epigastric tenderness on pressure. We decided to favour the differential diagnosis of a kidney or liver cyst infection and changed the antibiotic treatment to levofloxacin. The liver cyst infection was confirmed by an 18-F-Fluorodeoxyglucose (FDG) positron emitting tomography – computed tomography (PET-CT) (fig. 2). Besides clinical and laboratory follow up we repeated the PET-CT six weeks after antibiotic treatment was started. Antibiotic treatment was stopped after 11 weeks. Five weeks later the liver cyst showed only minimal activity.
Results: There is no reliable diagnostic tool to identify infected cysts in ADPKD. Even in magnetic resonance imaging (MRI) over 60% infected cysts can be missed. Recently PET-CT scans were used to detect sources of infections and also infected cysts. In a recent study, Sallé et al demonstrated that PET-CT-scans are very efficient to identify infected cysts in ADPKD.
Conclusion: FDG-PET-CT is a promising method to detect cyst infections in ADPKD.

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Patient Preferences on ESA Dosing Interval in Outpatient Treatment of Renal Anemia in Switzerland

A. Kneubühl[1,2], I. Koneth[3], D. Hertner[4], S. Segerer[1], P. Meier[5], A. Komarek[6]
[1]Zurich, [2]Lachen, [3]St. Gallen, [4]Schwyz, [5]Sion, [6]Reinach

Purpose: Disparities of dosing intervals of erythropoiesis-stimulating agents (ESA) could have a major influence on patient's quality of life by constraining their lifestyle. The aim of this survey was to gather patient preferences on ESA therapy in the outpatient setting of renal anemia.
Methods and Materials: Patients with outpatient anemia treatment (pre-dialysis, with peritoneal dialysis, or after kidney transplantation) were surveyed by nephrologists with a questionnaire during regular follow-ups.
Results: 114 patients (pts) were included in the survey, of which 97 received an ESA therapy. 38 pts were treated once-monthly, 10 Q3W, 23 Q2W, 14 QW, 1 every 10 days and 7 pts had a prolonged interval of up to 8 weeks (4 n.a.). 80% of pts preferred a once-monthly interval (main factors: decreased number of injections/less pain and increased convenience/comfort). Table 1 shows patients assessment of intervals in regard to 4 statements.

Table 1
Interval assessment regarding 4 statements.

	Patient preferences			
With the following interval…	Once-monthly	Q2W	QW	TIW
…the treatment would be simplified the most.	79.2%	12.3%	7.5%	1.0%
...my motivation to carry out all injections would be the highest.	79.8%	9.6%	9.6%	1.0%
…the risk of forgetting an injection would be the lowest.	64.6%	9.1%	25.3%	1.0%
…my life would be least constraint.	85.9%	8.1%	5.1%	0.9%

While 93% of pts currently treated with a prolonged interval (≥ once-monthly) would still choose the once-monthly treatment, 54% of pts currently treated in a shorter interval (≤3 weeks) would prefer once-monthly treatment. The vast majority of pts already treated in a monthly interval (89%) see the risk of forgetting an injection as lowest in the monthly interval.
Conclusion: The majority of patients included in this survey prefer a once-monthly interval over bi-weekly or once-weekly treatment due to pain or convenience related factors. The risk of forgetting an application due to prolonged interval does not seem to be an issue for patients already in a monthly or longer interval.

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Chronic Lymphocytic Leukaemia Associated with Paraneoplastic MPO-ANCA Positive Microscopic Polyangiitis

K. Hübel, F. Hitz, I. Koneth, I. Binet
St. Gallen

Purpose: We report a case of a patient with newly diagnosed MPO-ANCA positive microscopic polyangiitis who initially presented with a pulmo-renal vasculitic syndrome in association with a newly diagnosed chronic lymphocytic leukaemia (CLL). To the best of our knowledge this is the first report of such an association.
Methods and Materials: Our case report will summarize initial clinical presentation, diagnostics, treatment and follow up. In addition literature concerning CLL and autoimmune phenomenon and the rationale behind treatment will be discussed.
Results: A 70 year old woman presented with acute severe renal failure, constitutional symptoms, pulmonary haemorrhage and diffuse lymph nodes enlargement. Kidney biopsy showed pauci-immune segmental glomerulonephritis with fibrinoid necrosis. MPO-ANCA were positive at 26.8 U/l. A CLL was diagnosed by bone marrow aspirate, lymph node biopsy and FACS of peripheral lymphocytes. Therapy included plasma exchanges, 3 cyclophosphamide pulses, 3 steroid pulses followed by tapered oral prednison and 4 weekly courses of rituximab. After 9 months under low dose prednisone the patient is free of symptom and has no longer any lymphadenopathy. The eGFR improved from 8 ml/min at presentation to >60 ml/min/1.73 m^2 with normal urinalysis, ANCA are negativ.
Conclusion: In addition to a pulmo-renal vasculitis a chronic lymphocytic leukaemia was diagnosed and supposed to be the trigger of the ANCA-associated vasculitis, thus representing a paraneoplastic autoimmune phenomenon.

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Acute Kidney Injury Crossing the Border: Hantavirus Complicated with Acute Pancreatitis

T. Oettl, D. Kiss
Liestal

Purpose: We present the case of a 29 year old man hospitalized by his general practitioner (GP) with abdominal pain, vomiting and unclear thrombocytopenia. The history consisted of a short episode of fever and chills one week earlier, followed by progressive paraumbilical and back pain. In the emergency room, surprisingly, acute kidney injury (AKI) with a glomerular proteinuria and microhematuria was diagnosed.

Methods and Materials: Case report and clinical outcome of nephropathia epidermica including serologic and histologic work-up.
Results: The patient was on holiday in his home country of Macedonia 3 weeks prior to his first severe symptoms. One week after his return, he complained of lack of energy, two weeks later he had the above mentioned symptoms. No recent intake of NSAID. The GP diagnosed an unclear thrombocytopenia of 20/nl and treated for gastroenteritis. On clinical examination, we saw a young, hypovolemic man, stable blood pressure of 133/72 mm Hg, pulse 80/min, afebrile. Epigastric pain without signs of peritonitis, no petechial bleedings were seen. Main laboratory findings were creatinine 1151 umol/l, urea 52 mmol/l, potassium 4.4 mmol/l, pH 7.42, HCO3- 20 mmol/l, thrombocytes 73/nl, lipase 1300 U/l, albuminuria 2.8 g/d. No fragmentocytes. After rehydration and analgetic therapy, the patient clinically improved, the diuresis improved from 1l to 6l/d. The kidney biopsy showed only mild interstitial nephritis and rare interstitial hemorrhages. Serological testing showed positivity of IgM and IgG against Hanta virus (HV) type Dobrava. Despite normalizing renal function from day 5 on and absence of abdominal pain, lipase and amylase continued to rise during hospitalization.
Conclusion: Although the pathway of infection may be unclear, AKI associated with abdominal pain and thrombocytopenia makes a HV infection possible especially in the light of a travel history into countries of a known high prevalence. Acute pancreatitis in this setting is not the cause of AKI but a rare comorbidity of HV infection.

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Ninety-Six Months of Peritoneal Dialysis – And Still Going on: A Single Case with a Favorable Long-Term Course on Peritoneal Dialysis

S. Farese, V. Reinmann, P. Sandoz
Solothurn

Purpose: Long-term peritoneal dialysis (PD) is often hampered by membrane failure, peritoneal infections or other complications associated with this dialysis modality.
Methods and Materials: Here, we report a case of 72 year old woman who started PD in 2003. Despite a single episode of a *staphylococcus epidermidis* peritonitis in 2004 and a surgical mesh-reinforced correction of a periumbilical hernia in 2004, PD was never interrupted.
Results: Today, after ninety-six months (8 years) of continuous treatment with 4 exchanges/d of biocompatible PD-fluids (3 x 2 L glucose 1.5% and 1x2 L glucose 4.25%) dialysis is still performed through the same catheter, the peritoneal function is intact (KT/V_{urea} 2.32 /week, creatinine clearance 75 L/1.73 m^2/week, high average transporter for urea, low average for glucose), residual renal function is maintained (urine output 1.4 L/d), blood pressure is controlled and the patient presents in an excellent health condition.
Conclusion: In most PD patients a decline in membrane function and a concomitant failure of the dialysis modality is observed after a few years. However, selected patients present with favorable courses and can therefore be safely managed for even very long time periods by this technique.

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Silica and Glomerulonephritis, Just an Association?

O. Phan, P. Gardiol, B. O'Callagan
Payerne

Purpose: Causal links have been documented between silica and rheumatoid arthritis, lupus erythematosus, systemic sclerosis and glomerulonephritis. Two different effects of silica have been suggested, an enhanced inflammatory response in the pulmonary region: activation of alveolar macrophages and dysregulation of autoimmunity.
Methods and Materials: We present the case of a 58-year-old man, who had worked for processing quartz-containing stones for more than 5 years, complained of low-grade fever, thoracic pain, dypnea and rapid deterioration of renal function.
Results: Urinalysis on admission showed proteinuria (294 mg/day), microhematuria (20–30/hpf), RBC cast and granular cast, serum creatinine 179 µmol/l. Mediastinal lymph nodes were markedly swollen with pleuritis on chest computed tomography. Pericarditis was diagnosed without cinetic compromission. A renal biopsy showed diffuse crescentic glomerulonephritis. Immunofluorescence and electron microscopic studies showed no significant deposits in the glomeruli. Myeloperoxidase-antineutrophil cytoplasmic antibody (ANCA) was positive. After a 6 month treatment with glucocorticoids and cyclophosphamide, radiological findings were minimal and stable, the renal function improved and microhematuria was resolved.
Conclusion: An occupational history must be obtained for all renal patients, checking particularly for exposure to silica, heavy metals, and solvents. Environmental triggers are thought to play a role in the development of an idiopathic expression of systemic autoimmune disease. In conclusion, at present there is evidence that occupational exposure to silicon-containing compounds could be related to the development of ANCA-associated glomerulonephritis and vasculitis, and silica is one of the first well-documented environmental triggers in these diseases.

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Case Report: Severe Renal Failure Due to Adrenal Insufficiency

H. Elsässer, W. Zimmerli, D. Kiss
Liestal

Purpose: Adrenal manifestation of recurrent urogenital Tuberculosis is a rare cause of renal insufficiency
Methods and Materials: Case report and discussion of the pertinent literature
Results: We report the case of a 73-year-old retired school-teacher who complained of increasing fatigue since 6 weeks. In addition, he reported increased thirst, loss of weight (–9 kg), nausea and vomiting. He presented in good nutritional condition (BMI 21), afebrile, dehydrated and hypotensive (90/65 mm Hg). A diffuse bilateral supraclavicular, and monolateral axillar and cervical lymphadenitis was observed. Initial laboratory findings revealed normal blood cell counts, severe renal insufficiency (s-creatinine 292 µmol/l ≈ eGFR (MDRD) 19 ml/min), moderate hyponatremia (132 mmol/l) and hypokaliemia (5.5 mmol/l) and only slightly elevated CRP (20 mg/l). Abdominal CT scan showed a tumor of the left kidney and enlarged adrenal glands. The findings led to the initial presumption of metastasing renal cell carcinoma. In consideration of the clinical course, laboratory findings and CT imaging, additionally (sub) acute primary adrenal insufficiency was suspected. The latter presumption was confirmed by diminished fasting cortisol-concentration (61 nmol/l [171–800 nmol/l]), diminished aldosterone- and renin-, as well as elevated ACTH-concentrations (88.5 pmol/l [2–11.5 pmol/l]). Hydrocortisol and fludrocortisol was started and the physical condition of the patient improved markedly. Left nephrectomy and adrenalectomy was performed. Surprisingly an oncocytoma and distended adrenal caseate tuberculoid necrosis was found. Tuberculostatic therapy was established for one year. Surgery as well as tuberculostatic and adrenal replacement therapy was well tolerated. Renal function significantly improved (eGFR (MDRD) up to 35 ml/min). In the following years the patient was in in good mental and physical condition. He died in his late 70's from sudden cardiac arrest while gardening.
Conclusion: Adrenal insufficiency is a rare and reversible cause of renal insufficiency.

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Nephrotic Syndrome and Knee Pain

I. Grendelmeier, M. Filipowicz, D. Kiss
Liestal

Purpose: A 55-year–old patient was brought to our emergency room following a collapse. He had been well except for increasing limb oedema over the past few weeks. The patient's medical history revealed a long standing history of psoriatic arthritis treated with Methotrexat and Prednison.The clinical and laboratory evaluation during admission revealed oedema of the lower limb, hypokalemia (2.2 mmol/l), moderate renal insufficiency,hypalbuminemia (18 g/l) and hypercholesterinemia (8.4 mmol/l). The spot urine showed proteinuria in the nephrotic range (17 g/d).
Methods and Materials: Renal biopsy revealed AA-Amyloidosis which was likely to be secondary to the psoriatic arthritis and we went in more detail about the patient's history which revealed only few symptoms of knee pain and painful finger joints at the onset of the disease. But the review of the CRP over the past 20 years showed high values between 14 and 160 mg/l and X-ray of the hand was typical for destructive psoriatic arthritis. The serum Amyloid concentration was increased with 555 mg/l (normal <6.8 mg/l).
Results: Anti TNF alpha therapy with Etanercept in combination with prednisone was started. The CRP value returned to normal but the patient's kidney function worsened and he developed multiple pulmonary embolisms. Despite adequate anticoagulation the patient died one week after beginning of anti TNF-alpha therapy.
Conclusion: AA-Amyloidosis is the result of deposition of amyloid fibrils derived from acute phase reactant serum amyloid A (SAA) as a complication of many chronic inflammatory disorders. Renal prognosis and mortality correlate with the total amyloid burden quantified and monitored by Serum Amyloid A protein concentration and/or Serum Amyloid P (SAP) component scintigraphy. If inflammation remains uncontrolled, 50% of patients die within 10 years after diagnosis. Primary goal of treatment is to control the inflammatory disease to suppress the production of SAA. Yet likely, chronic psoriatic arthritis remains a rare cause of AA-Amyloidosis.

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Intraperitoneal Application of Ceftriaxone for Longterm Antimicrobial Treatment of Pulmonary Nocardiosis

P. Grosse
Basel

Purpose: ***Background:*** Peritoneal application of certain antibiotics has been shown to be successfully used in treating systemic infectious diseases.
Methods and Materials: Clinical case report
Results: ***Case:*** 41 year old, HIV positive woman admitted due to pneumocystis pneumonia. Incidental finding of co-infection with nocardia species. Discontinuation of first-line treatment for pulmonary nocardiosis with cotrimoxazol and establishment of intraabdominal ceftriaxone with consecutive clinical improvement.
Conclusion: To our knowledge there are no case reports so far describing the intraabdominal application of ceftriaxone in the treatment of pulmonary nocardiosis. We hope to encourage the use of ip-administration of suitable antimicrobial agents in CAPD patients for making ambulatory treatment of systemic infections more feasible.

Posters – Hypertension

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11-Year Trends (1999-2009) in Major Modifiable Chronic Kidney Disease Risk Factors in the Geneva Population

I. Guessous[1,2], M. Bochud[2], J.-M. Gaspoz[1], A. Pechère[1]
[1]Geneva, [2]Lausanne

Purpose: To report the 11-year trends in major modifiable CKD risk factors in the Geneva population.
Methods and Materials: Population-based health study (Bus Santé) of a representative sample in the Canton of Geneva, Switzerland. Blood pressure (BP) was measured thrice using validated devices. Hypertension (HTN) was defined as mean systolic/diastolic S/DBP ≥140/90 mm Hg or presence of anti-hypertensive medication (HTN Rx). Diabetes was self-reported. Obesity was defined as a measured BMI ≥30 and sedentarity as ≤10% total daily energy expenditure (kcal/day) spent in 4 or more METs. Multiple (age, HTN, diabetes, BMI, phyisical activity level (kcal/day), alcool consumption (kcal/day), smoking, education level) linear regression was used to assess annual changes and p value for trends.
Results: We analyzed 9320 subjects (50% women) aged 35–74 years (37.2% aged >55) between 2001 and 2009. In men aged >55, HTN prevalence increased from 1999 to 2009 (adjusted annual change +3.7% (95%CI 0.1–7.1, P = 0.04), which was mainly driven by increased HTN Rx use (+7%, 3.2–10.9, P <0.001)), while no change was reported for women or younger men. The adjusted (including HTN Rx use) annual change in mean SBP remained stable in men age >55 and women aged <55. It decreased in women age >55 (beta coefficient β = –0.62, P <0.001) and increased in men aged <55 (β = 0.34, P <0.001). The adjusted annual change in mean DBP decreased in all groups (range of β, –0.22 to –0.71 mmHg/year). In all groups, diabetes, obesity, and sedentarity prevalences did not change. Smoking prevalence decreased in men and women aged >55 years (adjusted annual decrease: 4.0% (1.4–6.5, P = 0.003) in men and 4.1% (1.5–6.6, P = 0.02) in women) and remained stable in younger participants.
Conclusion: 11-year data showed that HTN increased in men aged >55 and that smoking decrease in men and women aged >55, while other CKD modifiable risk factors remained stable. Most of the increase in HTN prevalence is explained by increased HTN Rx use.

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Palatability of Crushed Beta–Blockers, Converting Enzyme Inhibitors and Thiazides

L. Zgraggen[1], P. B. Faré[1], S. A. G. Lava[1,2], G. D. Simonetti[2], M. G. Bianchetti[1]
[1]Bellinzona, [2]Berne

Purpose: A problem that often affects antihypertensive drugs is the lack of formulations appropriate for childhood. Parents therefore crush tablets and administer the antihypertensive drug mixed with solid food or a palatable drink. It is well known that palatability represents one of the major factors affecting compliance to drugs, especially in childhood. The palatability of crushed ß–blockers, converting enzyme inhibitors and thiazides was therefore assessed among adult volunteers.
Methods and Materials: The palatability of crushed atenolol, bisoprolol, enalapril, lisinopril, ramipril, chlorthalidone and hydrochlorothiazide was evaluated among 20 (12 female and 8 male subjects) blinded healthy adult volunteers by means of a facial hedonic scale that depicted 5 grades of pleasure. For purposes of comparison, the calcium channel-blockers amlodipine (which is poorly appreciated in childhood) and lercanidipine (which is appreciated in childhood) were also tested. A concealed random allocation procedure was used.
Results: The palatability scores assigned to chlorthalidone, hydrochlorothiazide and lisinopril were superior (P <0.002) to those assigned to atenolol, bisoprolol, enalapril and ramipril. Like in childhood, the palatability score of lercanidipine was superior to that of amlodipine (P <0.002). No significant score differences were found between women and men.
Conclusion: The taste differences of the tested drugs might provide useful information in the selection of a pulverized antihypertensive agent in pediatric clinical practice.

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Important Differences in Acid Uric Levels and Risk of Hyperuricemia in Linguistic Regions of Switzerland

I. Guessous[1,2], D. Hayoz[3], P. Greminger[4], A. Gallino[5], P. Erne[6], on behalf of the Swiss Survey on Salt Group[7]
[1]Geneva, [2]Lausanne, [3]Fribourg, [4]St. Gallen, [5]Bellinzona, [6]Lucerne

Purpose: Association between serum uric acid (SUA) and CVD has been demonstrated. We investigated the level of SUA, the prevalence of hyperuricemia (HU), and their determinants in a representative sample of the Swiss population.
Methods and Materials: We analyzed data from the Swiss Salt Study, a population-based study conducted in the three linguistic regions. Possible determinants of SUA levels were assessed by questionnaires or measured. HU was defined as SUA levels ≥420 and ≥320 µmol/L in men and women, respectively. Adjusted median and logistic regressions were used.
Results: We analyzed 1'248 participants. The SUA medians (IQR) were 347 (304–395) in men and 251 (216–290) µmol/L in women. The prevalence of HU was 25.2% (21.9–28.5) in men and 18.7% (15.8–21.5) in women, with differences across linguistic regions; 25.7%, 28.3%, and 13.3% in the French, German, and Italian regions in men (p <0.01), and 20.1%, 21.6%, and 5.4% in women (p <0.001). In men, the risk of hyperuricemia increased with BMI (adjusted odds ratio OR, 1.17 [1.00–1.05]), systolic BP (OR = 1.03 [1.00–1.05]), heart rate (OR = 1.03 [1.00–1.05]), beer consumption (OR = 1.06 [1.00–1.11]), and decreased with age (OR for every 1 year increase = 0.95 [0.93–0.97]), diastolic BP (OR = 0.95 [0.92–0.98]), and CKD-epi (OR = 0.94 [0.92–0.96]). In women, the risk of HU increased with BMI (OR = 1.17 [1.10–1.24]), beer consumption (OR = 1.61 [1.13–2.29]), and decreased with CKD-epi (OR = 0.96 [0.93–0.98]). Compared to women in the French and German linguistic regions, the adjusted risk of HU was lower among women in the Italian linguistic region (French OR = Ref, German OR = 0.66 [0.33–1.32], and Italian linguistic region OR = 0.24 [0.06–0.94]).
Conclusion: The prevalence of HU is high in Switzerland and important differences in HU prevalences across linguistic regions exist, with the lowest prevalence in the Italian linguistic region. Even after adjustment for major confounders, women in the Italian linguistic region have a 70% lower risk of HU than women in the French linguistic region.

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Prevalence of Chronic Kidney Disease in the Population-Based Swiss Survey on Salt

V. Forni[1], N. Glatz[1], D. Conen[2], H. Stettler[3], F. Paccaud[1], M. Burnier[1]
[1]Lausanne, [2]Basel, [3]Zurich

Purpose: Chronic kidney disease (CKD) is an important burden in the general population and an independent marker of cardiovascular morbidity and mortality. Population-based data are scarce in Switzerland. We aimed to reassess the prevalence of CKD and its determinants in the general Swiss resident population, using the recently validated CDK-EPI equation.
Methods and Materials: The cross-sectional population-based Swiss Survey on Salt included a random population-based-sample of 1377 individuals from the three linguistic regions of Switzerland, assessed between 01.2010 and 07.2011. Data from 1247 subjects (605 men and 642 women) aged 15–95 years, were available for the present analysis.The estimated glomerular filtration rate (eGFR) was obtained

using the CKD-EPI equation. Subjects with CKD Stage 3 to 5 according to NKF KDOQI (eGFR <60 ml/min/1.73 m^2) were considered for the analysis. We used multiple logistic regression to analyze the determinants of CKD Stage 3–5, including age, sex, BMI, smoking and diabetic medication use.
Results: The total prevalence of CKD Stage 3–5 was 7.7% (7.5% stage 3, 0.2% stage 4, 0% stage 5). By age group, CKD Stage 3–5 was more prevalent among persons aged ≥60 years (21.7%) than persons aged 45–59 years (2.4%), 30-44 years (0.3%) or 15–29 years (0%). There were no significant gender differences, with an overall prevalence of 6.4% in men and 7.5 % in women, 21.9% and 21.5% in men and women ≥60 years respectively. Prevalences across the linguistic regions were similar. In multiple logistic regression analysis, age (OR [95%CI] =1.13 [1.10–1.16], p <0.001) and diabetes medication use (OR [95%CI] = 2.42 [1.03–5.63], P = 0.041) were significantly associated with CKD Stage 3–5.
Conclusion: This study indicates a total CKD Stage 3–5 prevalence of 7.7% in the Swiss population aged ≥15 years, with no differences between sex and linguistic region. Age and diabetes medication use, but not gender, BMI, hypertension and smoking, were independent determinants of CKD Stage 3–5.

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11-Year Trends (1999–2009) in Hypertension Awareness in the Geneva Population

I. Guessous[1,2], M. Bochud[2], J.-M. Gaspoz[1], A. Pechère[1]
[1]Geneva, [2]Lausanne

Purpose: To report the 11-year trends in awareness of having arterial hypertension and its determinants in the Geneva population.
Methods and Materials: Population-based study (Bus Santé) of a representative sample in the Canton of Geneva, Switzerland. Self-reported notion of hypertension (HTN)/using anti-hypertensive drug was compared to HTN based on blood pressure (BP) measurements. BP was measured thrice using validated device and HTN defined as mean systolic/diastolic BP ≥140/90 mmHg. Diabetes was self-reported. Sedentarity was defined as ≤10% daily energy expenditure (kcal/day) spent in 4 or more METs. Adjusted (age, HTN, diabetes, BMI, phyisical activity level (PAL) (kcal/day), alcool consumption (kcal/day), smoking, education level) logistic regression was used to assess the associations of survey year and other determinants (accounting for secular trends) with HTN awareness.
Results: We analyzed 9320 subjects aged 35–74 years between 2001 and 2009. Overall, 34.4% (3199) had HTN (self-reported or measured). 34% of the participants with HTN were not aware of having HTN. This prevalence decreased from 37.6% to 16.7% between 1999 and 2009 (41.1% to 16.8% in men and 32.4% to 16.4% in women). The adjusted risk of being unaware of having HTN decreased with survey year (OR = 0.88, 95%CI 0.85–0.91, trend p <0.001, in men; OR = 0.90, 0.86-0.94, <0.001, in women), continuous BMI (OR = 0.88, 0.85–0.91 in men; OR = 0.97, 0.94–1.00, in women) and diabetes (OR = 0.36, 0.25–0.51 in men; OR = 0.48, 0.28–0.83 in women). In men, smokers were more likely to be unaware of having HTN than never/exsmokers (OR = 1.30, 1.02–1.66). In women, increased PAL was associated with increased risk of being unaware of having HTN (OR = 2.38, 1.21–4.71). HTN awareness was not associated with education level.
Conclusion: HTN awareness considerably increased between 1999 and 2009. Efforts made at the individual/population levels seemed to have succesfully improved awareness in the general population of Geneva. Smokers remain more likely to be unaware of having HTN.

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Estimation of Salt Intake in Switzerland Using 24-Hour Urine Collection

A. Chappuis[1], L. Gabutti[2], I. Binet[3], I. Guessous[1,4], P. Erne[5], M. Bochud[1]
[1]Lausanne, [2]Locarno, [3]St. Gallen, [4]Geneva, [5]Lucerne

Purpose: The Swiss Federal Office of Public Health has launched a salt strategy, the main objective of which is to reduce population dietary salt intake to 8 g/day in the period 2008–2012 and achieve WHO-recommendation of <5 g/day on the long run. We conducted a national survey to estimate salt intake in the population living in Switzerland aged 15 years and over.
Methods and Materials: The population-based survey included 11 study centers, covering 9 cantons and the 3 main linguistic regions. Participants were recruited using a 2-level sampling strategy. Subjects collected 24-hour urine; collections <300 ml were excluded from the analysis (n = 3). Urinary sodium was measured using indirect potentiometry. The study is still ongoing, these results are therefore preliminary.
Results: Data from 662 men and 696 women out of 1377 participants were available for the analysis. The mean (sd) urinary salt excretion was 10.6 (4.2) g/24h in men and 7.8 (3.3) g/24h in women (p <0.001). In the 15–29, 30–44, 45–59 and ≥60 year-old groups, salt excretion was 9.8, 11.0, 11.4 and 10.1 g/24h in men and 7.9, 8.1, 8.2 and 7.0 g/24h in women. The age-, sex-, and BMI-adjusted mean urinary salt excretion in the German-speaking region (9.4 g/24h) was higher than in the French- (8.7 g/24h) but similar to the Italian (9.2 g/24h) speaking region. Cantons of Luzern and St.Gallen had significantly higher salt excretion (mean 9.8 g/24h) than Zürich and Basel (mean 9.0 g/24h), which highlights heterogeneity within the German-speaking region. A large proportion of men and women had a urinary salt excretion above the WHO recommendation of 5g/day (93.8% and 79.0% resp, p <0.001); 71.0% of men and 41.2% of women (p <0.001) were also above the national short-term objective of 8g/day.
Conclusion: Similar to what is found in other Western countries, 24-hour urinary salt excretion, which reflects dietary salt intake, is above the recommended thresholds in a large part of the population of Switzerland, especially in men and middle-aged people.

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Knowledge on Salt-Related Health Conditions in Switzerland

H. Stettler[1], A. Chappuis[2], P. Suter[1], P. Erne[3], P. Meier[4], F. Paccaud[2]
[1]Zurich, [2]Lausanne, [3]Lucerne, [4] Sion

Purpose: The Swiss Federal Office of Public Health has launched a strategy to reduce dietary salt intake in the Swiss population (2008–2012). Within this framework, it is important to assess knowledge on salt-related health conditions.
Methods and Materials: Cross-sectional population-based survey in 11 Swiss centers. Participants (≥15 years old) were recruited using a 2-stage sampling strategy. A standardized questionnaire included questions on knowledge on salt intake and related health conditions. Participants collected 24-hour urine.
Results: The 656 men and 693 women had mean (SD) age 49(18) and 48(18) years. Urinary salt excretion went from 6.4 to 10.0 g/24h in women, and from 9.7 to 11.7 g/24h in men who reported very low to very high salt intake, respectively (P ≤0.0 01). Those reporting a high salt intake had higher odds of having urinary salt excretion over 5 g/24h (OR [95%CI] = 6.27 [2.19–17.9]) than those reporting low intake. Three out of four participants believed that high salt intake may impact on health. Salt intake was related to hypertension by 81% of participants, to stroke by 21%, to cardiac diseases by 40% and to myocardial infarction by 21%. More than 90% of participants correctly classified several conditions as being unrelated to dietary salt intake. For most questions, German-speaking participants had lower knowledge on salt-related health conditions. Older age, female sex and Italian language were associated with higher odds of correctly reporting the maximum recommended dietary salt intake (5 g/24h). People with older age, female sex, non-German language and lower education level were more likely to report trying to limit their salt intake.
Conclusion: Knowledge on salt and salt-related health conditions is moderate-to-high in this population. Further health education campaigns are likely to have only limited impact on salt consumption. However, there are substantial differences across linguistic regions and sex that should be taken into consideration when designing the salt-related policies.

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Association between High Blood Pressure and Family History of Hypertension in Switzerland

N. Glatz[1], P. Erne[2], R. Meier[3], T. Schoen[4], I. Binet[5]
[1]Lausanne, [2]Luzern, [3]Sion, [4]Basel, [5]St. Gallen

Purpose: Having a first-degree relative suffering from high blood pressure (BP) is an independent risk factor for hypertension (HT). We used data from the Swiss Survey on Salt, a national population-based survey, to explore associations between HT and self-reported family history of HT.
Methods and Materials: The survey included 11 centers, covering 9 cantons and the 3 main linguistic regions. Participants aged 15 years and over were recruited using a 2-stage sampling strategy. We measured BP using an oscillometric BP device 5 times during each of the 2 study visits. The first measure of each visit was excluded and HT was defined as mean systolic BP (8 measures) ≥140 mm Hg or mean diastolic BP (8 measures) ≥90 mm Hg or self-reported current anti-hypertensive treatment. A standardized questionnaire included questions on parents and siblings history of HT.
Results: Data from 667 men and 703 women out of 1377 participants were available for this analysis. The proportion of subjects reporting a positive maternal history of HT was 23.7% a paternal history 20.9% and a sibling history (at least one) 11.3%. In multiple regression analysis with sex, age and BMI as covariates, reported high BP in

the mother (OR[95%CI] = 1.88 [1.33–2.66], p <0.001), in the father (OR[95%CI] = 1.59 [1.09–2.31], p = 0.016), in siblings (OR[95%CI] = 2.08 [1.36–3.19], p = 0.001) or in at least one first-degree relatives (OR [95%CI] = 2.53 [1.85–3.46], p <0.001) were significantly associated with HT. Compared to having no relative with HT, having one (OR[95%CI] = 2.06 [1.45–2.92], p <0.001), two (OR[95%CI] = 3.41 [2.11–5.50], p <0.001) or three (OR[95%CI] = 5.30 [2.35–11.96], p <0.001) relatives was associated with a higher risk of HT.
Conclusion: Similar to what was found in other studies, having a first-degree relative suffering from high blood pressure increases the risk of hypertension. When several relatives are concerned, the risk further sharply increases. Family history of HT represents a useful and inexpensive screening tool for HT.

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The Influence of Dietary Salt Restriction on Renal Sodium, Urea and Potassium Excretion in Hypertensive Patients

V. Sibalic[1,2], G. Stoffel[3], S. Henzen[4], D. Reuss[1], M. Zeppetzauer[2]
[1]St. Gallen, [2]Triesen/FL, [3]Winterthur, [4]Sevelen

Purpose: A salt reduced diet is recommended in most hypertensive patients. Physiological renal parameters could identify idiosyncratic renal effects in hypertensive patients with a successful blood pressure reduction after a sodium depleted diet.
Question: How does fractional excretion of sodium (FENa), the quotient of urinary sodium/urinary potassium (UNa/UK) and the fractional excretion of urea nitrogen (FEUN) change in hypertensive patients with a blood pressure reduction after a salt restricted diet?
Methods and Materials: 11 ambulatory patients with elevated blood pressure without antihypertensive medication collected a 24h-urine twice. The first urine collection was done after 7 days of a regular diet, the second urine collection was performed after 7 days of a moderate self-guided salt restricted diet at home. The blood pressure was monitored by repetitive daily self-measurements on a checkerboard-pattern for 14 days.
Results: The FENa under regular diet was 0.93%, after 7 days of diet the value came to 0.48% (p = 0.009). The quotient FENa/FEUN under regular diet was 0.003, after the diet it run up to 0.191 (p = 0.004). The quotient UNa/UK under regular diet was 4.10, after the diet it was lowered down to 2,35 (p = 0.029).
Conclusion: The study was performed with ambulatory patients with a newly diagnosed hypertension without an antihypertensive therapy. The successful salt diet was proved by 24h-urine collections. Because salt restriction is known to influence the renin-angiotensin-aldosterone homeostasis, it is feasible that the parameters FENa, UNa/UK, FEUN displayed significantly different values after dietary salt restriction, since they represent the sum of renal hormonal effects on salt homeostasis. The renal parameters FENa, UNa/UK, FEUN should be examined further in order to show their ability to identify hypertensive patients who profit most from a salt reduced diet.

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Measurement of Renal Function in Hypertensive Patients with Cimetidine

V. Sibalic[1,2], G. Stoffel[3], S. Henzen[4], D. Reuss[1], M. Zeppetzauer[2]
[1]St. Gallen, [2]Triesen/FL, [3]Winterthur, [4]Sevelen

Purpose: Glomerular filtration rate (GFR) is recognized to be the best way to assess renal function. Because the ability of Cimetidine (CM) to block tubular creatinine secretion, CM is thought to enable the physician to assess GFR easily, conveniently and accurately. Creatinine clearance (Ccr) after administration of CM approximates GFR. The ideal CM-dose for a 24h-urine collection is still uncertain. How does 1.8 g CM affect Ccr, when the drug is taken 8 hours before 24h-urine collection?
Methods and Materials: 11 newly diagnosed hypertensive patients with normal renal function, not on antihypertensive medication, collected a 24h-urin at home twice, once with CM, once without CM. The patients swallowed 1.8 g of CM at 10 pm and started the 24h-urine-collection the next morning at 6 am. Statistical analyses for paired 24h urine samples were performed.
Results: 24h-Ccr did not show a statistically significant difference with CM and without CM intake (p = 0.350).
Conclusion: Cimetidine is rapidly absorbed after oral administration and peak levels occur in 45 to 90 minutes. Blood concentrations remain above the therapeutically effective blood for 4 to 5 hours following a dose of 300 mg. Walser Mackenzie suggested 1200 mg CM 2 hours before urin collection as suitable. Roubenoff administered 400 mg CM 4 x daily. Hilbrands gave 3x CM with a total dose of 1.2–2.0 g. None of these protocols seemed to be convenient for daily use in practice. Our regimen failed to show a significant influence on Ccr after administration of 1.8 g CM. Because the half -life of CM is approximately only 2 hours, repetitive doses of CM should be administered for measurement of Ccr and GFR-Estimation. But the cumulative dose should not exceed 2.4 g per day.

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Challenges in Recruiting Participants in a Population-Based Survey Including 24-Hour Urine Collection: Example from the Swiss Survey on Salt Intake

A. Chappuis, N. Glatz, P. Vuistiner, V. Forni, F. Paccaud, M. Burnier, M. Bochud
Lausanne

Purpose: We conducted a national population-based examination survey in eleven Swiss centers, which aimed at estimating dietary salt intake using 24-hour urine collection in the population aged 15 years and over. The survey started in 2009 and is still ongoing. We present data of the canton of Vaud to illustrate the practical challenges encountered during the recruitment process.
Methods and Materials: We chose a two-stage sampling strategy similar to the one used during the Swiss Health interview Surveys. We sent an information letter to a random sample of households from the Swisscom directory (fixed lines) and subsequently contacted them by phone. After having defined the household composition, we randomly selected a single individual to participate in the survey, within 8 predefined age and sex strata. The study included 2 hospital visits and a 24-hour urine collection.
Results: A total of 1729 households were contacted in the canton of Vaud, 34.3% of which could not be reached after 3 phone call attempts. Of the reached ones, 66.7% agreed to define the composition of their household, adding up to 1296 individuals. The 15–29y age category represented 16.1% of this sample but only 3.2% of the persons in the phone directory. Of the 334 randomized persons, 195 (58.4%) agreed to participate and completed the study; sex or age did not predict agreement at that stage. The overall household participation rate was 11.3% (195/1729).
Conclusion: Overall, participation rate is low, which highlights the difficulty to conduct a population-based survey including 24-hour urine collection and 2 hospital visits. Young people are difficult to reach when recruitment is based on a fixed-line phone directory.
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Regional Differences in Urine Flow Rate in the Population-Based Swiss Salt Survey

T. Schoen[1], N. Bianda[2], P. Greminger[3], M. Bochud[4], P. Suter[4], D. Conen[1]
[1]Basel, [2]Bellinzona, [3]St. Gallen, [4]Lausanne

Purpose: Urine flow rate (UFR) is a major determinant of urine concentration, which has been postulated to influence progression toward chronic kidney disease. We therefore aimed to study determinants of UFR in a representative sample of the Swiss population.
Methods and Materials: The cross-sectional Swiss Salt Study included a random population-based sample of 1377 (671 men and 706 women) individuals from the three linguistic regions of Switzerland. Data from 1219 subjects, aged 15–95 years, were available for the present analysis. After a 24-hour urine collection, UFR was calculated by the ratio of urine volume and duration of urine collection. One-way analysis of variance was used to compare UFR across study centers. Determinants of UFR were analyzed using linear regression models that included age, sex, body mass index, prevalent hypertension, diabetes, smoking, urinary sodium excretion, creatinine clearance (ml/min) and study center.
Results: Mean UFR was significantly different across study centers (BS = 82.0 ml/h; GE = 68.6 ml/h; LU = 91.0 ml/h; SG = 90.4 ml/h; TI = 69.4 ml/h; VD = 69.5 ml/h; VS = 73.4 ml/h; ZH = 91.1 ml/h; p <0.0001). In multivariable regression models, all individual German-speaking cantons (BS, LU, SG, ZH) had higher UFR than individual non-German speaking cantons (GE, VD, VS, TI). In combined analyses, mean UFR (SD) were 89.0 ml/h (39.8) and 70.4 (33.1) for German-speaking and non-German speaking cantons, respectively. In multivariable regression analyses, independent predictors for UFR were German-speaking cantons (β =15.8 [12.0–19.6] p <0.001), female sex (β = 16.1 [11.8-20.4] p <0.001), body mass index (β = –0.9 [-1.4-(-0.4)] p <0.001), urinary sodium excretion (β = 0.2 [0.16–0.23] p <0.001) and age (β = 0.2 [0.07-0.34] p = 0.0034).
Conclusion: We found significant differences in UFR across different linguistic regions in Switzerland, with a higher UFR in German-speaking cantons. Other significant determinants included age, sex, body mass index and urinary sodium excretion.

The numbers refer to the pages of this supplement.