levels of the markers were also consistently different. At the follow-up, both LMWH and UFH produced a 100% increase in TFPI after 10 min of HD ($p<0.0001$). It was still evident after 180 min ($p<0.01$), and higher in pts maintained on UFH ($p<0.05$). The 10 min rise in TFPI correlated with the bolus dose of UFH ($r=0.700$, $p=0.011$). There were no changes in vWF and TF.
In conclusion, UFH induces a more sustained overdialytic increase in plasma TFPI compared to that due to LMWH. This reflects the more extensive release of TFPI from endothelial cells by UFH that reduces their antithrombotic potential. The repeated use of UFH also results in decreased plasma levels of anticoagulant TM. These novel endothelium-dependent mechanisms may account for better clinical effects of LMWH than UFH in HD pts.

O48 BLOOD PUMPS (BP) STRONGLY ACTIVATE COAGULATION DURING HAEMODIALYSIS (HD)

Christian Tielemans, Michele Warnimont, Cecile Husson, Jean-Marin Des Grottes, Joelle Nortier. *Nephrology, Hopital Erasme, Brussels, Belgium; Nephrology, Hopital Erasme, Brussels, Belgium; Nephrology, Hopital Erasme, Brussels, Belgium; Nephrology, Hopital Erasme, Brussels, Belgium; Nephrology, Hopital Erasme, Brussels, Belgium*

The AN69ST membrane adsorbs significant amounts of unfractionated heparin during a single pass priming. We have previously shown that such heparin-coated AN69ST allows to dialyze most patients without systemic anticoagulation (JASN 2001; 12:277A). However,plasma thrombin-antithrombin (TAT) levels increased progressively during HD from 4.6 to 36.2 μg/l, $p<0.001$ – reflecting the activation of the coagulation. To check which part of the extracorporeal circuit (ECC) is responsible we performed a HD session in 10 different patients and sampled blood at start (t0) and at 30 minutes (t30) and the end, at different points of the ECC: inlet of arterial line (IN), before BP (BBP), after BP (ABP), after dialyzer (AD) and at the end of venous line (OUT). A significant increase in TAT levels was observed in the BP (see Table, ABP vs BBP), while no TAT production was observed within the dialyzer, in the arterial or in venous blood lines (BL).

TAT (N:1-4.1 μg/l	IN	BBP	ABP	AD	OUT
t30	6.4±0.8	5.9±0.6	9.3±1.3*	10.6±1.1	10.4±1.3
end	57.9±13.8*	54±12	140±35**	110±31	116±28

P value: +<0.001 vs t0 (TAT 5.8±1.0), *0.03 and **<0.05 vs BBP, all others: BBP vs IN, AD vs ABP,and OUT vs AD are NS.

The HD sessions were performed with 2 needles but using a BL suited also for single needle HD, i.e. with a venous BL comprising a BP segment but that is not inserted in the BP (between AD and OUT). As TAT generation did not occur at that level but only in the arterial BP we speculate that the mechanical stress within the pump and not the material of the BP BL segment is responsible for the activation of the coagulation.

FC9 Peritoneal dialysis – Solutions & PET test

O49 ★ PERITONEAL ISCHEMIA AND PSEUDOHYPOXIA IN PERITONEAL DIALYSIS

Roos van Westrhenen [1], Machteld Zweers [1], Cindy Kunne [2], Rudi De Waart [2], Allard van der Wal [3], Raymond Krediet [1]. [1] *Dept. of Nephrology, Academical Medical Center (AMC), Amsterdam, Netherlands;* [2] *Dept. of Clinical Chemistry, AMC, Amsterdam, Netherlands;* [3] *Dept. of Pathology, AMC, Amsterdam, Netherlands*

Continuous exposure of the peritoneum to glucose-based, lactate-buffered dialysis solutions is likely to increase the intracellular NADH/NAD+ ratio of exposed tissues by stimulation of the sorbitol pathway and by inhibition the lactate dehydrogenase reaction. This pseudohypoxia may stimulate the formation of different growth factors involved in peritoneal angiogenesis and fibrosis. Therefore lactate was replaced by pyruvate as buffer of PD fluid in a chronic peritoneal infusion model.
Eighteen Wistar rats were daily i.p. infused with pyruvate buffered (P: n=9), or lactate buffered dialysate (L: n=9), both containing 3.86% glucose. After 20 weeks, a peritoneal permeability analysis was performed and omental tissue was examined for number of vessels per field (αSMA) and presence of fibrosis (Sirius Red). The latter was scored in submesothelial (SM), perivascular (PV) and intersegmental (IS) areas on a semiquantitative scale ranging from 0 to 3 (normal to severe fibrosis).
Histology revealed a significant difference in numbers of αSMA-positive vessels per field (P: 16±9 v/f vs. L: 40±8 v/f, $p<0.001$). Fibrosis was significantly different in SM (P: 1.3±0.8 vs. L: 1.6± 0.7, $p=0.05$)) and IS (P: 1.1±0.4 vs. L: 1.6±0.7, $p<0.01$) areas). Functional characteristics were not significantly different between groups except for D/P sodium, which is a reflection of aquaporin- mediated water transport (P: 84±5% vs. L: 90±2%, $p=0.01$).
Conventional lactate and glucose containing dialysate stimulates development of fibrosis and angiogenesis in the peritoneum, possibly mediated via pseudohypoxia. Replacement of lactate as a buffer in dialysis fluid with pyruvate reduced angiogenesis and fibrosis, possibly by reducing the NADH/NAD+ ratio.

O50 N-ACETYLGLUCOSAMINE (NAG) - AN ALTERNATIVE TO GLUCOSE OSMOTIC SOLUTE IN PERITONEAL DIALYSIS FLUIDS (PDF)

Andrzej Breborowicz [1], Kinga Witka [1], Paul Tam [2], George Wu [2]. [1] *Dept. of Pathophysiology, Poznan Medical School, Poznan, Poland;* [2] *University of Toronto, Toronto, Canada*

Glucose (GLU), despite vast knowledge about its local and systemic toxicity when used in high concentrations, is the most common osmotic solute in peritoneal dialysis fluids. We propose that NAG can be an alternative to GLU osmotic solute in PDF. We tested that hypothesis in a model of acute peritoneal dialysis in rats,which were infused with lab made PDF containing GLU or NAG (42.5g/L) as osmotic solutes. After 1 and 6hr dwell dialysate volume and transperitoneal equilibration of solutes as well as selected inflammatory parameters were studied. Transport results of the 1hr exchange are presented in table.

	NetUF (mL)	Na sieving	Urea [D/S]	Protein [D/S × 10^3]
GLU	27.7±1.1	0.96±0.04	0.78±0.20	51.0±23.2
NAG	28.2±0.7	0.96±0.05	0.83±0.16	28.2±10.3*

*$p<0.01$ vs.GLU

After 6hr dwell drained dialysate volumes were comparable (34.5±2.5 mL in GLU vs. 36.1±1.7 mL in NAG) but transperitoneal equilibration of protein ($D/Sx10^3$) was still lower in NAG: 27.4 ±8.0 vs. 37.5±6.2 in GLU,$p<0.02$. Dialysate cell count after 6hr dwell was comparable in both groups:933±261 in GLU vs. 933±266 in NAG. However dialysate hyaluronan concentration (ng/mL) was higher in NAG group: 54.6±15.1 vs. 35.4±7.2,$p<0.001$. In blood insulin concentration (ng/mL) was lower in NAG: 4.6±1.0 as compared to GLU: 6.4±2.0,$p<0.05$.
Presented results confirm our previous findings that NAG is a comparable to GLU osmotic solute. In addition it serves as substrate for hyaluronan synthesis within peritoneal cavity,what explains the reduced peritoneal permeability to protein.NAG is weaker than GLU stimulator for insulin synthesis what may result in long term beneficial metabolic effects. We conclude that NAG can be considered as an effective and safe osmotic solute in PDF.

O51 ★ RANDOMIZED CROSS-OVER ADMINISTRATION OF PH-NEUTRAL, BICARBONATE BUFFERED PD SOLUTION IN CHILDREN ON APD

Claus Peter Schmitt[1], Susanne Haas[1], Thomas Schaub[2], Franz Schaefer[1], Mid European PD Study Group (MEPPS). *[1]Pediatric Nephrology, University Children's Hospital, Heidelberg; [2]FMC, Bad Homburg, Germany*

PH-neutral fluids are more biocompatible since they are virtually free of glucose degradation products and preserve peritoneal cell functions in vitro. Children on APD may benefit particularly from the introduction of pH-neutral PD fluids since, due to their short dwell times, they are continuously exposed to an acidic intraperitoneal pH with conventional PD solutions. In a prospective, randomized cross-over trial we treated 34 children (0.5-15.7 years) in randomized order during 2 consecutive 12-week study periods with a pH-neutral PD fluid containing 34 mM bicarbonate (BIC 170/180) or a conventional lactate solution (35 mM, pH 5.5; CAPD 17/18). Serum biochemistry and capillary BGA were obtained every 4 weeks, PETs at study entry and at the end of either treatment period.

Using the bicarbonate dialysate we observed a steady increase in serum bicarbonate 23.7±5.7 to 24.6±2.3 mM) and base excess (-0.9±2.5 to 0.8±2.7), but a decline using the lactate solution (23.7±5.7 to 21.9±3.1, p=0.01 and -0.4±5.7 to -2.3±3.4, p<0.01 for intraindividual comparison). No differences were observed with respect to ultrafiltration rate, peritoneal solute transport kinetics, small solute clearances, dialytic protein loss, and concomitant medications. The outflow of CA125, a marker of mesothelial cell mass, was significantly increased by bicarbonate PD fluid (21.6±1.2 vs. 11.2±5.4 kU/m^{2}BSA, p<0.05). Peritonitis episodes occurred in 4 patients on bicarbonate and 7 patients on lactate PD fluid.

In conclusion, pH-neutral, bicarbonate buffered PD fluid is well tolerated in children on APD. Whereas solute and water transport capacity is similar, correction of metabolic acidosis appears to be more effective and mesothelial cell mass better preserved with the bicarbonate-based PD fluid.

O52 ICODEXTRIN IMPROVES FLUID BALANCE IN PD PATIENTS

Simon Davies[1], Graham Woodrow[2], Catherine Johansson[3], Paul Williams[4], Jose Divino[5]. *[1]Nephrology, North Staffordshire Hospital, Stoke-on-Trent, Staffordshire, United Kingdom; [2]Nephrology, Leeds General Infirmary, Leeds, Yorkshire, United Kingdom; [3]Nephrology, Sahlgrenska Sjukhuset, Goteborg, Sweden; [4]Nephrology, Ipswich Hospital, Ipswich, Suffolk, United Kingdom; [5]Renal, Baxter, Brussels, Belgium*

Worsening fluid balance reduces patient and technical survival in patients with increased solute transport. We have undertaken a randomised, double product blinded controlled trial (icodextrin v. glucose 2.27%) to establish whether icodextrin improved fluid status.

50 patients, (urine output <750 mls, high or high average solute transport and either treated hypertension, untreated BP>140/90 or requiring the equivalent of all 2.27% glucose exchanges) were randomised and evaluated at 1, 3 and 6 months. Endpoints included drained weight, total body water using both deuterium dilution (TBW-D) and multi-frequency bioimpedance (Xitron) (TBW-B), extra-cellular water (ECF-B), achieved ultrafiltration and total sodium losses. Data was analysed on an intention to treat basis, using between group comparisons of their change from baseline at each time-point.

Randomisation was well balanced for age, sex, race, comorbidity, renal disease and APD use (32% both groups). The icodextrin group lost weight whereas the control group tended to gain during the study. Between group differences in weight from baseline were -1.3kg, P=0.006, -1.67kg, P=0.008 and -2.0kg, P=0.014 at 1, 3 and 6 months respectively. Similar differences in TBW-B were observed: -1.7kg, P=0.006, -1.53, P=0.003 and -1.39, P=0.036. This was largely attributable to the changes in the ECF-B: -1.06kg, P=0.008, -0.85kg, P=0.035, -0.82kg, P=0.1. Differences in TBW-D at 3 months -1.1kg, P=0.047 and 6 months -0.38, P=0.2, provided independent evidence of change in body composition. The icodextrin treated group achieved consistently better ultrafiltration and total sodium losses throughout the study. We conclude icodextrin causes a sustained improvement in fluid balance.

O53 REPEATING THE PET: AT WHAT INTERVAL?

S. Bozfakioglu[1], F. Ersoy[2], T. Arinsoy[3], I. Karayaylali[4], C. Ozener[5], M. Yavuz[6], M. E. Yilmaz[7], T. Akpolat[8], R. Ataman[9], Z. Aydin[10], S. Mujais[11]. *[1]IU Med Fac; [2]Akdeniz U. Med.Fac; [3]Gazi U Med Fac; [4]Cukurova U Med. Fac; [5]Marmara U.Med.Fac; [6]Uludag U.Med Fac; [7]Dicle U Med. Fac; [8]19 May??s U.Med Fac; [9]Cerrahpasa U.Med Fac, Eczacibasi Baxter Hastane Urunleri; [10]Eczacibasi Baxter Hastane Urunleri; [11]Baxter Healthcare Corp*

Clinical guidelines on repeating the PET test are variable and mostly based on opinion. The logistic burden of the test is not insignificant and recommendations on repetition should rest on a valid expectation of change. We examined the stability of transport classification in 230 pairs of PET at intervals ranging from 1 to 24 months. Comparisons were made between initial PET and corresponding repeat within defined intervals. Results are shown in the table:

Interval (months)	N pairs	D/D0 4h		D/PCr 4h	
		Initial	Repeat	Initial	Repeat
<6	52	0.43±.01	0.44±.01	0.61±.01	0.60±.02
6-12	95	0.41±.01	0.44±.01	0.64±.01	0.62±.01
12-18	53	0.41±.01	0.43±.01	0.61±.01	0.60±.01
18-24	30	0.42±.02	0.42±.01	0.67±.01	0.61±.02*

* p=0.011

The mean D/D0 for glucose was not different in pairwise comparisons at any time interval. Mean D/P creatinine was different only in the 18-24 interval. The mean change in D/D0 in each paired comparison was less than 0.03 for all intervals, and the mean change in D/PCr was less than 0.02 for all intervals except for 18-24 months where it was 0.064. Categorical changes in classification were usually "shifts around the cusp" in contiguous groupings and were similar for all intervals examined. Our results suggest that transport classification by the PET is stable for up to 2 years and this interval may be used as a minimum interval to repeat the PET unless required by clinical profile in individual patients.

O54 FAST-FAST PERITONEAL EQUILIBRATION TEST (FAST-FAST-PET): A SIMPLE METHOD FOR PERITONEAL HYDRAULIC PERMEABILITY STUDY

Vincenzo La Milia, Monica Crepaldi, Salvatore Di Filippo, Giuseppe Bacchini, Francesco Locatelli. *Nephrology and Dialysis, Alessandro Manzoni Hospital, Lecco, Italy, Italy*

Loss of ultrafiltration (UF) capacity is one of the most important causes of CAPD failure. The use of dialysate/plasma sodium ratio (D/PNa) is an useful mean to study free water transcellular transport through acquaporin channels. However, D/PNa is not always able to predict total UF (TUF) rate and does not exactly quantify free water transport.

With the aim of assessing the reliability of D/PNa to predict TUF in a large sample size, we performed 164 standard PETs (sPET) (4 hours long with 3.86% glucose concentration) in 64 CAPD patients.

D/PNa had the highest degree of correlation with TUF at 240'. However, even if statistically significant, the overall correlation coefficient was not very high (TUF=3728-3263*D/PNa240'; R2=0.21, p<0.005).

In order to quantify transcellular water transport, we shortened the duration of sPET with the aim of significantly reducing "pure" diffusive sodium transport.

In 26 patients we performed Fast-Fast-PET (1 hour long with 3.86% glucose concentration). We then measured sodium removal (NaR), cal-

culated UF through "small pores" (NaR*1000/plasma Na) (UFSP) and UF through "ultra-small pores" (TUF-UFSP) (UFUSP).
TUF during Fast-Fast PET was 504±200 ml, UFSP was 300±153 ml and UFUSP was 204±104 ml.
These findings allowed us to conclude that Fast-Fast PET is a simple and rapid method to quantify UF through acquaporin channels without the need of intraperitoneal markers. It could be an useful tool to assess UF failure in CAPD patients.

FC10 Transplantation – Immunosuppression

O55 EFFECTS OF THREE IMMUNOSUPPRESSIVE REGIMENS ON IMMUNOLOGICAL RISK PARAMETERS: RESULTS OF A PROSPECTIVE RANDOMIZED STUDY IN RENAL TRANSPLANT RECIPIENTS

Rolf Weimer[1], Anne Staak[1], Sabine Streller[1], Hartmut Dietrich[1], Volker Daniel[2], Andreas Feustel[1], Lucie Rainer[1], Stefan Zinn[1], Shirin Friemann[3], Wolfgang Ernst[4], Helmut Grimm[5], Gerhard Opelz[2].
[1]Department of Internal Medicine, University of Giessen; [2]Institute of Immunology, University of Heidelberg; [3]Dialysis Center, Wetzlar; [4]Dialysis Center, Langenseelbold; [5]Department of Surgery, University of Giessen, Germany

We found previously that pretransplant CD4 helper activity predicts the risk of acute renal transplant rejection. To analyze the effect of CsA/Aza, CsA/MMF and Tacr/Aza therapy on CD4 helper function, B cell/monocyte and cytokine responses, 82 renal transplant recipients were randomized to one of the three regimens and immunological tests were performed before and 4 months after transplantation. A PWM-driven allogeneic coculture system was used to assess helper function of CD4+ T cells and T cell-dependent B cell responses. B cell differentiation was assessed in a reverse hemolytic plaque assay.
Pretransplant CD4 helper defects, low IL-10 (<100pg/ml) and enhanced IL-4 responses (≥2.5pg/ml) of CD4 cells predicted a low risk of acute rejection ($p<0.05$). One of the 34 (3%) patients exhibiting at least one of the three low-risk parameters experienced acute rejection (AR) in contrast to 15 of 48 (31%) patients who did not ($p=0.001$). Only Tacr based immunosuppression resulted in an increased incidence of CD4 helper defects 4 mo. posttransplant compared to the pretransplant incidence ($p<0.005$). However, Tacr/Aza treatment was associated with an increase in CD4 cell ($p<0.05$) and B cell IL-10 responses ($p<0.01$) and occurrence of acute vascular rejection in 3 patients. Six patients who were switched to Tacr/MMF showed no increase of in-vitro IL-10 responses.
Our data show that pretransplant helper defects, low IL-10 and enhanced IL-4 responses of CD4 cells predict a low risk of acute rejection. Tacr results in suppression of CD4 helper activity but should probably be combined with MMF in immunological high-risk patients, as in-vitro IL-10 responses increased on Tacr/Aza treatment.

O56 NO BENEFIT FROM MYCOPHENOLATE MOFETIL IN RENAL TRANSPLANT RECIPIENTS WITH CHRONIC ALLOGRAFT NEPHROPATHY

G. Asci, H. Toz, E. Ok, M. Sezis, A. Basci. *Nephrology, Ege University Medical School, Izmir, Turkey*

Although it has been claimed that conversion to mycophenolate mofetil (MMF) from azathioprine (Aza) might improve renal function in renal transplant recipients (RTR) with chronic allograft nephropathy (CAN), there is no prospective controlled study.
In this prospective controlled study, 38 RTR with biopsy-proven CAN on triple therapy (Cyclosporin, Aza, and corticosteroid) were randomized to continuing Aza (1.59±0.30 mg/kg) or switched to MMF (21.50±4.76 mg/kg). There were no differences in age, gender, donor age, HLA-matching, cold-ischemia time, transplant duration, serum creatinin (Cr) levels, number of previous acute rejection episodes, and histopathological scores between two groups. Cyclosporin (CsA) doses were reduced 25% in each group resulting in similar CsA levels (95±62 ng/ml in MMF group, 110±45 ng/ml in Aza).
Mean follow-up period was 10.5±1.2 months. No AR rejection episode occurred during the study. At the end of study, the mean serum Cr levels were not different between MMF and Aza groups (2.14±0.6, and 2.14±0.5, respectively). Renal function, as reflected by serum Cr levels, worsened in 8 RTR (5 in Aza group, 3 in MMF group), improved in 13 (6 in Aza group, 7 in MMF group), and was unchanged in 13 (6 in Aza group, 7 in MMF group). Two graft losses were seen in each group.
These data suggest that the addition of MMF provides no clear benefit in RTR with CAN.

O57 PERFERENTIAL SYNERGISM OF SIROLIMUS AND FK506 COMPARED TO ITS COMBINATION WITH NEORAL IN THE DEVELOPMENT OF INTIMAL HYPERPLASIA

Julian Waller, Gareth Bicknell, Nicholas Brook, Michael Nicholson.
Division of Transplant Surgery, University of Leicester, United Kingdom

Aims: Allograft vasculopathy, a central feature of chronic rejection in all solid organ allografts, remains the leading cause of late graft failure following heart transplantation. The anti-proliferative drug sirolimus has been shown to inhibit the development of intimal hyperplasia, a central feature of allograft vasculopathy. This study aims to assess the efficacy of dual combination of sirolimus and calcineurin inhibitors on the development of intimal hyperplasia, reflective of modern clinical immunosuppressive practice.
Methods: Male Sprague-Dawley rats were assigned to receive sirolimus (0.05mg/kg/day) and either FK506 (0.1mg/kg/day) or cyclosporin (5mg/kg/day) and compared to an untreated control group. All animals underwent left common carotid artery balloon angioplasty. After explantation, intima medial ratios were calculated and pro-fibrotic gene expression was measured (RT-PCR for MMP2, MMP9, TIMP-1, collagen III and TGF-beta). The extracellular matrix accumulation was quantified using pico-sirius Red.
Results: Sirolimus in combination with FK506 was associated with the greatest reduction in intimal thickening, median intima medial ratio 0.68 (range 0.36-0.94) compared to both cyclosporin, 1.12 (range 1.06-1.68, $P<0.032$) and untreated controls, 1.47 (1.02-2.04, $P<0.005$). Pro-fibrotic gene expression was significantly reduced compared to positive controls ($p<0.05$) when sirolimus was used in combination with the calcineurin inhibitors. Furthermore, treatment with sirolimus and FK506 significantly attenuated extracellular matrix deposition compared to sirolimus and cyclosporin ($P<0.023$).
Conclusion: The synergistic benefits of sirolimus in combination with FK506 are preferential over those observed with cyclosporin. Randomised trials are warranted to assess if FK506 should be the primary calcineurin-inhibitor of choice when used in combination with sirolimus.

O58 A RANDOMISED, OPEN-LABEL, PILOT STUDY TO COMPARE THE SAFETY AND EFFICACY OF TACROLIMUS (TAC) ELIMINATION WITH TAC DOSE REDUCTION IN DE NOVO RENAL ALLOGRAFT RECIPIENTS, RECEIVING SIROLIMUS, TAC AND CORTICOSTEROIDES IN THE POSTOPERATIVE PERIOD. PRELIMINARY RESULTS

J. Paul, J.M. Grinyo, J.M. Campistol, J. García, J.M. Morales, M. Arias, D. Prats. *Nephrology, H. Miguel Servet, Zaragoza, Spain*

Pilot study to evaluate renal graft function, severity of acute rejection, patient and graft survival at 3 and 12 months after transplantation,in patients receiving induction therapy with TAC and Sirolimus followed by discontinuation of TAC.
Group I: Sirolimus 2 mg/day PO following a single loading dose of 6 mg on day 1, trough levels (4-8 ng/ml), TAC (0.1 mg/kg/d) trough levels (8-12