16th Annual Meeting of the International Society of Blood Purification

Abstracts

October 4–6, 1998
Newport, R.I.

Guest Editor
Michael J. Lysaght
Brown University
Providence, R.I.

2 figures, 9 tables, 1998

The organizers would like to thank the following organizations for their generous support of ISBP '98:

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Basel · Freiburg · Paris · London · New York · New Delhi · Bangkok · Singapore · Tokyo · Sydney
Program

Sunday, October 4, 1998

12:00–19:00 Registration
12:00–17:00 Poster Setup
13:30–16:30 Welcoming Tour and Visit to Hammersmith Farm
17:30–19:30 Welcome Wine and Cheese Reception

Monday, October 5, 1998

08:45–10:15 Symposium: Therapeutic Options for the Early Stage ESRD Patient
  Chairs: K. Koch (Germany) & L. Dworkin (USA)
  - Outlook in 1998 on the Impact of Nutrition on Management and Outcome of Renal Disease (J. Bergström, Sweden)
  - Rationale for the Early Initiation of Dialysis (T. Golper, USA)
  - BMP and Related Recombinant Growth Factors as Possible Modulators of the Progression of Renal Disease (M. Charette, USA)

10:15–10:45 Coffee Break

10:45–12:00 Award Lecture & Prize Presentations
  Chairs: M. Lysaght (USA) & S. Shaldon (Monaco)
  - Award Presentation (Transplant Immunobiology): Sir Roy Calne
  - Prize Presentations
    - Cardiovascular Effects of Recombinant Human Erythropoietin in Predialysis Patients (T. Akiba, T. Takamoto, M. Hiroe, F. Marumo and Predialysis EPO Study Group, Japan)
    - Continuous High Flux Hemodialysis (CHFD) Improves Whole Blood TNFα Production in Septic Patients (G. Lonnemann, M. Bechstein, S. Linnenweber, M. Burg, Germany)

12:00–13:30 Poster Sessions with boxed lunch

Access (see page VI)
  Chairs: T. Golper (USA) & F. Locatelli (Italy)

Clinical (see pages VI–VII)
  Chairs: J. Bergström (Sweden) & K. Leunissen (The Netherlands)

13:30–15:00 Free Communications 1
  Chairs: H. Klinkman (Germany) & V. Tesar (The Czech Republic)
  - Cytokine mRNA Expression Patterns and Levels in End-Stage Renal Failure and Renal Replacement Therapy (I. van Riemsdijk, E. Loonen, C. Baan, R. Zietse, W. Weimar, The Netherlands)
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Plasma Homocysteine Level (sHCY) in Patients on Hemodiafiltration (HDF)

M. Gonella, G. Calabrese, M. Scancarello, A. Mengozzi, G. Vagelli, P. Deambrogio (Italy)

New Generation of Steam Sterilized Dialysers

H. Göhl, R. Buck, M. Storr, R. Deppisch (Germany)

May Albumin Loss through Dialyzer Membrane Contribute to Low Serum Albumin Levels in Hemodialysis Patients?

W. Beck, R. Deppisch, H. Göhl (Germany)

Can Sterile and Pyrogen-Free Substitute Be Consistently On-Line Delivered?

L. Vaslaki, A. Karátson, P. Vörös, L. Major, F. Pethő, E. Ladányi, C. Weber, R. Mitteregger, D. Falkenhagen (Germany)

15:00–15:30 Coffee Break

15:30–17:00 Panel: Present and Future Trends in the Management of ESRD

Chairs: S. Shaldon (Monaco) & E. Lowrie (USA)

Panelist & Discussants

J. Bosch, M. Lazarus, J. Newmann (USA)

17:15–18:00 ISBP Business Meeting

19:30–23:30 Festive Banquet at Rosecliff

Tuesday, October 6, 1998

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10:30–11:00 Coffee Break

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<td>Announcement of Posterpresentation Awards</td>
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<td>Special Lecture: Cytokines in the Pathogenesis and Treatment of Renal Failure</td>
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<td>R. Deppisch (Germany)</td>
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16th Annual Meeting of the ISBP
## Poster Sessions

**Monday, October 5, 1998**

### 12:00–13:30 Access

**Chairs:** T.A. Golper (USA) & F. Locatelli (Italy)

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**Chairs:** J. Bergström (Sweden) & K. Leunissen (The Netherlands)

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Tuesday, October 6, 1998

Bioengineering/CAPD
Chairs: L. Henderson (USA) & S. Jörstad (Norway)

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Comparison of Microbiological Quality of Dialysate and Replacement Fluid in On-Line Hemodiafiltration (HDF) vs. Conventional Hemodialysis (HD) and HDF in Clinical Application
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1 Cardiovascular Effects of Recombinant Human Erythropoietin in Predialysis Patients

T. Akiba, T. Takamoto, M. Hiroe, F. Marumo and Predialysis EPO Study Group
Tokyo Med. & Dent. Univ., Tokyo, Japan

Cardiovascular diseases account for more than half of deaths in end-stage renal disease patients, suggesting a particular importance to prevent cardiovascular damages in predialysis patients. We studied predialysis patients with serum creatinine (Cr) of ≥2 mg/dl or with creatinine clearance of ≤30 ml/min, and a hematocrit (Hct) of <30%. They were administered 6,000 IU of Epoetin-ß (EPO) once a week until their Hct levels reached ca. 30% (initial phase, IP). Then, the Hct levels were maintained for 8 weeks with decreased dose or frequencies of EPO (maintenance phase, MP). Nineteen patients were administered EPO and their cardiac function sequentially estimated by echocardiography. Their serum Cr were 5.1±2.0 mg/dl (mean±SD), and Hct were 24.9±2.7% before EPO. Hct increased to 30.9±1.9% at the end of IP, and maintained to 31.3±2.7% at the end of MP. Blood pressure did not change during the study. Echocardiography showed significant decreases in LVDD, LVFT, LVMASS, CO and HR (p<0.05), but no changes in AOD, LVDS, LVST, PWT, FT, RVD, LAD, Max-AOV, and A/R. We conclude that the administration of EPO to predialysis patients improves renal anemia, ameliorates hyperkinetic state of heart and reduces cardiac volume. These improvements might decrease cardiovascular risk both in predialysis and dialysis patients.

2 Clinical Effect of a New Triacetate (CTA) Membrane with Microgradient Structure for Hemodialysis (HD)

Fujigaoka Hosp., Showa Univ., Rokkou Island Hosp., Yokohama, Japan

CTA membrane ordinarily has a skin membrane structure. The performance and biocompatibility of new CTA membrane with micro-gradient porous membrane structure were evaluated for 30 regular HD patients for 1–3 months. In addition to the high clearance (CL) for small molecules (urea nitrogen CL: 182±4 ml/min under 200 ml/min dialysate flow rate), CL and reduction rate of β2-microglobulin (β2M) reached 74.4±11.1 ml/min and 69.0±2.4%, respectively. This dialyzer demonstrated a high sieving coefficient (SC) for β2M (0.98±0.10 at 1 hr after the start of HD), and did not show any significant reduction even at 4 hr (0.93±0.07). SC of myoglobin and α1-microglobulin at 1 hr was 0.57±0.23 and 0.19±0.08. Despite the high removal capacity for low molecular protein fractions, albumin loss in dialysate remained 2,053±722 mg/HD. These results suggest that new CTA membrane realized the high removal capacity for uremic substances without the risk of albumin deficiency.

3 Quality of Life (QoL) in Patients with Chronic Renal Failure (CRF)

C. Avanzi for the A.S.P.N.A.T. Group
San Severo, Italy

Aim of the study was to evaluate the QoL of patients affected by different levels of severity of kidney diseases. SF-36 questionnaire was submitted to control group (A), was evaluated by G. Apolone et al., and to patients with CRF treated by diet (B), by dialysis (C), by kidney transplant (D) (see table).
SF-36, though generic questionnaire, is a good tool to differentiate, among kidney patients and control subjects, the self-perception of QoL.

### 4 Survival of Prosthetic Grafts in Chronic HD Patients with Compromise of the Endogenous Venous System (VS)

G. Bacchini, S. Andrulli, M. Corti, L. Del Vecchio, F. Locatelli
Nephrology and Dialysis Division, Hospital of Lecco, Lecco, Italy

The compromise of VS is a common problem in HD pts and the construction of prosthetic graft has been considered a valid alternative. During the period 1991–1997, we prospectively evaluated 40 pts (23 F, 17 M, age 69 ± 10 years, time on dialysis 6.25 ± 5.5 years) who underwent prosthetic surgery for hemodialysis vascular access (VA) in the right or left arm, with compromise of VS due to distal and proximal fistulas. We used PTFE (n = 45), reinforced PTFE (n = 8) and biological (n = 5, mesenteric bovine vein) materials to perform 92 surgeries for vascular access (58 constructions and 34 revisions). VA survival, as measured by Kaplan-Meyer analysis, was 2.8, 4.2 and 17.8 months (75, 50 and 25 percentiles, respectively). Each patient had a median of 2 surgeries (max 6) lasting between them 2.3, 3.1 and 9.2 months (25, 50 and 75 percentiles). Total VA survival (that is VA survival apart from the number of re-interventions in each patient) was 81%, 75% and 65% at 1, 2 and 3 years, respectively. Our experience showed that the probability of VA failure, after compromise of VS, was of 50% at 4 months.
6 Comparison of Microbiological Quality of Dialysate and Replacement Fluid in On-Line Hemodiafiltration (GDF) vs. Conventional Hemodialysis (HD) and HDF in Clinical Application

R. A. Heidler, W. Beck, R. Deppisch, J. Braun
Hemodialysis Unit Nürnberg, Gambro R&D, Hechingen, Department of Medicine IV, Division of Nephrology, University of Erlangen-Nürnberg, Germany

HDF is being used as an efficient treatment method for long-term ESRD patients. Convective removal of uremic toxins such as β2-microglobulin requires high volumes of replacement fluids, which can be produced economically by an on-line three-step ultrafiltration system. The use of ultrapure dialysate may also lower the risk of exposure to substances causing monocyte activation, which has been thought to contribute to long-term complications in ESRD patients. In this study we compared the microbiological quality of dialysate and replacement fluid in different treatment modes, i.e. conventional HD, HDF and on-line HDF. Stable ESRD patients (n = 29) were treated in 3 parallel groups for 5 months: (i) conventional HD (GFS+), (ii) conventional HDF (Polyflux 14S) using bags for reinfusion and (iii) on-line HDF (Polyflux 14S) using AK100 ULTRA machine. Bicarbonate dialysate prepared from dry powder was used in all treatments. 50 ml dialysate and substitution fluid were taken at the dialyzer inlet and infusion line, respectively, after 4 h treatments at the beginning of the study and after 5 months. Microbiological testing was performed under optimized cultivation conditions for detection of water/dialysate-borne (gram-negative) bacteria, i.e. nutrient-poor tryptone-glucose-agar, 25°C and 7 days cultivation. Endotoxins were analyzed using a kinetic LAL-assay (Chromogenix, det. limit 0.01 EU/ml). Analysis of gram-negative bacteria in dialysate gave the following results: 1 of 23 samples was positive in the on-line HDF group, whereas in the HD group and the conventional HDF group 21 of 28 and 20 of 28 samples, respectively, contained gram-negative bacteria. No endotoxins could be detected in the dialysate and replacement fluid of the on-line HDF group. In contrast, in 8 of 17 dialysate samples of the conventional HD and in 10 of 19 samples of the conventional HDF group endotoxins could be detected in low concentrations (0.01–0.05 EU/ml). 1 of 19 samples of the reinfusion bag used for conventional HDF contained 0.02 EU/ml. No febrile episodes were reported during the treatments. Our data show that on-line preparation of dialysate and substitution fluid enables HDF treatments without the risks of bacterial and endotoxin contamination. Long-term investigations are needed to document clinical benefits of ultrapure dialysate/infusate on monocyte activation and related long-term complications in ESRD patients.

7 Trace Elements in Serum of Chronic Hemodialysis and CAPD Patients

M. Benedik, A. Briški, R. Ponikvar, A. Guček
University Clinical Center, Ljubljana, Slovenia

In the study 127 patients on chronic HD program and 46 stable CAPD patients were included. In HD patients 6 ml of blood was taken before the beginning of HD. In CAPD patients 6 ml of blood was taken in the morning before the first exchange. For blood collection Becton-Dickinson Vacutainer tubes No 12200 were used. Serum was separated from red cells within two hours of collection. Serum levels of Se, Zn and Cu were analyzed by electrothermal atomic absorption spectrometry (ETAAS). The results are in the table.

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<th>Median</th>
<th>Min.</th>
<th>Max.</th>
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<td>Se1 (μg/l)</td>
<td>55.1</td>
<td>14.7</td>
<td>54.0</td>
<td>25.0</td>
<td>103.0</td>
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<tr>
<td>Zn1 (μg/l)</td>
<td>538.7*</td>
<td>112.4</td>
<td>527.5</td>
<td>369.3</td>
<td>1,164.9</td>
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<tr>
<td>Cu1 (μg/l)</td>
<td>1,014.7</td>
<td>232.6</td>
<td>985.5</td>
<td>584.6</td>
<td>1,942.4</td>
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<td>Se2 (μg/l)</td>
<td>59.6</td>
<td>15.5</td>
<td>56.5</td>
<td>33.0</td>
<td>104.0</td>
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<tr>
<td>Zn2 (μg/l)</td>
<td>645.2</td>
<td>106.6</td>
<td>633.4</td>
<td>466.1</td>
<td>916.5</td>
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<td>Cu2 (μg/l)</td>
<td>1,004.6</td>
<td>229.4</td>
<td>970.3</td>
<td>301.8</td>
<td>1,588.5</td>
</tr>
</tbody>
</table>

Se1, Zn1, Cu1-HD pts; Se2, Zn2, Cu2-CAPD patients; *Zn1/Zn2: p < 0.0001.

We can conclude that serum Zn levels are significantly lower in HD patients.
Inflammation, Malnutrition, Cardiac Disease and Mortality: An Integrated Hypothesis

Jonas Bergström, Bengt Lindholm
Div. of Renal Med. and Baxter Novum, Karolinska Institute, Stockholm, Sweden

Malnutrition and hypoalbuminemia, which are prevalent in patients with end-stage renal disease (ESRD), are strong predictors of increased mortality. However, cardiovascular disease predominates among direct causes of death, whereas malnutrition appears to be of minor importance in this respect. Reports in the literature demonstrate that cardiac failure may cause malnutrition and that infection/inflammation may predispose to atherosclerosis as well as protein catabolism and hypoalbuminemia. Cytokines, generated in response to cardiac failure, infection and other inflammatory stimuli, may cause muscle wasting, hypoalbuminemia and anorexia as well as reduced cardiac contractility and atherosclerosis. We propose that malnutrition in ESRD patients is largely the consequence of cardiac failure or is caused by factors (infection, inflammation) which also trigger the development of atherosclerotic cardiovascular disease, in which scenario proinflammatory cytokines have a pivotal role. Malnutrition may rarely be the direct cause of death, except in elderly dialysis patients, but may contribute to a poor prognosis by aggravating pre-existing heart failure and increasing the susceptibility to infections.

Compartment Effects Influence Lean Body Mass Estimates in Hemodialysis (HD) Patients

W.R. Clark, R.J. Hamburger, J.K. Leypoldt
Baxter Healthcare Co., Indiana Univ., and Univ. of Utah/VAMC, USA

Estimates of lean body mass (LBM) derived from creatinine kinetics (CK) are dependent on the specific CK model used in chronic HD patients. Using both single-pool (SP) and double-pool (DP) methods, we determined CK parameters in 20 patients receiving 41 high-flux HD treatments. Serum C at 20 sec (SP) or 80 min (DP) post-HD was used with the subsequent pre-HD serum C to estimate C generation rate (Gc), from which C index (CI) and LBM were derived. Patient characteristics were: sex (M/F), 12/8; age, 51.1 ± 15.3 yrs; dry body weight (BW), 79.4 ± 17.5 kg. Overall DP CI was 20.6 ± 6.5 mg/kg/d (M/F: 23.8 ± 6.1/16.5 ± 4.5; p < 0.001). The SP/DP estimates of Gc and LBM were 1.09 ± 0.40/0.91 ± 0.32 mg/min and 61.0 ± 19.1/54.1 ± 15.9 kg, respectively; SP vs DP, p < 0.0001. Linear regression analysis revealed systematic overestimation of LBM by the SP methodology: DP = 0.83·SP + 3.6 (r = 0.99, p < 0.0001). Normalization of LBM to dry BW confirmed this overestimation: 0.79 ± 0.22 vs. 0.70 ± 0.19 kg/kg; SP vs DP, p < 0.0001).

Conclusions: (1) CK methods providing estimates of somatic protein nutritional status in chronic HD patients must account for C’s multi-compartment kinetics; (2) use of SP CK methods results in significant overestimation of LBM.

Relationship between Urea and Creatinine Rebound in Hemodialysis (HD)

W.R. Clark, R.J. Hamburger, J.K. Leypoldt
Baxter Healthcare Co., Indiana Univ., and Univ. of Utah/VAMC, USA

Although numerous studies have measured post-HD urea rebound (UR) and its effect on delivered HD close, little is known about the R kinetics of larger uremic solutes. We studied the relationship between UR and creatinine R (CR) in 20 patients (12 M/8 F; age, 51.1 ± 15.3 yrs; mean ± SD) receiving 41 high-flux HD treatments. BUN and serum C were measured 20 sec and 30 min post-HD, the latter assumed to be U equilibration (eq) time. Based on our prior two-compartment modeling (Clark et al, ASN 1997), an 80 min eq concentration for C was derived from the measured 30 min values. The following concentrations were used to determine R (corrected for generation): [(eq – 20 sec)/20 sec] × 100%. Treatment characteristics were: time, 3.8 ± 0.3 hrs; dialysate U/C clearance, 230 ± 40/184 ± 44 ml/min; double-pool Kt/V, 1.42 ± 0.30 (BioStat™, Baxter). Post-HD CR was significantly greater than UR (29.3 ± 11.3 and 17.6 ± 9.4%, respectively; p < 0.0001). Regression of CR with UR revealed a relatively weak linear relationship: CR = 0.73·UR + 16.5 (r = 0.60, p < 0.0001).

Conclusions: (1) CR is greater than UR, consistent with different intercompartment mass transfer rates for U and C during HD; (2) the relatively weak relationship between UR and CR suggests different factors determine U and C intercompartment mass transfer.
11 In vitro Metabolic Activity of the HepatAssist® Liver-Assist System

Linda Custer, Claudy Mullon
Circe Biomedical, Lexington, Mass., USA

Previously cryopreserved primary porcine hepatocytes have been placed in the extrafiber space of a polysulfone hollow-fiber cartridge. The device is similar in size and configuration to a hemodialyzer, except that its membrane is microporous rather than ultrafiltrative and that it has been designed to contact plasma rather than whole blood. It is placed in a HepatAssist® flow circuit comprising a pump and a combined heat-gas exchanger and used to treat patients with acute liver failure. This therapy has bridged patients to successful orthotopic liver transplants or spontaneous recovery. In laboratory studies to investigate the potential detoxification and metabolic activities of this system, the metabolism of diazepam, glucose, galactose, ammonia, and oxygen were measured. Typical observed rates of metabolism were:

<table>
<thead>
<tr>
<th>Substance</th>
<th>Metabolism Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>diazepam</td>
<td>3,000 mg/h converted to metabolites</td>
</tr>
<tr>
<td>glucose</td>
<td>100 mg/h produced</td>
</tr>
<tr>
<td>galactose</td>
<td>100 mg/h consumed</td>
</tr>
<tr>
<td>ammonia</td>
<td>150 µmol/h consumed</td>
</tr>
<tr>
<td>oxygen</td>
<td>800 µg/min consumed</td>
</tr>
</tbody>
</table>

12 Arrhythmia in Hemodialysis Patients

Cosenza, Italy

It is a well-known fact that patients in hemodialysis are exposed for various reasons to the risk of cardiac arrhythmia. The aim of this paper is to evaluate the incidence and the type of arrhythmia in a selected group of hemodialysis patients through electrocardiographic monitoring according to Holter. 14 patients undergoing hemodialytic treatment three times a week (9M, 5F; age: 54.4 ± 12.9 years old; duration of dialysis: 94.4 ± 48.8 months) were subjected to dynamic ECG according to Holter at the beginning and during the hemodialytic treatment and the interdialytic period during the week a continuous 24-hour registration for each period. Not all the patients were suffering from previous myocardial ischemic disease, arterial hypertension, diabetes, or severe anemia (Hb ≥ 10 mg/dl; HCT ≥ 25). Supraventricular hyperkinetic arrhythmias were present in 11 patients out of 14, equal to 78%, with an equivalent frequency between the inter- and intra-dialytic period, and hyperkinetic arrhythmia was present in 12 patients out of 14 equal to 85%, in the intradialytic period and in 9 patients out of 14, equal to 64%, in the interdialytic period. All the types of ventricular arrhythmia according to the classification in degrees by Lown were present. In our study we noted a greater incidence of ventricular arrhythmia in the intradialytic period compared to the interdialytic period but no substantial difference in the type or in the severity of the arrhythmia. In addition, no statistically significant correlation was found between arrhythmia and age and duration of dialytic treatment. In conclusion, hemodialysed patients, without cardiac diseases, present an elevated risk of arrhythmia. The continuous monitoring of the cardiac rhythm according to Holter can indicate the patients with more severe arrhythmia and, therefore, exposed to the risk of clinical cardiological emergencies during hemodialysis.

13 New Generation of Steam Sterilized Dialysers

H. Göhl, R. Buck, M. Storr, R. Deppisch
Gambro R&D, Hechingen, Germany

The evolution of polyamide membranes started with membranes developed for hemofiltration and ultrafiltration. Both applications were characterized by high ultrafiltration, respectively by high retention for microbiological substances like bacteria, endotoxins or cytokine inducing substance. In further steps the membrane has been optimized towards high removal rate for low and high molecular weight uremic toxins in hemodiafiltration and high flux dialysis, e.g. β2-M, factor D, GIP etc. It has been sterilized with γ-radiation or ethylene oxide. In the new Polyflux ‘S’ the membrane is steam sterilizable through alloying the polyamide with a heat resistant polymer, the polyarylethersulfone. The good endotoxin retention and the good biocompatibility of the polyamide membrane was kept in the membrane structure, by enrichment of the content of polyamide at the inner surface (whereas the outer surface is poor on polyamide). The third alloy component PVP forms together with the hydrophobic components microdomain structured surfaces which have been proven to be highly biocompatible. The good blood compatibility is achieved in the steam
sterilized Polyflux low flux version (UF coefficient of 6 ml/mmHg·m²) as well as in Polyflux S high flux (UF coefficient of about 50 ml/mmHg·m²) at the same high level which has not been reached for another synthetic polymer system. In vitro data for both types exhibit lowest generation of terminal complement complex (TCC), no activation of the kallikrein system, low thrombin generation (TAT) and low release of platelet factor 4. The low thrombogenicity allows reduced use of heparin during dialysis. Removal rates of the high flux membrane for low molecular weight as well as for high molecular weight substances are increased for the steam sterilized dialyser, i.e. urea clearance at Q _b _= 300 ml/min and UF = 0 for Polyflux S (1.7 m²): 257 ml/min, and for Polyflux ETO: 243 ml/min. The sieving coefficient for β_2-M could be optimized for Polyflux S, i.e. 0.75 compared to 0.6 for Polyflux-ETO. Although permeability increased, albumin loss through this 3-layer membrane structure could be kept below approximately 150 mg/l filtrate. The 3-layer structure enables in the low flux as well as in the high flux version constant performance with time (sieving, clearance, filtration) over the whole treatment period by preventing penetration of proteins into the membrane structure. For the first time a synthetic membrane has been developed towards clinical requirements. The 3-layer structure combined with a microdomain surface is the core element of this new generation of steam sterilizable membranes.

14 Plasma Homocysteine Level (sHCY) in Patients on Hemodiafiltration (HDF)

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Servizio di Nefrologia e Dialisi, Ospedale S. Spirito, Casale Monferrato, Italy

High sHCY in RDT pts is considered a risk factor for atherosclerosis. sHCY is reduced by folate (FA) supplements and removed by dialysis in a range of 11–49%. In this study sHCY was evaluated in pts on high-flux HDF. In 36 anuric pts (F 19, M 17, age 69 ± 14 yrs, BW 65 ± 11 kg, dialytic age 74 ± 58 mo) on HDF (with synthetic membranes, exchanging 18 l for each session lasting 247 ± 16 min), receiving 1.5 mg of FA and 16 ug of vit B12/week, keeping their plasma values (7.8 ± 2.9 ng/ml, 613 ± 274 pg/ml) normal, pre-post-dialysis sHCY was measured (HPLC, Biorad, n.v. 11 ± 2 μmol/l) and correlated with other parameters. HDF sessions lowered sHCY from 33 ± 10 to 16 ± 5 μmol/l (52%). Predialytic sHCY correlated with vit B12 (p < 0.01) and sCr (p < 0.05) but not with dialytic age and plasma FA. This study confirms high sHCY in RDT pts and an efficient removal by HDF. The combined effect of larger FA and vit B12 doses and high-flux HDF on sHCY should be evaluated.

15 Poly(Ethylene Oxide) – Polysulfone Block Copolymer Membranes

S.M. Fagan, K.A. Gagnon, L.F. Hancock, C.J.-P. Mullon
Circe Biomedical, Inc., Lexington, Mass., USA

A variety of surface modification post treatments have been used to improve the bio/hemocompatibility of materials. Membranes are an especially difficult challenge for surface modification. The high surface area and sub-micron dimensions of membrane pores make it difficult to ensure a uniform surface modification on a membrane. The present work overcomes this difficulty by covalently linking the surface modification agent to a base polymer and using the material directly for the manufacture of membranes. The presentation will report the synthesis of poly(ethylene oxide)/polysulfone block copolymer (PEO-b-PSF) and its utility for the manufacture of PEO surface modified membranes. PEO’s unique aqueous solution behavior is known to limit protein adsorption when it is used as a surface modification. Membranes manufactured from PEO-b-PSF possess an enriched PEO surface which reduces protein adsorption by ~ 50%. Micro-porous, immunorejection and dialysis membranes have been manufactured with EPO-b-PSF. A novel bioreactor membrane is being developed for application in a bioartificial liver.

16 Vascular Refilling Monitoring in Dialysed Children Using Bioimpedance and Continuous Hematocrit Measurements

Michel Y. Jaffrin, C. Fournier
UTC Compiègne, France

Continuous hematocrit measurements by optical methods in the blood line of dialysed patients can serve to monitor the relative plasma volume changes.
However attempts to correlate occurrence of hypotension solely with plasma volume reduction have not been successful. We have attempted to combine continuous hematocrit measurements with the monitoring of extracellular fluid volume (ECV) by bioimpedance using an extrapolation at zero frequency in order to obtain information on interstitial fluid variation and to what extent it participates to vascular refilling. Since dialyzed children are particularly prone to hypotension, a study was performed on 11 pediatric patients aged from 12 to 21 years. The extracellular resistance is converted into percent changes in ECV using our previously published method (Ve/Veo = R_eo/Reo, MBEC, 1997, p. 266) and absolute changes (in liters) of plasma volume and ECV are determined from initial estimates of these volumes using standard correlations from the literature after correction to take into account initial excess fluid. It is found that patients suffering from hypotension have on average a higher percentage of ultrafiltered volume lost by ECV (105% versus 92%), less reduction in intracellular fluid and a larger reduction in interstitial fluid volume than those without hypotension.

17 Clinical Evaluation of a New Synthetic Steam Sterilized Low-Flux Dialyzer

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Department of Internal Medicine III, University of Tübingen, Germany

Low-flux hemodialyzers made of cellulose, modified cellulose or synthetic polymers (e.g. cuprophan, cellulose acetate, polysulfone) do not reach the level of biocompatibility which has been achieved with synthetic high-flux membranes, e.g. Polyflux, Polysulfone. Therefore a synthetic low-flux membrane has been developed incorporating an asymmetric three layer structure combined with a hydrophilic/hydrophobic microdomain surface. In vitro analysis during dialyzer development revealed significantly reduced terminal complement activation as well as thrombogenicity in mini-module devices. Clinical investigations were performed to analyse permeability and biocompatibility, esp. complement activation. Stable ESRD patients (n = 8) were treated in two centers applying an A-B-A cross-over design (A: low flux Polyflux L14; B: lowflux Polysulfone HP86) using bicarbonate dialysate at Q_B 280–330 ml/min for 4–5 h. To assess complement activation and leukocyte counts EDTA-blood samples were taken at t = 0 and t = 15 min from the arterial and venous lines. EDTA plasma samples were analyzed for C3a (ELISA, Progen), C5a (ELISA, Behring) and TCC (sandwich ELISA using monoclonal anti-TCC antibody and polyclonal anti C5 antibody). Leukocyte drop observed at 1.5 min was below an average level of 25%, but many treatments with Polyflux L14 were below 10%. Data for generation of complement activation products (venous samples at t = 15 min) are given in the table below:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Significance*</th>
<th>Polyflux L14</th>
<th>Polyflux L14</th>
<th>HP86</th>
</tr>
</thead>
<tbody>
<tr>
<td>C3a [ng/ml]</td>
<td>p &lt; 0.01</td>
<td>1.237 ± 0.329</td>
<td>1.719 ± 0.178</td>
<td>1.301 ± 0.359</td>
</tr>
<tr>
<td>C5a [ng/ml]</td>
<td>n.s.</td>
<td>5.0 ± 1.7</td>
<td>5.8 ± 1.8</td>
<td>3.9 ± 1.3</td>
</tr>
<tr>
<td>TCC [ng/ml]</td>
<td>n.s.</td>
<td>689 ± 384</td>
<td>801 ± 317</td>
<td>578 ± 292</td>
</tr>
</tbody>
</table>

*Wilcoxon test for paired data

Our data show that surface induced complement activation is significantly lower for the new Polyflux L14 membrane compared to Polysulfone. Since leukocyte drop shows a non-significant difference in this study it seems to be reasonable to screen for other leukocyte activation parameters which have so far not been considered for biocompatibility evaluation of dialyzer membranes.

18 Ten-Year Experience with Extracorporeal Treatment of TTP/HUS

D. Beuno Jr., J. Reardon, J. Sevigny, A.A. Kaplan
Univ. Conn. Hlth Ctr, Framington, Conn., USA

From 1989 until 1998 we treated a total of 22 patients presenting with 24 episodes of thrombotic microangiopathy compatible with a TTP or HUS-like syndrome. 10 patients presented after bone marrow transplantation or chemotherapy (BM/C), 8 patients with ‘community-acquired’ idiopathic disease (CA), 2 patients were in the peripartum period (PP), one with a HELLP-like syndrome and 2 patients had a background of scleroderma (SC). 19 episodes were treated exclusively with therapeutic plasma exchange (TPE) using fresh frozen plasma. In the BM/C group, 4 were treated consecutively with TPE and the Prosorba protein A column, while one received only the Prosorba treatment. Successful outcome required up to 57 treatments.

Results: Only 1/10 BM/C patients survived (she received 26 TPE rxs), only 4/8 CA patients survived,
both PP patients survived, both SC patients survived, but with ESRD.

Conclusions: Despite aggressive extracorporeal therapy, TTP/HUS remains a deadly disease. Treatment with the Prosorba column was unsuccessful in reversing the dismal prognosis of patients with BM/C-associated TTP/HUS.

19 Hemodialysis (HD) Decreases Elevated Plasma Levels of the NO-Synthase Inhibitor Asymmetric Dimethylarginine (ADMA) in ESRD Patients
J.T. Kielstein\(^a\), R.H. Böger\(^b\), S.M. Bode-Böger\(^a\), K.M. Koch\(^b\), J.C. Frölich\(^a\)
\(^a\) Institute of Clinical Pharmacology and \(^b\) Division of Nephrology, Medical School Hannover, Germany

Endothelial dysfunction due to a lack of biologically active NO may be involved in the pathogenesis of hypertension and cardiovascular diseases in ESRD. ADMA is an endogenous inhibitor of endothelial NO-synthase. We measured plasma levels of L-arginine and ADMA by HPLC in HD patients (HD, \(n = 43\)) and matched controls with normal renal function (C, \(n = 37\)). NO synthesis was assessed as plasma nitrate by GC-MS. In a subgroup of 10 HD patients the same parameters were determined 1, 5 and 18 hours after end of HD sessions. Results are given in \(\mu\)mol/l, mean \(\pm\) SEM. Compared to controls, HD patients had six-fold elevated ADMA levels (HD: 5.95 \(\pm\) 0.49 vs. C: 1.29 \(\pm\) 0.18, \(p < 0.05\) by ANOVA) and lower nitrate levels (HD: 23.9 \(\pm\) 1.7 vs. C: 39.1 \(\pm\) 1.9). L-arginine, the substrate for NO-synthase, was not decreased in HD patients (HD: 75.9 \(\pm\) 7.2 vs. C: 75.5 \(\pm\) 3.9). In the time course study, ADMA levels were pre HD: 5.2 \(\pm\) 1.4; 1 hour post-HD: 6.5 \(\pm\) 0.7; 5 hours post-HD: 2.3 \(\pm\) 0.3; and 18 hours post-HD: 3.1 \(\pm\) 0.4. Although ADMA (MW: 202.3 Dalton) should easily be removed by HD, ADMA plasma levels were not lowered until 5 hours after end of HD session. This delayed decrease may in part be explained by redistribution.

Conclusion: (1) ADMA accumulates in ESRD patients. (2) Elevation of ADMA levels is accompanied by decreased plasma nitrate, suggesting ADMA to be a possible cause for reduced NO synthesis in ESRD patients. (3) HD significantly reduces ADMA plasma levels.

20 Changes in the Sigmoidal Relationship between PTH and Serum Ca by the Intravenous Treatment of 22-Oxacalcitriol (OCT)
Fujigaoka Hosp., Showa Univ., Eda Clinic, Yokohama, Japan

OCT is a new synthesized vitamin D analogue for intravenous administration. The effect of OCT treatment on parathyroid (PT) function was evaluated by PTH-Ca ion sigmoidal curve (S). Six hemodialysis (HD) patients with severe secondary hyperparathyroidism received 5–10 \(\mu\)g OCT at the end of every HD for 26 weeks. S was examined at the start, 12 weeks and the end of OCT treatment by changing dialysate Ca concentration from 0 to 4.5 mEq/l. Mean intact PTH levels were decreased from 678 at basal to 414 pg/ml at week 12. Maximal PTH secretion by hypocalcemic challenge (PTH max) tended to decrease from 1,722 to 1,164 pg/ml at week 26 as well as minimal PTH secretion by hypercalcemic challenge (PTH min) from 340 to 242 pg/ml. Despite the reduction of cellular mass of PTH secretion demonstrated by the decrease in PTH max and min, no significant change was observed in set-point Ca level and the slope of S. These results suggest that OCT suppresses PTH secretion not by the improvement of PT cell sensitivity for serum Ca, but by the reduction of PT cell mass secreting PTH.

21 The Influence of Increasing Dialysis Time Leads to Better HD Quality: An Intra-Individual Comparison
W. Kleophas\(^a\), D. Bach\(^b\), T. Wessels\(^c\), G.v. Endert\(^a\), A. Westhoff\(^a\), B. Grabensee\(^c\)
\(^a\) Dialysis Center Düsseldorf Karlstrasse, \(^b\) Krefeld Hospital Dept. of Nephrology, \(^c\) Dept. of Nephrology and Rheumatology, Univ. Düsseldorf, Germany

The aim of the study was to evaluate whether increasing dialysis time leads to better dialysis quality. Five patients were investigated (m/f 4/1, anurics, age 50.8 \(\pm\) 7.5 years; dialysis since 48.4 \(\pm\) 25.3 months). During a preliminary phase of 6 months, patients were dialyzed with polysulfon membranes, bicarbonate buffer and batch-type dialysis machines 3 \(\times\) 5 h per week with a dose of 75 litres and a blood flow of 250 ml/min. Afterwards patients were dialyzed 3 \(\times\)
8 h per week with the same equipment. Initially a dose of 72 litres was used; blood/dialysate flow at 150 ml/min. After 3 months the dose was increased to 90 litres with blood/dialysate flow at 190 ml/min. Blood samples were drawn pre- and post-dialysis for Kt/V and PCR calculations, PO4 and albumin. Blood pressure was taken before and after every dialysis. Statistical analysis was performed by using adjusted t-test, p-value < 0.05 regarded to be statistically significant.

### Results:

<table>
<thead>
<tr>
<th>Time, Flow</th>
<th>1 month pre</th>
<th>3rd month</th>
<th>4th month</th>
<th>6th month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time, Flow 5:00 h, 250 ml</td>
<td>8:00 h, 150 ml</td>
<td>8:00 h, 190 ml</td>
<td>8:00 h, 190 ml</td>
<td>8:00 h, 190 ml</td>
</tr>
<tr>
<td>PCR (p)</td>
<td>0.85 ± 0.01</td>
<td>1.03 ± 0.07</td>
<td>0.90 ± 0.09</td>
<td>1.02 ± 0.22</td>
</tr>
<tr>
<td>Albumin</td>
<td>4.01 ± 0.19</td>
<td>4.51 ± 0.13</td>
<td>4.507 ± 0.29</td>
<td>4.74 ± 0.15</td>
</tr>
<tr>
<td>PO4, mg/dl</td>
<td>2.47</td>
<td>2.37</td>
<td>2.22</td>
<td>2.15</td>
</tr>
<tr>
<td>SYSP pre</td>
<td>154.8 ± 16.8</td>
<td>148.5 ± 9.0</td>
<td>145.5 ± 9.4</td>
<td>145 ± 15.9</td>
</tr>
<tr>
<td>SYSP post</td>
<td>128.7 ± 17.2</td>
<td>124.5 ± 13.3</td>
<td>117.6 ± 15.2</td>
<td>119.7 ± 17.1</td>
</tr>
<tr>
<td>DIAP pre</td>
<td>85.6 ± 5.2</td>
<td>83.2 ± 1.1</td>
<td>82.2 ± 3.9</td>
<td>83.3 ± 4.6</td>
</tr>
<tr>
<td>DIAP post</td>
<td>78.3 ± 9.0</td>
<td>75.8 ± 9.7</td>
<td>72.4 ± 7.3</td>
<td>69.9 ± 10.8</td>
</tr>
</tbody>
</table>

Our data show that increased dialysis time together with decreased blood flow may lead to significantly better results in dialysis quality.

### 22 The Effect of Dialysate Temperature on Energy Transfer during Hemodialysis (HD)

**J. Kooman, F. van der Sande, J. Buurma, P. Hamelers, A. Kerkhofs, J. Barendregt, K. Leunissen**

University Hospital Maastricht, The Netherlands

It is well known that the use of low temperature (T) dialysate has a positive impact on hemodynamic stability during HD. However, little is known on the energy transfer (ET) from the extracorporeal system to the patient in relation to variations in dialysate T (Tdial). In this study, we assessed ET, body T (Tbody), and blood pressure (BP) during dialysis with Tdial = 37.5°C and Tdial = 35.5°C. Nine patients (4 males, 5 females; mean age: 68 years) were studied with the patient as his/her own control. Bicarbonate dialysate and hemophane membranes were used. HD time varied between 180 and 240 minutes. Dialysate contained <100 CFU/ml. Ultrafiltration volume was comparable between both treatments. ET was assessed by continuous measurement of T in the arterial (Tart) and venous side (Tvem) of the extracorporeal system (Fresenius BTM®) according to the formula: ET = (Tvem – Tart) - blood flow - treatment time-specific thermal capacity (3.64 kJ/kg·°C) - blood density (1,052 kg/m³).

### Conclusion:

Body remained stable during Tdial = 35.5°C despite a major energy loss and even increased during Tdial = 37.5°C despite a negative ET from the patient to the extracorporeal system. The latter suggest that the HD procedure itself leads to intrinsic heat generation in the patient. The beneficial effects of low T dialysate on BP during HD may be due to the counter-action of the negative hemodynamic effects of this phenomenon in combination with the cardiovascular response evoked to maintain Tbody.

### 23 Docusate Sodium (DSS) Increases Peritoneal Clearances (K) by Increasing Surface Area (A)

**J.K. Levold, M.F. Flessner, J.F. Gilson, C. Chen**

Salt Lake City, Rochester & McGaw Park, USA

While previous strategies for enhancing peritoneal solute K or permeability-area products (PA) have focused on increasing permeability (P), our goal was to investigate the effect of intraperitoneal (IP) administration of DSS, a surface-active agent, on peritoneal solute transport. PA for creatinine (Cr) and glucose (G) and K for total protein (TP) were evaluated in a rabbit model without (n = 9) or with (n = 10) 0.005% DSS given IP. DSS increased (p < 0.01) PA for Cr from 0.83 ± 0.23 (mean ± SD) to 1.41 ± 0.44 ml/min, PA for G from 0.52 ± 0.10 to 0.97 ± 0.38 ml/min and K for TP from 0.023 ± 0.007 to 0.030 ± 0.009 ml/min. Median percentage increases in PA for Cr and G and K for TP were similar (65, 66 and 48%), suggesting that...
these increases were the result of increasing A. Additional experiments were performed in a rat model to directly evaluate the effect of 0.005% DSS on P for mannitol (M) using special diffusion chambers affixed to a given A of the peritoneum (n = 3 without DSS vs. n = 3 with DSS). DSS had no effect on P for M in the rat (16 ± 2 μm/min without DSS vs. 16 ± 3 μm/min with DSS). These results demonstrate that increases in peritoneal K or PA after IP administration of DSS result from increasing A, not from increasing P.

24 Effects of Ligustium-Contained Peritoneal Dialysate on Adequacy and Ultrafiltration Volumes (UF) in CAPD Patients

J. Li, C.S. Lu, R.G. Ye, L. Sun, H.Q. Li
Nat. Inst. of Kidney, Sun Yat-sen Univ. of Med. Sci., Guangzhou, PR China

Ligustium is a substance extracted from a common Chinese herb, Rhizoma Ligustici. It has been proved to have anti-coagulant, anti-spasm, anti-inflammation effects. We did a prospective, self-controlled study to compare the effect of ligustium-contained peritoneal dialysate (40 mg/l ligustium) versus standard peritoneal dialysate on adequacy and UF in CAPD patients. Methods: 24 stable CAPD patients were divided into 4 groups, H (high), Ha (High average), La (low-average) and L (low transport) based on PET. Each patient used standard dialysate for two weeks, then the ligustium-contained dialysate for the next two weeks. UF of each dialysis exchange was recorded and urea kinetics (KT/V) was calculated once a week. The mean UF per exchange and mean weekly KT/V are shown in table 1.

Table 1. Peritoneal UF and KT/V between the two solutions

<table>
<thead>
<tr>
<th>Group (n)</th>
<th>Standard dialysate</th>
<th>Ligustium dialysate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UF (ml)</td>
<td>KT/V (l)</td>
</tr>
<tr>
<td>H (4)</td>
<td>26 (8-46)</td>
<td>1.59 ± 0.08</td>
</tr>
<tr>
<td>Ha (11)</td>
<td>254 (170-367)</td>
<td>1.77 ± 0.10**</td>
</tr>
<tr>
<td>La (8)</td>
<td>395 (242-546)</td>
<td>1.74 ± 0.13*</td>
</tr>
<tr>
<td>L (1)</td>
<td>412</td>
<td>1.67</td>
</tr>
<tr>
<td>Total (24)</td>
<td>184.4</td>
<td>1.64 ± 0.15</td>
</tr>
</tbody>
</table>

*p < 0.05, **p < 0.01 compared to their respective controls.

Conclusions: Addition of ligustium to standard dialysate can improve adequacy and ultrafiltration in CAPD patients.

25 Influence of Fluid Status on Blood Pressure (BP) and Serum Albumin (ALB) in CAPD

Div. of Baxter Novum and Renal Medicine, Karolinska Institute, Huddinge University Hospital, Huddinge, Sweden

Recent data suggest that removal of fluid and control of BP may be more important for the clinical outcome of CAPD than small solute clearances. A low ALB is a strong risk factor for mortality in CAPD, but it is not clear whether this is due to malnutrition, inflammation or fluid overload. We studied 26 CAPD patients (age 54 ± 10 years, 13 men) treated >1 year. Fluid status was assessed using simultaneous measurements of extracellular volume (ECV) by multiple frequency bioimpedance and lean body mass (LBM) by dual energy x-ray absorptiometry. 24 h BP was monitored, and drained night ultrafiltration (nUF), ALB and C-reactive protein (CRP) were measured.

Results: ECV/LBM (0.38 ± 0.033, used as an index of fluid status) was negatively correlated with S-ALB (33.7 ± 3.7 g/l, r = -0.45, p = 0.02) and tended to correlate with CRP (median 10.0 mg/l, range <10.0 to 73.0 mg/l, r = 0.35, p = 0.09). The drained nUF (median –80 ml, range –480 to +450 ml) correlated with systolic BP (136 ± 21 mm Hg, r = -0.52, p < 0.01), mean BP (103 ± 17 mm Hg, r = -0.44, p = 0.025) and ALB (r = 0.43, p = 0.028).

Conclusions: ALB, a well established marker of survival, is related to fluid status in CAPD patients. A negative night UF is associated with increased BP and as well as with a low S-ALB. These findings highlight the importance of the night dwell in CAPD. Strategies such as use of polyglucose solution or use of a night exchange device should be introduced to improve night UF in CAPD patients.
26 Nutritional Status, Inflammation and Clinical Outcome in CAPD Patients

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A cross-sectional study of nutritional status was performed in 36 unselected patients treated with CAPD, and the clinical outcome of the patients was evaluated prospectively.

Methods: Nutritional status was evaluated by the subjective global nutritional assessment (SGNA), anthropometrics including hand-grip strength (HGS) and several laboratory values, including s-albumin (ALB) and C-reactive protein (CRP). Dialysis dose (Kt/V) and the protein equivalent of nitrogen appearance (nPNA) were evaluated by urea kinetic modelling. The patients were divided into three groups based on SGNA: group I (n = 11; 31%) normal nutritional status and group II (n = 16; 44%) mild/moderate and group III (n = 9, 25%) severe malnutrition.

Results: Malnutrition was associated with: high age, cardiovascular disease (CVD) and diabetes mellitus, low nPNA, Kt/V, HGS, ALB and bicarbonate, and high CRP and haptoglobin levels. Elevated CRP (>120 mg/l) was also strongly associated with low ALB, HGS and nPNA. Overall survival was 48% (70% in group I) at 40 months, and was negatively associated with malnutrition, age, diabetes, low Kt/V and ALB, and high CRP.

Conclusions: Malnutrition among CAPD patients is multifactorial, and is associated with clinical factors (age, CVD, diabetes, Kt/V), anthropometric factors (HGS), and biochemical factors (acidosis, low ALB, and inflammation as assessed by high haptoglobin and CRP levels). The only factor found to negatively affect protein intake (nPNA) was a high CRP level.

27 Evaluation of Erythropoietin Level in High-Flux Dialysis Patients

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Formosan Blood Purification Foundation, a Provincial Taipei General Hospital, Taiwan, Taipei

Insufficient secretion of erythropoietin (EPO) is the primary cause of anemia in end-stage renal disease. The goal of this study is to evaluate whether the level of EPO and removal of EPO by high-flux membrane could cause a decrease of EPO concentration in dialysis patients. The relationships between such removal process and severity of anemia were investigated. The study focused on 126 high-flux dialysis patients with 68 males and 58 females. All of the 126 patients did not receive EPO treatment before this study. The RBC, Hb, Hct, and MCV counts and the level of EPO were measured before and after dialysis. To compare the results, 56 healthy individuals form the control group. It is found that the average EPO concentration in the blood of healthy individuals is 15.43 ± 9.37 mU/ml as compared to 14.50 ± 9.50 mU/ml of the dialysis patients prior to dialysis (p, NS). Although after dialysis the average value for EPO concentration in the blood decreased from 14.50 ± 9.50 mU/ml to 13.42 ± 9.10 mU/ml, the EPO concentration is still within normal range (3.3–13.5 mU/ml). Before dialysis, the average concentration of EPO in the male patients in lower than that of the female patients (13.11 ± 8.9 mU/ml vs. 16.13 ± 10.11 mU/ml; p = 0.077); however, the RBC, Hb, and Hct counts for men is higher than that for women (p < 0.0001). The results indicate that although high-flux dialysis can lower the EPO concentration, the EPO level in dialysis patients still remains within the normal range (3.3–13.5 mU/ml). Thus, high-flux dialysis does not cause insufficient erythropoietin in the patients. Insufficient level of EPO is not the main factor which cause anemia. These anemia-causing factors must be eliminated (via uremic toxin removal, exercise, and iron supplement, etc.) in order to improve the quality of dialysis and reduce the cost of EPO treatment.

28 Continuous High Flux Hemodialysis (CHFD) Improves Whole Blood TNFα Production in Septic Patients

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Suppressed ex vivo endotoxin (ET)-induced TNFα production in whole blood (WB) is associated with fatal outcome in sepsis. We showed previously that standard CVVH (ultrafiltrate volume 36 liters/day) only transiently improves WB-TNFα production in septic patients with acute renal failure (ARF). We now tested the effect of CHFD on WB-TNFα production using a closed loop single-pass batch hemodialysis system (Genius). 5 patients with oliguric ARF and sepsis were studied. CHFD was performed with polysulfone
F60 dialyzers. Blood flow was equal to countercurrent dialysate flow with 70 ml/min (75 liters of dialysate/18 h). Ultrafiltration rates were 100–250 ml/hour. Blood taken from the afferent blood lines after 5 minutes, 3, 6 and 18 hours of CHFD was incubated with 1 ng/ml of ET for 3 hours at 37 °C. TNFα and inhibitory TNFsRI were measured in WB culture supernatants by ELISA. Cytokine levels (ng/ml) are given in the table, median (range), * p < 0.05 versus 5 minutes of CHFD:

<table>
<thead>
<tr>
<th>Time of CHFD</th>
<th>WB TNFα (ng/ml)</th>
<th>WB TNFsRI (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 minutes</td>
<td>0.5 (0.1–1.8)</td>
<td>8.0 (4.4–12.0)</td>
</tr>
<tr>
<td>3 hours</td>
<td>1.1 (0.2–2.3)*</td>
<td>8.8 (4.1–11.6)</td>
</tr>
<tr>
<td>6 hours</td>
<td>1.6 (0.5–2.8)*</td>
<td>9.0 (3.7–12.8)</td>
</tr>
<tr>
<td>18 hours</td>
<td>1.5 (0.8–2.4)*</td>
<td>7.8 (3.7–11.0)</td>
</tr>
</tbody>
</table>

Suppressed ET-induced WB TNFα production increased significantly during CHFD. There was no change in WB TNFsRI production. These data suggest that high volume CHFD effectively removes a suppressing factor of proinflammatory cytokines. It remains to be shown whether this immunomodulation during CHFD improves outcome in septic patients.

### 29 Free Fatty Acids and Hemodialysis: Cardiovascular and Hormonal Effects

R. Marangoni, R. Savino, F. Masi, A. Manfredi, R. Cimino, R. Colombo, L. Maltagliati, F. Marangoni, C. Galli
Ospedale di Bollate, Bollate, Italy

During HD plasma lipid profile undergoes acute changes, such as a decrease in triglyceride (TG) levels and a marked increase in free fatty acids (FFA), included free arachidonic acid (FAA), the precursor of eicosanoids. Aim of this study was to assess the effects of the FFA rise on the concentrations of thromboxane A2 (TxA2), a potent vasoconstrictor and inducer of platelet aggregation, and aldosterone (A). We determined TG, FFA, TxB2 (stable metabolite of TxA2), A, and renin in plasma of 8 chronically anuric uremic patients undergoing bicarbonate hemodialysis, before and after the first weekly dialytic session, maintaining stable K concentration, in order to exclude any influence on A secretion. We observed that the increase of FFA is associated with a rise of TxB2 and a fall of A, while renin remained stable throughout HD. The modifications occurring in TxB2 and A appeared significantly correlated with FFA increase, positively and negatively respectively. These changes, which seem to be interdependent, repeated over time in chronically HD treated patients, can be responsible for cardiovascular risk (the rise of FFA and TxB2) and for alteration of hormonal regulation (the A fall).

### 30 Plasma Lipid Profile Changes during Different Blood Purification Methods

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Ospedale di Bollate, Bollate, Italy

During hemodialysis (HD) treatment plasma lipid profile shows rapid modifications especially characterized by an increase of free fatty acids (FFA) and a decrease of triglycerides (TG). Aiming at verifying if these changes even happen (and to what degree) during other extracorporeal treatments, we determined TG, total FFA and single major FFA, total cholesterol (T.CHO) and HDL (HDL.CHO) cholesterol in 18 chronically anuric uremic patients (before and after treatments performed either with or without heparin) undergoing: 6 of them: hemofiltration (HF); 6: Acetate Free Biofiltration (AFB); 6: Paired Filtration Dialysis, i.e. hemodialysis-hemofiltration in series (PFD). The results showed: FFA increase and TG decrease happen, in the same degree, in all tested methods. Among the major FFA stearic acid and arachidonic acid, precursor of eicosanoids, showed the higher increase in HF. T.CHO and HDL.CHO did not show significant modifications in all tested methods. Heparin administration seemed not to modify the above-described changes significantly. These changes, repeated over time, must be considered the cause of high cardiovascular risk, whether for the arrhythmogenic effects of FFA, or for the increased production of eicosanoids, among them thromboxane, a potent vasoconstrictor and inducer of platelet aggregation.
31 Hemodialysis (HD) Access with the Dialock™ Device

J. Megerman, N.W. Levin, T.S. Ing, B. Canaud, H. My
Biolink Corporation, Middleboro, Mass., USA

The Dialock™ HD access device was developed to overcome the main problems with current modes of access, i.e., failure due to infection and poor flow. It consists of a titanium port with a mechanical valve attached to 11F twin silicone catheters, contains no degradable septum, and provides a linear flowpath that avoids clotting and damage to red cells. The port is fully implantable below the clavicle, and the catheters are tunneled to the IJ vein with their tips placed in the right atrium. Special needles are used for percutaneous access, converting the device to a standard catheter system during dialysis. The Dialock was implanted in 21 patients in the US and France for 1–11 months (median 7.5 mos). After 2,000 accesses, blood flow averaged 330 ± 40 (US) and 315 ± 25 (Fr) ml/min and the infection rate was 2.3 per 1,000 patient-days. All infections were resolved with local plus systemic antibiotics without removing the device. Fibrin sheath stripping was performed in 2 patients and one devide was removed following the visualization of an asymptomatic ball thrombus at the catheter tip. Two patients died from unrelated causes. The Dialock may represent a substantial improvement over conventional devices used to provide hemodialysis access.

32 Diagnosis and Treatment of Renal Vein Thrombosis (RVT)

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Al Hada Hospital, Taif, Saudi Arabia

Diagnosis and treatment of RVT remain a matter of debate. One patient presented with acute renal failure and nephrotic syndrome post-partum (patient 1), and a second with flank pain and a non-functioning left kidney, complicating uncontrolled diabetes mellitus (patient 2). MRI of patient 1 showed an inferior caval vein (IVC) thrombus, partial right RVT, while the left kidney was swollen and the left renal vein could not be identified. In patient 2 there was a partial left RVT. Both patients received a combination of systemic urokinase (4,400 IU/kg as a bolus, followed by 4,400 IU/kg/hr for 24 hrs), i.v. heparin (for one week), and oral anticoagulation. The renal function of patient 1 improved markedly and the proteinuria disappeared. Follow-up MRI’s in patient 1 showed complete resolution of the right RVT and IVC-thrombus and partial reperfusion of the left renal vein with an atrophic left kidney, and complete resolution of the unilateral RVT in patient 2. MRI (if available enhanced MR angiogram) will facilitate the diagnosis and obviate the need for conventional angiography. Systemic thrombolytic therapy in combination with i.v. heparin might be the preferred treatment modality.

33 A New Subcutaneous Vascular Access Device for Hemodialysis

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VascA Inc., Topsfield, Mass., USA

The VascA Venous LifeSite™ is a subcutaneous port, with an internal valve that is actuated with a standard 14-ga dialysis needle, connected to a single lumen catheter placed in the central venous circulation for hemodialysis (HD).

Methods: The LifeSite was implanted in pairs in 10 patients with immediate dual needle HD use with the same-site needling technique. The catheters were placed in either the jugular, preferred, or subclavian veins and the ports were placed below the clavicle.

Results: After an average device implantation of 3 months per patient, the LifeSite achieved prescription HD blood flow rates averaging 384 ± 99 ml/min at draw and return pressures of –273 ± 32 and 225 ± 62 mm Hg, respectively. After 30 patient-months, one catheter-related infection occurred due to catheter tunnel erosion. Patient and nurse acceptance has been consistently high.

Conclusions: The VascA Venous LifeSite is capable of providing repetitive, reliable blood access and sustained blood flow sufficient for effective hemodialysis and also a closed system that is protected from external contaminants.
34 The Role of Comorbidity on Survival of Patients with End-Stage Renal Disease (ESRD)
M. Querques, A. Pappani, G. Di Francesco, P. Strippoli, D.A. Procaccini
Foggia, Italy

A cohort retrospective study was used to analyze the effect of comorbidity on survival of ESRD patients undergoing dialysis. We analyzed the survival of 286 patients (155 men, 131 women; median age 56 years; range 8–83 years) followed in Foggia, Italy, over a 21-year period (median follow-up 36 months; range 1–210 months). Two subscales assessing the overall severity of the identified coexistent diseases and overall physical impairment, and a composite four level index of coexistent diseases (ICED) were assembled using information recorded at the time of admission. The Cox proportional hazard model was applied to evaluate the association of various patient characteristics with the probability of death. Mortality risk for all patients was associated with higher level of ICED (RR = 2.6 for ICED = 2; RR = 3.3 for ICED = 3). ICED > 2 was associated with a significant higher survival in patients treated by haemodialysis (ICED = 2 – HD vs DP: log rank 13.7 p < 0.002; ICED = 3 – HD vs DP: log rank 6.65 p < 0.009). Comorbidity is a powerful independent prognostic factor in determining the mortality of ESRD patients.

35 An Innovative Approach to Temporary Vascular Access
Jamie L. Ross, Catherine Staffeld, Jill S. Lindberg, Mary Lee
Ochs wen Clinic, New Orleans, La., USA

In the era of the Dialysis Outcomes Quality Initiative (DOQI), the expectations are for nephrologists to improve outcomes in all aspects of dialytic care. The recommendations for temporary and chronic vascular access are extensive and explicit. In an organized effort to comply with the recommendations outlined by DOQI for temporary hemodialysis vascular access, two interventional nephrologists performed all of our central venous access procedures over a 12-month period. We performed 402 central venous catheter procedures using strictly controlled conditions and technique. We were testing the hypothesis that by utilizing such strict control we would reduce both infectious and procedural complications. The expected serious procedural complication rate is 2% as outlined in the DOQI standards. Our complication rate was 0.07%. The expected rate of infections for hemodialysis catheters is between 8% and 25%. We were asked to change lines for suspected infection in hemodialysis catheters in only 5.9% of our hemodialysis patients in whom we placed temporary catheters. We have concluded that the use of interventional trained nephrologists and strict control of technique can improve outcome in temporary vascular procedures.

36 Effect of On-Line Hemodiafiltration Modality on Removal Characteristics
Y. Takemoto, K. Tsuchida, O. Fu, T. Nakamura, S. Yamagami, T. Kishimoto
Osaka City University Hospital, Osaka, Japan

There are three modalities of on-line hemodiafiltration (on-line HDF): 1. Predilution method (Pre), 2. Pre and Post dilution method (Pre & Post), 3. Postdilution method (Post). When we performed the on-line HDF the substitution fluid was prepared from dialysate. The dialysate flow rate was set to 500 ml/min. Therefore if the substitution fluid flow rate was increased, the dialysate flow rate was decreased. The diffusive process is more effective for the removal of small molecular solutes, whereas the convective process is more effective for the removal of middle molecular solutes. This study was conducted to elucidate the appropriate substitution fluid flow rate in on-line HDF. We compared the removal rate of various solutes on each HDF. The degree of the removal of small molecular solutes is as follows: Post > Pre & Post > Pre. In contrast, the degree of the removal of middle molecular solutes is as follows: Pre & Post > Pre = Post. Therefore, Pre & Post HDF is an effective modality for removal of a wide range of solutes with small to middle molecular weights.
The pain caused by SC of EPO cannot be neglected for renal anemic patients, because they have to receive it 2 to 4 times a month. We compared the pain caused by SC of two different EPOs, epoetin α (α) and epoetin β (β), which are available in Japan. Ten renal anemic patients were chosen for this study. SC of α and β (6,000 IU, 0.5 ml) were done on their right and left or left and right forearms respectively at random. Each pain was evaluated using non-divided 100 mm visual analogue scale (VAS) and 5 point verbal descriptive scale (VDS) during injection, 1 and 5 minutes after SC. VAS showed that α caused significantly more pain than β 1 minute after SC (p < 0.05). In VDS 5 patients did not feel any pain within 1 minute, and all did not within 5 minutes after SC of β, although pain disappeared in only one patient within 1 minute after SC of α. The type of pain caused by SC of α was longer lasting and more expanding than that of β. However, the pain caused by SC of β was slight and limited at the injection site. In conclusion, SC of α causes more and longer lasting pain than that of β. It may be due to any differences of the component in preparation as citrate buffer of pH.

Plasma Leptin in Patients with Renal Diseases
V. Tesarš, V. Chábová, J. Perusičová, V. Bradová, T. Zima, E. Jelínková, J. Žabka, M. Merta
Charles University, Prague, Czech Republic

Leptin, a newly discovered hormone of the satiety, is metabolised predominantly by the kidneys, and so its plasma levels are supposed to be changed in patients with renal diseases. We measured plasma leptin by ELISA in 36 fasting diabetic patients with different stage of diabetic nephropathy, 12 men with nephrotic syndrome caused by membranous nephropathy, 15 dialyzed patients and 11 control healthy subjects. As expected leptin levels were higher in women compared to men (17.6 ± 6.5 vs. 7.7 ± 4.3 ng/ml, p < 0.001) and in dialyzed compared to non-dialyzed patients (19.6 ± 2.1 vs. 10.7 ± 3.7 ng/ml, p < 0.05) and dialyzed men compared to non-dialyzed men (15.1 ± 2.9 vs. 5.9 ± 3.3 ng/ml, p < 0.05), the difference did not reach statistical significance in women. There was no significant difference between patients with diabetic and membranous nephropathy and controls. There was no correlation of plasma leptin with age, body mass index and serum lipids, but there was a positive correlation between plasma leptin and serum creatinine in nondialyzed women (r = 0.68, p < 0.001). In conclusion: plasma leptin levels seem to be influenced in patients with renal diseases predominantly by sex and renal function, the influence of metabolic parameters (BMI, serum lipids) seems to be less important.

Supported by grant of MH No. 3587-3 and 4856-3.

Urinary IL-6/EGF Ratio in ANCA-Positive Renal Vasculitis, Lupus Nephritis and IgA Nephropathy
V. Tesarš, E. Jelínková, M. Merta, M. Jirsa, J. Žabka, A. Stejskalová
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Increased urinary excretion of IL-6 and decreased urinary excretion of EGF with increased IL-6/EGF ratio was found in patients with severe IgA nephropathy. We were interested if these changes are also present in patients with other glomerulonephritides (GN) and if there is any effect of immunosuppressive treatment (IST) on these markers. Urinary IL-6 and EGF were evaluated by ELISA in freshly frozen urine of 32 patients (pts) with IgA nephropathy (IgAN), 23 pts with ANCA-positive renal vasculitis (ANCA-RV), 10 pts with lupus nephritis (LN) and 11 healthy controls (Co). Effect of IST was also evaluated in 36 patients with these types of GN. Urinary IL-6 excretion was increased in active ANCA-RV compared to controls (8.42 ± 2.50 vs. 0.51 ± 0.13 g/mol creat, p < 0.01) and also to IgAN (1.49 ± 0.38, p < 0.001). Urinary EGF excretion was again severely depressed in active ANCA-RV compared to controls (611.3 ± 282.0 vs. 1,776.5 ± 336.7 g/mol creat, p < 0.01) and also IgAN (1,133.5 ± 158.7 g/mol creat, p < 0.05). These effects persisted even when IL-6 and EGF excretion was calculated per unit of GFR. Short-term IST and plasma exchange had no effect on urinary EGF excretion in active ANCA-A despite improved renal excretion in active ANCA-A despite improved renal...
40 Pulmonary Function in Patients with ARDS during Hemofiltration (HF)

E. A. Tishkov, O. B. Bukaev, S. V. Kapunov
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The aim of the study was to evaluate the effects of HF on pulmonary function in patients (n = 25) with ARDS (abdominal postsurgical complication, multiple organ failure). All patients required mechanical ventilation with F102 0.65 ± 0.07, PEEP was 7.5 ± 1.6 smH2O. X-rays of all patients revealed pulmonary edema. HF was performed in all cases (ADM-08, hemofilter HF-60, deficit ultrafiltrate 1,500–2,000 ml). Assessment of the effect of HF on the lung showed changes in near of 8–12 h: PaO2 increased (by 25%) reliably, PaO2/ F102 and Qs/Qt increased by 30 and 28% respectively (p < 0.05), AaD02 dropped (by 13%) reliably. PaCO2 decreased from 45 ± 5.1 to 36 ± 2.5 mm Hg. The PVR decreased from 288 ± 25.3 to 175 ± 20.4 mm Hg. With ultrafiltration the extravascular lung water increased significantly (p < 0.05). The X-rays of all patients revealed a reduction of edema after HF. We conclude that HF has a rapid, profound effect on the pulmonary circulation, improved gas exchange and O2-transport. The HF increasing fluid removal may reduce alveolar edema and interstitial lung water, this is an effective method of treatment of ARDS.

41 Lixelle Adsorbent to Remove Inflammatory Cytokines

K. Tsuchida, Y. Takemoto, O. Fu, T. Nakamura, S. Yamagami, T. Kishimoto
Osaka City University Hospital, Osaka, Japan

β2-microglobulin (BMG) selective adsorbent (Lixelle) for direct hemoperfusion has been used for the treatment of hemodialysis patients with long-term complication of dialysis-related amyloidosis (DRA). But there is no significant correlation between the serum level of BMG and the occurrence of DRA. Inflammatory cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor necrosis factor-alfa (TNF-α) are related to the cause of DRA. We studied the adsorptive rates of cytokines in vitro by using Lixelle adsorbent. The adsorptive rates were 98.5% in IL-1B, 98.0% in interleukin-1 receptor antagonist (IL-1Ra), 82.9% in IL-6, 99.9% in IL-8, 31.2% in TNF-α, and 46.1% in soluble TNF receptor (sTNFRII), respectively. As molecular weights of cytokines increase, the adsorptive rates decrease. Lixelle column adsorbed BMG and various inflammatory cytokines as well. Therefore, the removal of both BMG and inflammatory cytokines may play an important role in the treatment of DRA.
vein. The patient was put on heparin. After 5 days retrograde flebography showed a long stenotic part of iliac vein with very rough and altered vessel wall surface. Two stents were put in a vessel and good venous blood flow was obtained, providing a good function of PTFE graft again. Actual information provided by CDU was helpful in therapeutic efforts done to improve patient outcome and salvaging the PTFE graft.

43 High β-2-Microglobulin Adsorption on AN69 Dialyser Can Be Regenerated – In vitro Study
A. Urbancič, J. Buturović, R. Ponikvar, A. Bren
Dept. of Nephrology, Medical Centre Ljubljana, Slovenia

Adsorption of β-2-microglobulin (B2M) on polyacrylonitrile membrane and its possible reversibility was evaluated in an in vitro study in the absence of diffusion and convection. Uremic plasma obtained after therapeutic plasma exchange was processed in a single pass way during the procedures, using AN69 dialyser (Filtral 12, Hospal) and a constant plasma flow of 100 and 150 ml/min. After 15 minutes the dialyser was rinsed with 1 liter of 0.9% NaCl solution. The procedure was repeated for the next 15 min. B2M concentrations (mg/l, RIA, Pharmacia, Uppsala) were taken from the plasma before the procedures and from the outlet line and collected plasma after 2, 5, 10, 15 min and at the end, before and after rinsing of the dialyser. Adsorption (mg/min) was estimated. It was highest in the 2nd min using 100 and 150 ml/min of plasma flow; in the 2nd min after rinsing of dialyser it was significantly higher than in the last min before rinsing, but lower than in the 2nd min from the beginning of the procedure. In the in vitro study the adsorption of B2M on the AN69 dialyser membrane was the only way of B2M removal from the plasma. No marked differences were observed during the procedures with 100 and 150 ml/min of plasma flow. The highest adsorption capacity at the beginning of the procedures was markedly reduced for 15 min, but was in greater part regenerated for another 15 min by rinsing of the AN69 dialyser with saline. We think that this fact could be useful in clinical conditions of the dialytic treatment with AN69 dialyser membrane.

44 Effect of iv Fluids on Plasma Volume Preservation during Dialysis
F.M. van der Sande, J.P. Kooman, J.N.M. Barendregt, F.H.M. Nieman*, K.M.L. Leunissen
Dept. of Internal Medicine and *Staff Bureau, Univ. Hosp. Maastricht, The Netherlands

Saline (0.9%) or albumin (20%) infusions are generally used during symptomatic hypovolemia. Because of the attendant side effects and/or costs they are limited for chronic use. Hydroxyethylstarch (Haes) is used on the ICU in the management of hypovolemia with a potent volume effect up to 4 hours. It can be expected that Haes might also be of clinical importance in dialysis patients. Therefore, the efficacy of 3 solutions on plasma volume preservation (PV) and blood pressure (SBP) in 10 stable dialysis patients during 3 ultrafiltration/hemodialysis (UF+HD) sessions was compared. An iv injection (t = iv) of 100 ml saline (0.9%), albumin (20%) or Haes (10%) was given when relative blood volume (BV) decreased more than 10%, measured with Critline (In-line Diagnostics). Dialysis was standardized: individual bicarbonate, sodium and temperature. Statistical analysis: Manova. Time of in-
fusion was comparable between saline, albumin and Haes (140, 155 and 151 min). BV decreased significantly during UF+HD notwithstanding the infusion of the 3 fluids (fig. 1). However, the decrease was significantly higher when using saline compared to albumin and Haes. Between albumin and Haes there were no significant differences. With saline, SBP tended to decrease more as compared to albumin and Haes, although the difference was not significant (fig. 2). We conclude that Haes is an effective solution in preserving plasma volume being comparable to albumin but superior to saline. Further studies in hypotensive prone patients are needed to look at the clinical effect on blood pressure course during hemodialysis.

**45 Cytokine mRNA Expression Patterns and Levels in End-Stage Renal Failure and Renal Replacement Therapy**

Dept. of Internal Medicine, University Hospital Rotterdam-Dijkzigt, The Netherlands

Patients with ESRF suffer from general immunedeficiency, resulting in susceptibility for infections and a decreased response on T-cell dependent antigens, such as hepatitis B vaccination. Cytokines play a central role in activation of the immune system. In this study we measured cytokine-mRNA-profiles in peripheral blood mononuclear cells (PBMC), in order to find out, whether their immunedeficiency could be linked to a defect in their cytokine gene expression.

*Patients:* In stable pre-dialysis ESRF (n = 10), on CAPD (n = 10) and CIHD (n = 15), we measured mRNA-expression of IL-1β, IL-2, IL-4, IL-6, IL-10, IL-15, TNF-α and IFN-γ. Measurements were performed using the RT-PCR method. 11 healthy subjects served as controls.

*Results:* mRNA-expression for IL-2 (not detectable) and IFN-γ (73% vs 90–100%) was comparable in PBMC of controls and patients. However, significantly more patients had positive mRNA-expression of IL-1β, IL-4 and IL-6 compared to controls.

<table>
<thead>
<tr>
<th></th>
<th>IL-1β</th>
<th>IL-4</th>
<th>IL-6</th>
<th>IL-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>18</td>
<td>27</td>
<td>18</td>
<td>36</td>
</tr>
<tr>
<td>ESRF</td>
<td>100*</td>
<td>75*</td>
<td>20</td>
<td>70</td>
</tr>
<tr>
<td>CAPD</td>
<td>90*</td>
<td>80*</td>
<td>30</td>
<td>80</td>
</tr>
<tr>
<td>CIHD</td>
<td>100*</td>
<td>50</td>
<td>87*</td>
<td>60</td>
</tr>
</tbody>
</table>

Percentage positive samples with RT-PCR; * p < 0.01.

As in most samples of both patients and controls mRNA expression for TNF-α and IL-15 was present, we performed a quantitative RT-PCR for these cytokine genes and found significantly more IL-15 and TNF-α in patients compared to controls (p = 0.03, p < 0.001, respectively).

**Conclusion:** We were not able to correlate the general immunedeficiency of ESRF, CAPD or CIHD patients with a deficient expression of cytokine genes. On the contrary, our data suggest an activation rather than a suppression of the immune system at the mRNA level. This implies that other factors, e.g. directed at the protein production or at the bioavailability of cytokines, play the major role in the immunosuppressive state of ESRF, CAPD and CIHD patients.

**46 Can Sterile and Pyrogen-Free Substituate Be Consistently On-Line Delivered?**

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On-line hemodiafiltration (HDF) bears microbiological risks due to the preparation of huge amounts of substituate from contaminated dialysis fluid (DF). We have examined 30 machines with a two-stage filtration system (DIASAFE® and HDF filter) in 6 centers for 6 months. Samples were taken monthly from the inlet DF (A), the ultrafiltered DF (B) and the on-line substituate (C), and assayed for microbial counts, endotoxin concentration and cytokine-inducing activity. Pyrogenic reactions were not observed during the study. Ultrafiltration of DF (A: <1–895 CFU/ml, 0.003–4.682 EU/ml) resulted in sterile substitute with LAL reactivities not different from pyrogen-free saline (C: 0.006 ± 0.003 vs. saline: 0.007 ± 0.004 EU/ml). Likewise, cytokine-inducing activity was the same for
both solutions (C: 416 ± 179 vs. saline: 390 ± 247 pg IL-1Ra/10^6 WBC). In addition, the high microbiological quality of ultrafiltered DF (B), which did not differ from substitute quality (C), translates into both the absence of cytokine induction via dialyzer backtransport, and a redundant safety mode of the on-line system used. We conclude that on-line HDF is microbiologically safe.

47 No Difference in Cytokine Induction between Patients on On-Line Hemodiafiltration (HDF) and Low-Flux HD

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Chronic inflammation causes various long-term complications of ESRD patients and may increase mortality. Influx of microbial substances from contaminated dialysate fluid (DF) and on-line substitute is a major source of cytokine induction, the initial inflammatory process. We have compared patients on on-line HDF and low-flux HD with respect to (a) spontaneous and (b) LPS-induced in vitro whole blood IL-1Ra and TNFα synthesis, and (c) cytokine production capacity. Both groups (n = 15) were treated with ultrapure DF and polysulfone membranes. Cytokine induction was found elevated in ESRD patients compared to healthy subjects, with no differences between the treatment modalities. Intradiallytically, white blood cells became slightly, albeit not significantly activated, as measured by LPS-induced cytokine synthesis. There was no decline in cytokine production capacity of leukocytes during the treatment, indicating that the proportion of less mature or functionally impaired cells did not increase as a result of stimulated cell sequestration. We conclude that infusion of large volumes of on-line substitute does not provoke chronic inflammation.

48 Abnormal Blood Pressure Response during Dobutamine-Atropine Stress Echocardiography in Patients with Hemodialysis-Induced Hypotension

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Underlying coronary artery disease may play a role in the complex pathophysiology of hemodialysis-induced hypotension. Dobutamine stress echocardiography can be used to evaluate both left ventricular function and presence of coronary artery disease. We studied 36 patients of whom 18 were normotensive and 18 were severely hypotensive during hemodialysis. Dobutamine infusion was started with 5 up to 40 μg/kg/min with additional atropine, if necessary, to achieve 85% of age and sex predicted maximal heart rate, in absence of signs or symptoms of ischemia or side effects. At rest and at the end of every dose step heart rate, blood pressure and echographic images were recorded. Echo images of the left ventricle were scored using a 16-segment model and a 5-point score at rest and at peak stress. Ischemia was present if a worsening of wall motion occurred during stress. At rest, during 10 μg/kg/min dobutamine and peak stress stroke volume was calculated using the bi-plane discs-method. Normotensive patients had more often beta blockers therapy (12/18 vs 6/18). Hypo- and normotensive patients showed no difference in rest wall motion score (1.42 vs 1.44) and stress induced ischemia (4 vs 3 patients). However, there was a significant difference in blood pressure and stroke volume during dobutamine stress. In hypotensive patients both blood pressure (133/74 to 127/71 mmHg) and stroke volume (55 vs 42 ml) decreased from rest to peak stress, whereas in normotensive patients blood pressure (149/86 to 155/86) and stroke volume (67 to 62 ml) were significantly higher. We conclude that hypotensive patients both blood pressure (133/74 to 127/71 mmHg) and stroke volume (55 vs 42 ml) decreased from rest to peak stress, whereas in normotensive patients blood pressure (149/86 to 155/86) and stroke volume (67 to 62 ml) were significantly higher. We conclude that hypotensive patients during hemodialysis showed no difference in rest wall motion score and stress induced ischemia compared to normotensive patients. However, both blood pressure and stroke volume decreased significantly during dobutamine stress in hypotensive patients, indicating an inability to increase contractility to compensate for vasodilation.
Relative Blood Volume Changes during Dialysis without Ultrafiltration Do Not Only Depend on Changes in Osmolality

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Hemodialysis is predicted to cause fluid shifts between the extracellular and intracellular compartments, despite the absence of ultrafiltration. Using mathematical modeling of urea and sodium kinetics, the total fluid shift during a four-hour dialysis session is directed towards the intracellular compartment. As a result relative blood volume would decrease by approximately 2%. We attempted to validate these predictions in vivo. We therefore studied six patients on chronic hemodialysis (three times four hours a week, using bicarbonate as a buffer and polysulphone membranes) in which, due to residual renal function, ultrafiltration was not necessary. In all patients relative blood volume increased significantly during the first and second hours of treatment, by 2.5 ± 1.3 and 2.3 ± 2.4% respectively. Towards the end of dialysis relative blood volume decreased towards baseline. Blood pressure and heart rate remained unchanged during all treatments. Several mechanisms could explain the observed discrepancy between predicted and observed blood volume patterns. Dialysis induced vasoconstriction or vasodilation could induce a change in hydrostatic capillary pressure or changes in the distribution of blood flow that could in turn lead to alteration of hematocrit and/or total body hydraulic permeability. The present study however does not permit conclusions regarding the mechanism of the observed increase in relative blood volume. We conclude that during dialysis without the need for ultrafiltration relative blood volume is increased despite predictions to the contrary. Mathematical models should include more physiological variables to accurately predict changes in relative blood volume.