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Swiss Society of Nephrology

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Pigilozitane Improves Insulin Sensitivity, Reduces Visceral Fat and Stimulates Lipolysis in Non Diabetic Dialyzed Patients A. Zanchi, L. Tappy, N. Theumann, G. Halabi, C. Mathieu, T. Gauthier, S. Tremblay, P. Coti, M. Burnier, D. Teta

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 pigilozitane (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 1.56 ± 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

Purpose: Hemodynamic effects of changes in serum ionized calcium (iSCa) 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 changes in iSCa levels and arterial stiffness 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 iSCa 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 iSCa level, pulse wave velocity (PWV) was measured. Statistical analysis was performed with SAS 9.2 for Windows on an X86_VSPRO platform.

Results: iSCa levels were modified during sequence 1 (iSCa 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 (iSCa high-low), iSCa 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 iSCa 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.


Purpose: Hypercalcuria 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 lead to Na-transport independent 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. Tetrathydro (TH)-aldosterone was measured as the major urinary aldosterone metabolite. Apparent activity of the enzyme 11β-HSD2 was assessed by calculating F/Cortisol (F/C) + F/Cortisol (F/C) + cortisol (F) x THF/SAT (THF/SAT) x THE (THE)

Results: Calcium and magnesiumuria 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 cortisol (F/C) x THF/SAT/THF (F/C) x THF/SAT/THF (p = 0.0213) without effect on magnesiuria.

Conclusion: We conclude that enhanced F availability as indicated by a reduced 11β-HSD2 activity does lower calcium excretion. The paradoxical stimulation of systemic lipolysis by PIO may reflect adipose tissue remodeling.


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 angiomylipomas (n = 11); the remaining two turned out to be malignant tumors. Three persons had congenital agenesia 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).

<table>
<thead>
<tr>
<th>Overall</th>
<th>Men</th>
<th>Women</th>
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<tr>
<td>(n = 558)</td>
<td>(n = 264)</td>
<td>(n = 294)</td>
</tr>
<tr>
<td>Age (years) 50.8 (18–89)</td>
<td>51.2 (18–89)</td>
<td>50.2 (19–86)</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>25.4 ± 5.1</td>
<td>26.3 ± 4.2</td>
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<tr>
<td>kg/m²</td>
<td></td>
<td></td>
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<tr>
<td>eGFR (ml/min/1.73 m²)</td>
<td>92.3 ± 16.9</td>
<td>93.6 ± 17.3</td>
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<tr>
<td>Kidney length (cm)</td>
<td>110.4 ± 8.8</td>
<td>113.9 ± 8.1</td>
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<tr>
<td>Kidney volume (cm³)</td>
<td>138 ± 36</td>
<td>154 ± 35</td>
</tr>
<tr>
<td>Nephrolithiasis (%)</td>
<td>4.8</td>
<td>5.7</td>
</tr>
<tr>
<td>Simple renal cyst (%)</td>
<td>12.4</td>
<td>17.1</td>
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<tr>
<td>Renal mass (%)</td>
<td>2.3</td>
<td>1.9</td>
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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. Girard, E. 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 isothalamate renal clearance in infants’ GFR ranging between 15 and 75 ml/min per 1.73 m². 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 formula by using another gold standard method of GFR determination was applied 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.

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

F. Thomas1, B. Pannier1, A. Benetost1, U. Vischer2
1Paris/FR, 2Nancy/FR, 3Thônex

Purpose: Obesity is a strong risk factor for diabetes, CV diseases and death in the general population. However, its prognostic significance and 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/m² 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/m²). All-cause mortality was higher in patients with an elevated WC, but differences.

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.

Low Klotho Levels in Autosomal Dominant Polycystic Kidney Disease: Potential Mechanism of Resistance to FGFR23

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1Zürich, 2London/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 FGFR23/Klotho and renal phosphate handling.

Methods and Materials: Our study was conducted 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 m².

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 cyst growth, which can be explained by loss of GFR in patients with ADPKD.

Oral Presentations – Hypertension

Prevalence of Microalbuminuria in the Swiss Survey on Salt

P. Meier1, T. Schoeni1, V. Foroni1, A. Chappuis2, I. Binet1, A. Péchère-Bertschi2, Sion3, Basel, Lausanne, 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 (17) 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 (2.0–19.9), 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 homogeneous 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. Simonetti1, 2, N. Jech3, G. Kraus4, R. Schwetz5, M. Klett6, A. Schroer7, C. Kuhnen8, F. Schaefer9, E. Wühl10
1BIERN, 2Heidelberg/DE, 3Marburg/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 prestigeTM and Omron M311). 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 ± 0.3 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.

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. Ogna1, V. Forner2, V. Vuistiner3, D. Hayoz4, P. Suter5, 1Locarno, 2Lausanne, 3Pribourg, 4Zurich

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 formulae, 24-hour urine protein excretion was assessed and BMI was categorized in 3 groups: lean (<25 kg/m²), overweight (25–30 kg/m²) and obese (>30 kg/m²).

Results: The prevalences of overweight and obesity were 32.8% and 14.0%, respectively. Median CrCl [95%CI] was 135 ml/min [97–120] 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%, 10.7% and 14.0%, respectively). Median CrCl [95%CI] was 100 ml/min [97 –103] in lean, 117 ml/min [114–121] in overweight and 125 ml/min [120–132] in obese children. We used a CrCl ≥140 ml/min as cutoff for GHF. BMI was categorized in 3 groups: ≤24 kg/m², >25–30 kg/m² and >30 kg/m².

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

P. E. Cipolla, J. Chen, A. K. Kraus, P. D. Bardwell

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 by blood in FACS, donor-specific tolerance was confirmed 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 in 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. Bohlander, B. Pfanner, J. Patlích, J. Nußberger, G. Thalmann, H. Imboden

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 been reported.

Methods and Materials: Rat, pig and human kidney specimens were formaldehyde-fixed. Cryosections were investigated by fluorescent light or laser scanning microscopy. 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. Angiotensin fibers co-staining for CGRP but not for syntaphysin and anti-rein antibodies. Immunofluorescence detection was by fluorescent light or laser scanning microscopy.

Conclusion: The kidney harbors an important angiotensinergic postganglionic and sensory-sympathetic innervation. Ang II as a peptide co-transmitter may modulate sympathetic neurotransmission and kidney function independently from humoral Ang II including nephriusis, renin secretion, and renal adaptation of blood pressure.

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

D. Mardasini, M. Maillard, E. Hummler, M. Burnier, B. Vogt

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 biosynthesis enzymes. 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.


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

S. Nandul Khoda, E. Dizin, E. Feraillie, K. H. Krause, P.-Y. Martin, S. De Seigneur

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 is involved in apoptosis and survival pathways as well as in renin-angiotensin 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 NOX2/2 double-KO mice to decipher the role of these enzymes in kidney fibrosis progression in a tubular stress model. mCCDc1 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-1 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 kidneys of obstructed kidneys. Apoptosis, interstitial fibrosis and oxidative stress were attenuated in NOX2/NOX4 KO compared to NOX4 KO animals. In mCCDc1 cells NOX4 si-RNA silencing led to apoptosis in the presence of TGF-β1.

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 vasa vasorum and 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, vasa vasorum and NO2 activation may explain enhanced kidney fibrosis in UO NOX4 KO mice.

GlutU 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 hyperuricemia, a condition in which affected patients suffer from hyperuricemia, 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

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

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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
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.

Dnm-1 – A New Player in Renal Allograft Rejection
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¹Zurich, ²Hannover/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. DNM-1 (CD226) on T cells has been shown to play an important role for allogeneic graft-versus-host responses. 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.

Methods and Materials: Patients qualifying for AB0-incompatible kidney transplantation received Rituximab® 1 week before transplantation 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 CD112. The role of DNM-1 during renal allograft rejection is unknown.
Non-Invasive Detection of Subclinical Tubulo-Interstitial Inflammation by the Urinary Cxcl10 Chemokine: Validation in a Real-Life Setting

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1Basel, 2Winnipeg/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. Aliotraft 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 (11/86/3/25), 12: 16/362 (4%), 13: 5/362 (1%). t0-biopsies and t2-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 e1-microglobulin/creatinine ratios (4.5 vs 4.9 mg/mmol; p = 0.28). By contrast, urine CxCL10/creatinine ratios were significantly higher in t2-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 1.62 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 t2-biopsies (43%) would have been missed (11: 40; t2: 6).

Similar results were obtained if surveillance biopsies were grouped according to the combined Banff t- and s-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

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Zurich

Purpose: BK viremia and polymavirus-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 192 included patients, 49 (32%) tested positive for BK viremia, but only 8 developed biopsy-proven polymavirus-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 polymavirus 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

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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 (MF1 <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 predictive.

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

Basel

Purpose: Delayed graft function (DFG) 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 rejection.

Results: Sixteen of 345 recipients experiencing primary-non-function (5%) were excluded from the analysis. DGF occurred in 93/323 recipients (28%). 16/236 patients with DGF (6%) and 221/236 patients with no DGF (94%) had at least one allograft biopsy within the first year post-transplant (p = 0.6). Among the DGF and IFG 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 IFG (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 IFG group (45 ml/min vs 50 ml/min; p = 0.0001).

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.
A Label-Free Serum Test Measuring Overall Calcification Inhibition

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1Berne, 2Solothurn, 3Aachen

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 particles of 50–100 nm diameter. Subsequently, these primary CPPs undergo spontaneous transition to spindled 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-inhibitory properties contained in serum. The assay measures the formation of protein-mineral aggregates in real time.

Conclusions: 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.

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 apparatus. The aim of the study was to compare the effects of two vitamin 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-1-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: calcitrol (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:

<table>
<thead>
<tr>
<th></th>
<th>Heart Rate (BPM)</th>
<th>Systolic BP (mm Hg)</th>
<th>Diastolic BP (mm Hg)</th>
<th>Mean BP (mm Hg)</th>
<th>Heart weight (g)</th>
<th>PRA (ng/ml/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sham control</td>
<td>361 ± 13</td>
<td>142 ± 8</td>
<td>96 ± 8</td>
<td>113 ± 9</td>
<td>1.03 ± 0.1*</td>
<td>1.53 ± 0.38*</td>
</tr>
<tr>
<td>Clip control</td>
<td>366 ± 7</td>
<td>193 ± 9</td>
<td>141 ± 7</td>
<td>166 ± 8</td>
<td>1.36 ± 0.06</td>
<td>4.81 ± 1.27</td>
</tr>
<tr>
<td>Clip calcitriol</td>
<td>365 ± 8</td>
<td>182 ± 10</td>
<td>129 ± 7</td>
<td>154 ± 8</td>
<td>1.57 ± 0.07*</td>
<td>3.26 ± 0.48</td>
</tr>
<tr>
<td>Clip paricalcitol</td>
<td>364 ± 9</td>
<td>163 ± 7*</td>
<td>119 ± 6*</td>
<td>139 ± 7*</td>
<td>1.02 ± 0.06*</td>
<td>1.62 ± 0.3*</td>
</tr>
</tbody>
</table>

*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.

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

1Basel, 2Hamburg/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 deposition along the GBM. Despite IgG deposition (PDS) 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.

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

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Purpose: Periostin is a matricellular protein involved in tissue remodelling through the promotion of adhesion, cell survival, cellular differentiation, 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 peritoneal cavity in patients with EPS and with simple peritoneal sclerosis on PD. It might play a role in the progression of peritoneal injury.
Prevalence of Reduced Renal Function in Switzerland – Results of a Multicenter, Cross-Sectional Study

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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 m²
- Mildly reduced RF: eGFR 60-89 ml/min/1.73 m²
- Moderately reduced RF: CKD Stage 3: eGFR 30-59 ml/min/1.73 m²
- Severely reduced RF: CKD Stage 4-5: eGFR <30 ml/min/1.73 m²

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.

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

O. Phan, M. Maillard, F. Funk, M. Burnier
Lausanne, St. Gallen

Purpose: In a previous study, we demonstrated that PA21, a new calcium-free, iron based phosphate binder effectivelly 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 lantheinum (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:

<table>
<thead>
<tr>
<th></th>
<th>Body weight</th>
<th>Creatinine</th>
<th>P mmol/l</th>
<th>Ca mmol/l</th>
<th>iPTH pg/ml</th>
<th>U. P/creat</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRF</td>
<td>311 ± 8</td>
<td>157 ± 14</td>
<td>4.2 ± 0.6</td>
<td>2.8 ± 0.5</td>
<td>3704 ± 868</td>
<td>21 ± 4.6</td>
</tr>
<tr>
<td>CRF</td>
<td>300 ± 6.3</td>
<td>136 ± 14</td>
<td>2.8 ± 0.3</td>
<td>2.5 ± 0.5</td>
<td>1277 ± 411</td>
<td>4.6 ± 1.0</td>
</tr>
<tr>
<td>CRF</td>
<td>308 ± 5.8</td>
<td>144 ± 21</td>
<td>2.5 ± 0.3</td>
<td>2.5 ± 0.5</td>
<td>1100 ± 355</td>
<td>10 ± 1.1</td>
</tr>
<tr>
<td>CRF</td>
<td>305 ± 5.7</td>
<td>130 ± 8</td>
<td>2.4 ± 0.1</td>
<td>2.6 ± 0.1</td>
<td>1000 ± 212</td>
<td>7.3 ± 1.1</td>
</tr>
</tbody>
</table>

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.

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

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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.

Multiscale Hemodynamic Modeling of the Intrarenal Circulation

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, 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.

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. Using these flow parameters, the Reynolds number is 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 ultrason sound flow measurements.
I. Binet5, F . Frey1, P . Meier6, M. Magnin7, M. Burnier8, S. Favre1, S. Liniger1, A. Bock2, P .-Y . Martin3, A. Fischer4, L. Gerber1, A. Gaspert1, N. Müller1, H. Zwahlen2, T. Fehr1

Pharmacies in the Years 2008–2011
Consolidated Results from a Screening Project in
1Zurich, 2Bellinzona

Evaluation of a Renal Risk Score in the Swiss Population:
Recipie developed in 2008.
the context of the World Kidney Day (WKD) a renal risk score was
population motivated a pilot project for information and detection. In
ZG, GE, AG, BE and VS participated from 2008 to 2011 in this

Methods and Materials: 86 pharmacies in the cantons SG, VG, LD, 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: myocardiard 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.

Neutrophil-Gelatinase-Associated Lipocalin and Cystatin C vs. Creatinine-Based Estimates of the Glomerular Filtration Rate (eGFR)
Y. Tomonaga1, T. Szucs2, L. Rischi3
1Berne, 2Basel, 3Schaan, 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:

\[ \text{Normal RF: eGFR} \geq 90 \text{ ml/min/1.73 m}^2 \]
\[ \text{Mildly reduced RF: eGFR} 60–89 \text{ ml/min/1.73 m}^2 \]
\[ \text{Moderately reduced RF: CKD Stage 3: eGFR} 30–59 \text{ ml/min/1.73 m}^2 \]
\[ \text{Severely reduced RF: CKD Stage 4–5: eGFR} <30 \text{ ml/min/1.73 m}^2 \]

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.

Mycoplasma and Ureaplasma in Kidney Allograft Recipients: Innocent Bystanders or a Cause for Concern?
L. Gerber1, A. Gasper1, N. Müller1, H. Zwahlen1, T. Fehr1
2Zurich, 3Bellinzona

Purpose: Mycoplasma hominis and Ureaplasma urealyticum belong to the family of purely intracellular bacteria called Mycoplasmaeae. 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 sterile leucocyturia, Mycoplasma or Ureaplasma were considered the sole pathogens in the urine samples in immunocompetent hosts, they were further studied with the polymerase chain reaction (PCR) for Mycoplasma hominis and Ureaplasma urealyticum 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.

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 4,5 L HES 6% (Volunex®). After initial cardiac arrest, spontaneous circulation had returned and brain death was diagnosed by cerebral angiography. The recipient received an induction with Thymoglobulin, 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%
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-hydroxyvitamin 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 period 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.


Zurich

Purpose: Renal allograft recipients are at high risk for substantial bone mineral density (BMD) loss 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 randomised 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 serum vitamin D levels < 30 nmol/l at the primary endpoint are excluded from the study. The study protocol is still under evaluation by the ethics committee.

Results: At the time of abstract submission, 9 patients have been randomized (4 denosumab vs. 5 control). Their mean age was 47.75 ± 23.23 m/min, at day 30 ± 18 and at 1 year ± 25, not differing between groups.

Conclusion: Delayed graft function trends to happen more in cases with biopsy proven osmotic nephrosis compared to cases without. Results of fractures, and allograft function at one year.

Delayed graft function trends to happen more in cases with biopsy proven osmotic nephrosis compared to cases without. Results of fractures, and allograft function at one year.

Pharmacokinetic of Tacrolimus after Gastric Bypass Surgery

S. Pietthüller, D. Tsinaïlis, 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 biliopancreatic GBP 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.
Heart Failure and Mitral Insufficiency in a Renal Allograft Recipient
A. Schlechti, C. Kocher, S. Segerei, R. Caduff, L. G. Wyler, V. Müller, B. Beck, J. Blum, J. Kamarchev, N. Müller
1Zurich, 2Basel

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-aveolar 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 cardiacogenic shock. The autopsy confirmed disseminated trypanosomiasis with myocarditis.

Conclusion: Trypanosoma cruzi is 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 history of travel to endemic areas and the rising number of transplantations in patients with a history of travel to endemic areas, the risk of Chagas disease to be transmitted via an allograft has to be considered.

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

Purpose: Renal thrombotic micro angiopathy (TMA) in systemic lupus erythematosus (SLE) is associated with the presence of anti-phospholipid antibodies (aPL). In 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 motefili and methyl-prednisonolone, without calcineurin inhibitors. The graft produced urine immediately. As serum creatinine remained at 172 µmol/L at day 6, a graft biopsy was performed. Isoleted 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.
Epidemiological Trends in Maintenance Dialysis Treatment: 40 Years of Single Center Experience

P. Rhy, M. Ambühl, D. Corletto, 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.


Results:

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<tr>
<td>Age at initiation, yr</td>
<td>48.0 ± 14</td>
<td>49.7 ± 16</td>
<td>55.1 ± 15</td>
<td>63.9 ± 16</td>
<td>0.000</td>
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<tr>
<td>Time to TPL, mo</td>
<td>27.2 ± 42</td>
<td>29.0 ± 33</td>
<td>29.2 ± 28</td>
<td>29.8 ± 34</td>
<td>0.934</td>
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<tr>
<td>Time to death, yr</td>
<td>8.3 ± 8</td>
<td>7.6 ± 7</td>
<td>8.5 ± 8</td>
<td>2.9 ± 3</td>
<td>0.000</td>
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<tr>
<td>3–5-yr survival, %</td>
<td>62.5 / 38.8 / 27.2 / 24.2</td>
<td>65.8 / 44.4 / 38.2 / 24.2</td>
<td>46.0 / 25.3 / 38.8 / 24.2</td>
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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.

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

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1Lausanne, 2Sophia Antipolis/FR

Purpose: To evaluate the effects of Naproxinod (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 D1 to D4. On D8, natriuresis, plasma renin activity (PRA), and glomerular filtration rate (GFR), using insulin clearances, were measured before and after 40 mg of intravenous FUR.

Results: On D-1 24 h 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).

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.

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

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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 follows: 8 pts 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 dialysis and excluded from analyses. Factors influencing CysC were analyzed performing a linear mixed model to take into account the repeated measures during.

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 abnormalities, those who were susceptible to present a worse prognosis in renal function.
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.


Intracranial Arachnoid Cysts in Adpkd Patients

Purpose: Autosomal dominant polycystic kidney disease is the most common inherited renal affection and the most frequent cause of endstage renal disease at all. Using a multicentric system 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 middle and posterior fossa 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 extracerebral rim 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 patients 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 similar 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 arachnoid cysts compared to cysts in kidney or liver. However the cystic lesion can extend to bizarre dimensions.


Functional and Social Status, Actual and Perceived
Social Support in a Population of Swiss Maintenance Haemodialysis (HD) Patients
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1Baden, 2Zurich

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 (46%) 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 levels of social support and social status was detectable.

Conclusion: Swiss maintenance HD patients have a high level of instrumental and some basic 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.

A Comparison between Pediatric Renal Biopsy Findings in Zurich and Armenia
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1Yerevan/AR, 2Zurich

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 (E VN: age 1–18 years (11.1 ± 4.5); 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 5%) 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.

Nutritional Counselling of Stone Patients by the Physician – Is it Worth the Hassle?
K. Günther, D. Tsanlis, 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 volume). The second urine collection was lacking and further 16 due to inconsistencies in urine collections (>20% difference in daily urine volume). The mean urine volume was 1740 ± 718 ml/day. The mean calcium excretion decreased from 84 ± 2.5 mmol/d to 439 ± 153 mmol/d (p <0.05) representing about 30% difference in daily urine calcium 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/day. The mean calcium decreased from 84 ± 2.5 mmol/d to 439 ± 153 mmol/d (p <0.05) representing about 30% difference in daily urine calcium excretion). Thus 28 patients were analyzed before and after counselling regarding urine volume, natriuresis for salt intake and urea excretion for protein intake.

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.
A Prospective Analysis of Falls in Patients on Maintenance Haemodialysis (MHD)
A. Rossier, R. Bullani, M. Silva Pereira, S. Dubritt, 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 (mean age 64.9 y) underwent 65 falls. Incidence of falls and severe falls requiring presentation to an emergency department.

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 related morbidity by patients with kidney failure needing an emergency department.

Dialysis 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 an adapted PD (lower volume, frequent PD).

Methods and Materials: Between May 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 5 patients, the PD began after a catheter placement, for 7 after the operation. For 13 patients in the BSAP-based “low turnover” group, 2 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” group. Significant positive 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 = 0.003). 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 PTH (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 and spKt/V. IPHT was negatively correlated with serum ionized calcium, but not with phosphate.

Conclusion: BSAP and iPTH were correlated to some degree, but the BSAP and iPTH based bone turnover categories were hardly congruent. Of the 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” group. Significant positive 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 = 0.003). 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 PTH (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 and spKt/V. IPHT was negatively correlated with serum ionized calcium, but not with phosphate.

Conclusion: BSAP 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.

Small Solute and Ultrafiltration Kinetic Modelling in Capd Patients Using the Three-Pore Membrane Model – A Population Approach
R. M. Kalicki, D. E. Uehlinger Berna

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.

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 significant. In spite of reduction of the UF, MAP, the HR remained unchanged. There was a wide range of SV at the start of treatment (321–1294). 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 UF. TPR increased from 174 mmHg/L/min to 214. The increase in TPR correlated significantly with the reduction of the SV and total UF. The comparison of different age (<70/>70) groups revealed a significant difference between SV (813 and 673) 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 chronic 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 significantly higher 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 dry weight assessment should be improved.

Enhanced Suppressive Function of Tregs from Patients on a High Cutoff HD Technique

P. Meier

Purpose: Considering the effect of oxLDL accumulation on Tregs viability and function in chronic HD patients, a new generation of protein-energy dialyzers, with very large pores (i.e., HD 1100 Gambro), could be used 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 211 – Polyflux 210 H [regular membranes: RM] vs. HCO [high cutoff] 1100) in plasma oxLDL clearing, and to analyze the Tregs suppressive function to properly balance of immunity in ESKD patients.

Methods and Materials: Thirty ESKD patients on chronic HD (3 x 4 h weekly) were studied in three equal groups during three months. Plasma para-dialysate oxLDL concentrations were measured using a mAb-HEK-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. 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.

Conclusion

was ~5% of body weight (interquartile range –9.8 – 0.3%), which did not correlate with the clinical score. The impendence values (Ω), measured at 50 kHz, showed a linear correlation with the clinical score of the AAP (r = 0.30, p = 0.004). The group of children with mild dehydration had significantly lower impendence values at 50 kHz compared to the group of children with moderate dehydration (p = 0.008). A cutoff set by 810 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 impendence 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.
Impact of Systemic Inflammation on Anemia Status and Management in Hemodialysis Patients – A 12 Months Interim Analysis of the Swiss “Motion” Survey

P. M. Ambühl1, P. Meier2, Z. Fumeaux3, L. Gabuttì4
1Zürich, 2Sion, 3Nyon, 4Locarno

Purpose: A frequent complication in patients with kidney diseases, chronic anemia is commonly treated with erythropoetin 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 inflammatory 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

<table>
<thead>
<tr>
<th>CRP &lt;4 mg/L</th>
<th>4 ≤ CRP &lt;11 mg/L</th>
<th>CRP ≥11 mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 282</td>
<td>n = 281</td>
<td>n = 271</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 ≤ x ≤ 7</td>
<td>7 ≤ x ≤ 24</td>
<td>x &gt; 24</td>
</tr>
<tr>
<td>Serum ferritin (μg/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>502 ± 281</td>
<td>476 ± 262</td>
<td>526 ± 338</td>
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<tr>
<td>Hb (g/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>115 ± 12</td>
<td>116 ± 13</td>
<td>112 ± 14</td>
</tr>
<tr>
<td>ESA dose/week (μg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 ± 27</td>
<td>36 ± 34</td>
<td>53 ± 47</td>
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</tbody>
</table>

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.

Migraine Induced Kidney Stones?

L. Gerber, R. P. Wüthrich, N. Mohrbbi
Zürich

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 hypochloretria 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 carboxyhydrase inhibitor in the proximal and distal tubules, leads to an increased bicarbonate excretion, a higher urinary pH and a RITA 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.

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

T. Perrin, O. M. Hemett, M. Merth, 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 stenomies 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 elevated to 241 μg/l and after 3 days it was 161 μg/l. On the same day, an enteroclysis through the jejunostomy was performed with 300 ml of iopamiro300 (= 90 g of iodine) and showed no intestino-portal 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 rehydration 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 JNAG and lysozyme were markedly increased. Looking for a cause for ARF, it turned out that the radiographic contrast was present 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 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 presumably caused by the local inflammatory state. This mechanism seems to be quite rare, as we have found no similar report in the literature.

References:

Methods and Materials: Case report.

Results: NA.

Conclusion: Although no iv-radiocontrast had been administered, 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 presumably caused by the local inflammatory state. This mechanism seems to be quite rare, as we have found no similar report in the literature.

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 hyodoaldosteronism, pseudohydropertiglyceridemia 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), glycerokinase deficiency (GKD), psychomotor retardation and characteristic facial appearance.

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 hyodoaldosteronism. 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 hyodoaldosteronism and hyperlipoproteinemia (in fact a pseudohydropertiglyceridemia) was suspicious for contiguous gene deletion syndrome in Xp21. Family history disclosed mental retardation in the patient’s sister and mother. An array of contrasting genotypic hybridization confirmed the diagnosis with a microdeletion Xp21 associated as a contiguous gene syndrome in Xp21. It is characterized by congenital adrenal hypoplasia (CAH), Duchenne muscular dystrophy (DMD), glycerokinase deficiency (GKD), psychomotor retardation and characteristic facial appearance. Total body potassium content was normal. The child was treated with high dosage of desoxycorticosterone with normalization of potassium and serum creatine levels and improvement of muscle strength.
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.

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

J. Trachsel, S. Dimitrijevic, P. Koch, P. M. Ambühli
Zurich

Purpose: Reticulocyte 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, iron saturation 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 (Venoferrin®).

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 170 to 279% (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 B, 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).

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

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

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1Reinach, 2St. Gallen, 3Lugano, 4Interlaken
Zurich

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 (mth) 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; 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 naive. 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/m²/month and decreased to 125 ± 71 µg/m²/month (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 saturation (Ferritin >200 µg/L and TSAT <20%; B) iron deficiency (mean iron availability than ferritin and transferrin saturation (TSAT).)

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

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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 proposals. No significant difference was observed for total calcium targets.

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.

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. Franz1, A. Comenda2, P. Meier2, O. Phan4, A. Komarék1,*, G. Meffert1
1Reinach, 2Zurich, 3Sion, 4Payerne, *Interlaken

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 and 12.

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. CCI 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 at 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.

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 egipatic enic tent. 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 egipatic enic tent 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. Recent PET-CT scans were used to detect sources of infections and also infected cysts. In a recent study, Salté 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.

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

A. Kneubühl1,2, I. Koneth3, D. Hertner4, S. Segerer1, P. Meier5, A. Komarek6
1Liestal, 2Basel

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 Q2W, 14 QW, 14 Q, 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). Table 1 shows patients assessment of intervals in regard to 4 statements.

Table 1

<table>
<thead>
<tr>
<th>Interval assessment regarding 4 statements</th>
<th>Patient preferences</th>
</tr>
</thead>
<tbody>
<tr>
<td>With the following interval …</td>
<td>Once-monthly Q2W QW TIW</td>
</tr>
<tr>
<td>…the treatment would be simplified the most.</td>
<td>79.2% 12.3% 7.5% 1.0%</td>
</tr>
<tr>
<td>…my motivation to carry out all injections would be the highest.</td>
<td>79.8% 9.6% 9.6% 1.0%</td>
</tr>
<tr>
<td>…the risk of forgetting an injection would be the lowest.</td>
<td>64.6% 9.1% 25.3% 1.0%</td>
</tr>
<tr>
<td>…my life would be least constraint.</td>
<td>85.9% 8.1% 5.1% 0.9%</td>
</tr>
</tbody>
</table>

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.
Methods and Materials: Case report and clinical outcome of nephropathia epidemica 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/μl and treated for gastroenteritis. On clinical examination, we saw a young, hypovolemic man, stable blood pressure of 133/72 mm Hg, pulse 80/min, afibrile. Epigastric pain without signs of peritonitis, no petechial bleedings were seen. Main laboratory findings were creatinine 1151 μmol/l, urea 52 mmol/l, potassium 4.4 mmol/l, pH 7.42, HCO3- 20 mmol/l, thrombocytes 73/μl, lipase 1300 U/l, albuminuria 2.8 g/dl. No fragmentocytes. After rehydration and analgetic therapy, the patient clinically improved, the diuresis improved from 1 l/day to 6 l/day. The kidney biopsy showed only mild interstitial nephritis and rare interstitial hemorrhages. Serological testing showed positivity of IgM and IgG against Epstein-Barr virus (V) in Doxo. Despite normalizing renal function from day 5 on and absence of abdominal pain, lipase and amylas 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.

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

S. Far ese, V. Reinmann, P. Sandz Solotrun

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 1 x 2 L glucose 4.25%) a dialysis GL is still performed through the same catheter, the peritoneal function is intact (KT/V,urea 2.32/week), creatinine clearance 75 L/1.73 m²/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.

Silica and Glomerulonephritis, Just an Association?

O. Phan, P. Gardiol, B. O’Callagan

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, dyspnea 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 computed tomography. Percarditis was diagnosed without clinical complication. 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 improvement was remarkable.

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.

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 Prednisol. The clinical and laboratory evaluation during admission revealed oedema of the lower limb, hypokalemia (2.2 mmol/l), moderate renal insufficiency, hypercholesterolemia (8.4 mmol/l). The spot urine showed proteinuria in the nephrotic range (17 g/dl).

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.
Intrapерitoneal Application of Ceftriaxone for Long-term 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


I. Guessous1, M. Bochud2, J.-M. Gaspoz3, A. Pechère1
1Geneva, 2Lausanne

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, physical activity level (kcal/day), alcohol 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), which included 2040 (12 female and 8 male participants). The 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 younger or older males. The adjusted (including HTN Rx use) annual change in mean SBP remained stable in men aged >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.

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

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1Bellinzona, 2Berne

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 β-blockers, converting enzyme inhibitors and thiazides was therefore assessed among adult volunteers.

Methods and Materials: The palatability of crushed atenolol, bisoprolol, enalapril, ramipril, chlorothiazide 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, atenolol, bisoprolol, enalapril and ramipril were superior to that of amiodipine (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.

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

I. Guessous1, D. Hayoz2, P. Greminger3, A. Gallino4, P. Eme5, on behalf of the Swiss Survey on Salt Group
1Geneva, 2Lausanne, 3Fribourg, 4St. Gallen, 5Bellinzona, 6Lucerne

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 serum SUA ≥5.0 mg/dL.

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 [1.00–1.06]), 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 [0.90–0.97]), diastolic BP (OR = 0.95 [0.92–0.98]), and CVD-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.

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

V. Forn1, N. Glatz1, D. Gonet1, H. Steitler1, F. Paccoud2, M. Burnier3
1Lausanne, 2Basel, 3Zurich

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 CKD-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 K/F KDOQI (eGFR < 60 ml/min/1.73 m²) 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 diabetes 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 20–39 years (21.7%) than persons aged 45–59 years (2.3%), 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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I. Guessous1, M. Bochud2, J.-M. Gaspoz1, A. Pechère1

1Geneva, 2Lausanne

**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. Sedentariness was defined as ≤10% daily energy expenditure (kcal/day) spent in ≥4 or more METs. Adjusted (age, HTN, diabetes, BMI, physical activity level (PAL) (kcal/day), alcohol consumption (kcal/day), smoking, education level) logistic regression was used to assess the association of awareness every year and other determinants (accounting for secular trends) with HTN awareness.

**Results:** We analyzed 9320 subjects aged 35–74 years between 2001 and 2009. Cross-sectional data (1999) and 1st (2001–2002) (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 unawareness 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 successfully 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. Chappuis1, L. Gabutti2, I. Binet3, I. Guessous4, P. Erne5, M. Bochud6

1Lausanne, 2Locarno, 3St. Gallen, 4Geneva, 5Lucerne

**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. The Swiss Federal Office of Public Health has launched a strategy to reduce dietary salt intake in the Swiss population (2008–2012).

**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 < 0.001). Those reporting a high salt intake had higher odds of having urinary salt excretion over 5 g/24h (95% CI) = 6.27 [2.19–17.29]) 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 10 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 age, sex and region. Knowledge on 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. Knowledge on salt and salt-related health conditions 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. Glatz1, P. Erne1, P. Meier1, T. Schoen1, I. Binet2, I. Lausanne, Luzern3, Sion4, Basel5, St. Gallen6

1Lausanne, 2Luzern, 3Sion, 4Basel, 5St. 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 (SBP >=8 mmHg) or mean diastolic BP (DBP >=9 mm Hg) self-reported current known medical condition. The proportion of participants reporting a high blood pressure 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 20.8% and a sibling history [at least one] 11.3%. In multiple regression analysis with sex, age and BMI as covariates, reported high blood pressure history was associated with a higher family history of HT. This association was more pronounced in women.
Patients with Cimetidine

Measurement of Renal Function in Hypertensive Patients

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/urea nitrogen (UNa/U) and the fractional excretion of sodium (FENa) 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 24-h urin twice. The first urin 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 the patient in a prospective daily self-measurements on a checkboard-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/FENa under regular diet was 0.30 ± 0.00 (p = 0.004). The quotient UNa/U 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 24-h urine collections. Because salt restriction is known to influence the renin-angiotensin-aldosterone homeostasis, it is feasible that the parameters FENA, UNa/U, FENa 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/U, FENa should be examined further in order to show their ability to identify hypertensive patients who profit most from a salt reduced diet.

Regional Differences in Urine Flow Rate in the Population-Based Swiss Salt Survey

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 a 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.
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