P119

INTENSIVE DETOXICATIVE THERAPY BY XENOHEPATOCYTES
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Intensive detoxicative "cellular therapy" requires functioning bank of allocells with preserved organ-specific properties. We showed that donor allo- and xenohepatocytes, cryopreserved by routine technologies, by supraprapid freezing, maintain a high level of viable cells in suspension, thus providing for an active capture of xenobiotics. Application of supralow (-196°C) temperatures guarantees a long-term (10 years or more) maintenance of detoxicative properties of cryopreserved cells, making control over the composition of preserved medium, sterility and bio-sorbent viability unnecessary. Experimental studies using hepatocytes of rats, dogs, puppies, pigs and humans, and clinical experience on detoxicative therapy by donor "allocells" make it possible to recommend application of hepatocyte suspension in an "artificial liver" device or transport perfusion systems depending on the level of viable cells in suspensions: low-viability cells may be used only under indirect cell/blood contact (e.g. extracorporeal dialysis), thus excluding penetration of cell elements into organism during cell lysis. Reliability of maintaining organ-specific properties of cells in cryobanks provides for a timely treatment by effective natural biosorbents during intensive detoxicative therapy.

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Kidney

P121

CONTINUOUS VENO-VEINUS HEMOFILTRATION (CVVH)
VARIES THE HEIGHT OF THE ULTRAFILTRATE (UF) LINE.

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INTRODUCTION: The purpose of the present work is to evaluate the efficiency of the CVVH when the height of the UF line is changed.

METHODS: The CVVH through single-puncture with double light catheter (Mahurkar) was used, hollow fiber filter (Renaflo); pump (Dialyse Technik BN-11) and dialyse liquid (Peritofundina), were also used and varying: 1)- Pump speed, from 50 to 300 ml/min. 2)- Height of the UF line, from 0 to 120 cm. and 3)- The dialyse bath: 0.17 and 33 ml/min.

Statistic analysis was performed to determine the degree of correlation between pairs of measured variables (linear regression analysis); p-value < .05 was considered significant.

RESULTS: The height of the UF line varies the hydrostatic pressure, both being correlated: without dialyse bath, $r = .779$, with bath at 17 ml/min. $r = .996$ and with bath at 33 ml/min., $r = .998$ ($p < .001$). The more the hydrostatic pressure increases the less the UF volumen is, at to a point in which the dialyse balance becomes positive.

3 anuric patients were observed to have a better hemodialysis (clearance of urea, creatinine and potassium) by this technique.

CONCLUSIONS: 1- The hydrostatic pressure of the UF can be controlled by changing the height of the UF line. 2- When increasing the hydrostatic pressure, the UF volumen decreases. 3- The combination of the above with a dialyse bath, increases the CVVH efficiency.

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ACUTE ARSENIC POISONING IN A SUICIDE ATTEMPT: CASE REPORT.

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A 25-years-old-man was admitted to the ICU one hour after voluntary ingestion of 30 g of arsenic trioxide. On admission he was alert and cooperative; he had biliary vomiting with hematemesis, abdominal pain, watery diarrhea, arterial hypotension (blood pressure 90/50 mmHg) and sinus tachycardia (pulse 120 beats/minute) with CVP 0 cmH₂O. After gastric lavage with activated charcoal magnesium sulphate was administered enterally. He was treated with dimercaprol intramuscularly and intravenous fluids. Plasma expanders were perfused and a progressive rise of the central venous pressure (7 cmH₂O), without the reestablishment of diuresis, was observed. As he was anuric hemodialysis was carried out followed by diuresis. In the following days he underwent several plasma-exchanges to remove the As-BAL, with reinfusion of human albumin; the succession of the plasma-exchanges as well as the posology of dimercaprol depended on blood and urin arsenic level; diuresis was forced with diuretics. During the stay the patient showed: face congestion and edema with conjunctival hyperemia; mental confusion, for 24 hours, due to brain edema (CT-scan) were successfully treated with mannitol; hepatic failure with cytolysis and steatosis with splenomegaly (ultrasonography); left basal pneumonia with pleural effusion and polyneuropathy of lower limbs. Therapeutically, besides the specific antidote, N-acetylcysteine and reduced glutathione were used. Four weeks after admission the patient was discharged rather good health condition and is now being observed for continuous paresthesia of lower limbs and vertigoes. In this case the max. blood arsenic level was 2232 mcg/l while in urine it was 18560 mcg/l.

Conclusions: Although limited literature concerning massive acute arsenic poisoning and possible therapeutical approaches we can state that an early and effective therapeutical management is necessary with specific antidotes and the immediate use of extracorporeal detoxification such as the plasma-exchange, which is not yet sufficiently used in clinical toxicology.

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P122

PROSPECTIVE EVALUATION OF THE MECHANISM OF
HYPONATREMIA DURING MENINGITIS IN ADULTS WITH NORMAL
EXTRACELLULAR FLUID VOLUME (ECFV).

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The mechanism of hyponatremia during meningitis in adults is unclear since ECFV depletion is common in such patients. Therefore, the responsibility of inappropriate antidiuretic hormone (ADH) secretion is controversial. Hence, reports were mainly anecdotal and frequently involved patients with ECFV depletion. No study has prospectively addressed the mechanism of hyponatremia during meningitis in patients with normal ECFV. Therefore, we prospectively studied 8 consecutive patients (49 ± 7.8 y) with meningitis (3 bacterial, 1 tuberculous and 4 of viral or undetermined etiology), and hyponatremia with normal ECFV (normal clinical examination and renal function, elevated natriuresis). Determinations of plasma (P) and urinary (U) sodium and osmolality, and of P ADH were performed during meningitis and after recovery (both before and after a water-loading test).

Results (mean $\pm$ SE): *, †, #: different from the 2 other values at respectively $p < 0.05$, 0.01 and 0.001. (Friedmann analysis or ANOVA with repeated measures).

	P Na mmol/L	P. Osmo mOsm/kg	U Osmo Osm/kg	P ADH pg/ml
Meningitis	131.4 $\pm$ 0.6	273.1 $\pm$ 1.4	655 $\pm$ 73	11.1 $\pm$ 3.2*
Recovery: before load	136.9 $\pm$ 0.7#	281.9 $\pm$ 1.1†	532 $\pm$ 98	4.6 $\pm$ 0.7*
Recovery: after load	131.8 $\pm$ 1.1	271.3 $\pm$ 2.0	99 $\pm$ 28 #	3.3 $\pm$ 0.6*

Blood urea nitrogen, P renin activity and P aldosterone were identical during and after meningitis, further attesting to the unchanged (and normal) ECFV. P ADH and U osmolality were high during meningitis despite significant hyponatremia attesting to the presence of inappropriate ADH secretion. By contrast, after recovery the same level of hyponatremia (induced by water loading) was associated with significant decreases of both parameters indicating recovery of a normal P sodium level regulation. In conclusion, inappropriate ADH secretion is probably a constant feature during meningitis with hyponatremia in adults with normal ECFV. Both ADH secretion and renal diluting ability return to normal after recovery of meningitis.

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P123

INTENSIVE MANAGEMENT OF RHABDOMYOLYSIS IN PATIENTS WITH NO APPARENT TRAUMA.

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Rhabdomyolysis is a clinical entity usually related to crush-syndrome in severely traumatized patients. However, it must be suspected in not evident trauma ("auto-crush" in comatous patients); or in association to direct toxic effect of several substances (drugs, heroin, cocaine, ethanol, etc...). In a period of 18 months, 41 patients with no apparent trauma, with diagnostic criteria of rhabdomyolysis, were diagnosed. In 33 of them, the main datum in anamnesis was long-lasting decubitus secondary to low consciousness of variable aetiology. Seven patients were admitted to ICU (ages 17 to 30 years old). Their CPK titres at admission ranged from 7.320 to 112.000 UI/l; those of creatinine, 0,7 to 5,2 mg/dl. Myoglobinuria was present in all of them. Treatment or prophylaxis of renal failure was begun according with protocol (diuretics after volume repletion, urine alkalization, etc...). Despite early instauration of therapeutic measures, 5 patients required haemodialysis. One of them died because multi-organ failure. Two patients, with no apparent trauma at admission, developed compartmental syndrome which even required wide fasciotomy. In our experience, ruling out rhabdomyolysis is mandatory in patients with no apparent trauma but with factors inducing "auto-crush" (long-lasting decubitus in low consciousness of variable aetiology). This will make possible early treatment of renal failure, the most hazardous complication in these patients.

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P125

MYOGLOBIN AS AN EARLY INDICATOR OF PROGRESSIVE RENAL FAILURE FOLLOWING CARDIOTHORACIC INTERVENTION

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In 200 patients with normal renal function (RF) undergoing cardi thoracic intervention RF was controlled by measurement of serum creatinin (SC) and creatinin clearance (CC), and additionally serum and urinary myoglobin (M) levels, urinary-proteins (P) and -enzymes (E) were established. According to the renal dysfunction (RD) 2 groups were formed: group A [SC <2mg/dl at fifth pop day (n=174)] and group B [SC >2mg/dl at fifth pop day (n=26)]. Both patient groups did not differ in age and surgical indications. In both groups the levels of urinary M, E and P increased as expected (normal increase after extracorporeal circulation [ECC]), in group B the levels raised two to three times more. In both groups this development was accompanied by a significant decrease of CC (p < 0,01), this decrease was much more significant in group B. The RF recovered in group A after surgery within 5 days. On the other side group B showed increasing levels of M, urinary -P and -E after the fifth postoperative day. Time of ECC was longer and the dosage of nephrotoxic drugs significantly higher in this group. The acute periop. damage of RF is ensured to late by the increasing levels of SC and CC. A more sensitive and specific predictor for the development of ischemic renal dysfunction during ECC is the urinary-M. An indicator for drug-nephrotoxicity during therapy are the urinary-E. Recovery or worsening of RF is shown by the extent of albuminuria. In case of the evidence of unusually high levels of M in serum and urine we can expect an eminent reduction of RF up to an acute renal failure. In our opinion convenient forms of hemofiltration in time can limit extent and duration of renal dysfunction.

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P124

ACUTE RENAL FAILURE FOLLOWING RENAL TRANSPLANTATION.

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Aim: The acute renal failures (ARF) occurring within the first 3 months following renal transplantation (RT) were retrospectively assessed in order to determine: 1) specific risk factors, 2) impact on graft survival. **Methods:** 98 cadaveric RT were performed in 97 patients (mean age 41 years). Immunosuppressive treatment associated azathioprine, steroids, antilymphocyte globulin followed by cyclosporine. The ARF criteria were: serum creatinine (S.Cr.) still >200 µmol/l 8 days after RT, re-increasing S.Cr. >200 µmol/l (previous normal graft function) or >50% of basal value (previous impaired graft function). 50 ARF were recorded in 34 patients: 15 post-ischaemic tubular necrosis (PITN) including 8 patients needing transient hemodialysis, 21 rejections (18 patients) and 14 ARF of other origins (3 vascular complications, 3 urologic complications, 2 drug-induced ARF and 6 miscellaneous). Rejections (Group 1 = G1) were compared to all other patients (Control 1 = C1), as ARF of other origins (G2 and C2). PITN patients (G3) were compared to patients with immediate graft function only (C3). Statistical analysis used Chi2, Yates correction and t test. **Results:** Hyperimmunization before RT was the main risk factor for rejection occurrence (22% hyperimmunized patients in G1 vs 4% in C1, p=0.02). The differences concerning HLA-matching or other factors (number of blood transfusions, expecting time on dialysis, second graft...) did not reach the level of significance. Graft loss was more frequent (G1:45% vs C1:6%, p<0.01), and 1-year graft function was strongly involved (G1 mean S.Cr. 183 µmol/l vs C1 mean S.Cr. 138 µmol/l, p<0.001) in patients who experienced early rejection. ARF of other origins also had detrimental effect on 1-year graft survival (G2:77% vs C2:88%, p<0.001). Cold ischaemia was longer in PITN (29 h in G3 vs 23 h in C3, p<0.001). 1-year graft survival was not significantly worsened in PITN patients (G3:80% vs C3:90%). **Conclusion:** One third of patients are finally concerned, with a possible effect on long-term graft function. Prevention measures must be improved in order to decrease the incidence and the impact of early ARF after RT.

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THE EFFECTS OF FLUID AND DOPAMINE INFUSION TO OXYGEN CONSUMPTION (VO₂) AND OXYGEN DELIVERY (DO₂)

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The aim of this study was to evaluate the effects of fluid (4ml/kg) and dopamine infusion (10 µg/kg/min) on VO₂ and DO₂ on the patients who didn't had symptoms of ARDS, septicemia and lactic acidosis.

With the institutional approval and informed consent of relatives, 10 patients, mean age 44.7±16.5 who were treated in the ICU because of different pathologies were included in this study. Patients under ventilatory therapy were sedated with sodium thiopentone and/or morphine chloride and curarized. Arterial and pulmonary artery catheters were inserted in order to monitorize MAP, MPAP, PCWP and CVP. Cardiac output was measured with thermodilution technique, meanwhile the VO₂ measurements were done also with Datex Deltatrac metabolic monitor. Arterial and mixed venous gasses and hemoglobin levels were assessed for the calculations of DO₂I and VO₂I. Shortly after the control measurements 4 ml/kg of 6% hydroxyethyl starch was given to patients in 25-30 minutes and the measurements were repeated. After the stabilization of the patients the same steps were done this time with dopamine infusion rate of 10 µg/kg/min. Student-t test was performed for statistical analysis.

The rise in DO₂I with the fluid administration was statistically significant (control 278±110 ml/kg/m², test 388±156.9 ml/kg/m², p<0.01) but the increase in VO₂I was nonsignificant (control 112.9±23.9 ml/kg/m², test 119.8±27.3 ml/kg/m²). On the other hand with dopamine infusion the VO₂ (control 114.9±28 ml/kg/m², test 134.9±21.7 ml/kg/m²) and DO₂I (control 347.8±162 ml/kg/m², test 537±236 ml/kg/m²) values increased significantly when compared to controls.

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PERI-OPERATIVE RENAL
HEMODYNAMIC CHANGES IN
HYPERTENSIVE PATIENTS.

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Ten % of people are hypertensive and arterial hypertension could alter renal function. This study was undertaken to analyze renal hemodynamic changes in the peri-operative period in normotensive (N) and hypertensive (HT) patients.

METHODS: Sixteen patients were enrolled: 10 N and 6 HT patients. Hypertension was controlled by various antihypertensive drugs except diuretics. Surgery was scheduled cholecystectomy (13 cases) or hip prothetic replacement (3 cases). The study was approved by Ethical Committee (Univ. Lyon1). Renal tests were normal preoperatively. Anesthetic procedure was: premedication by 100 mg of hydroxyzine, induction by a bolus dose of propofol (2 mg.kg-1) with fentanyl (0.02 mg.kg-1) and vecuronium (0.08 mg.kg-1) followed by an infusion of propofol (3-6 mg.kg-1.h-1) with N2O (50% inspired). Fentanyl (0.05 mg) and vecuronium were injected if necessary. Ventilation was controlled and patients extubated immediately after the end of surgery. IV fluid replacement (0.9% NaCl solution) was approximately 500 ml.h-1. Samples were collected before anesthesia (C), after anesthetic induction and just before the beginning of surgery (A), just before the cholecystectomy or the hip replacement (S), 30 minutes and 2 hours after the end of surgery (R1 and R2). The following parameters were measured or calculated: mean blood pressure, heart rate, urine output, inulin and PAH clearances as glomerular filtration rate (GFR: ml.min-1.1.73m-2) and CPAH (ml.min-1.1.73m-2). Results, mean $\pm$ SEM, were compared with Mann-Whitney test (*: p < 0.05).

1.1.73m-2) and CPAH (ml.min-1.1.73m-2). Results, mean $\pm$ SEM, were compared with Mann-Whitney test (*: p < 0.05).

RESULTS: There is no difference in sex-ratio, type of surgery and total doses of anesthetic drugs. HT patients were significantly older: 69 ± 9 vs 51 ± 10.5 years. MBP and HB evolutions were not significantly different. In N group, renal parameters evolutions are in accordance with published data: a dramatic fall in V, GFR and CPAH. In HT group, V evolution was similar as in N group. The figure describe GFR and CPAH evolutions.

CONCLUSION: GFR had a greater fall and remain reduced at recovery time in the HT group. So, HT patients are at high risk of acute renal failure not only pre-operatively but also post-operatively.

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EFFECTS OF HYDROXYLETHYL STARCH USED
DURING BRAIN DEATH ORGAN DONORS RESUSCITATION
ON KIDNEY TRANSPLANT FUNCTION.

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Brain death organ donors require great fluids intake because of diabetes insipidus. We compared the effects of HAS (Elohes*) versus those of Albumin (ALB) used during organ donors resuscitation on the renal function of kidney recipients.

METHODS: We reviewed 26 kidney transplantations performed from September 1, 1991, to March 1, 1992, for which brain death organ donors received HAS as much as require to maintain a good volemic status (HAS group). They were compared to the 28 performed from January 1, 1991, to September 1, 1991, for which brain death organ donors did not receive HAS but 25 or 4 % ALB solution (ALB group). Resuscitation of the donors involved vasopressors (dopamine, dobutamine or epinephrine), red cells or fresh human plasma as required by hemodynamic or biological data. All transplantations and organ procurements were performed at our institution with the same procedures. Systolic arterial pressure, heart rate, last four hours urinary output (V), creatinemia (Creat.) and azotemia were measured just before surgery. In recipients, we measured: duration of cold and warm ischemia times, lower Creat. of the first week and number of patients with a V above 200 ml.h-1 on the first day. Results are expressed as mean $\pm$ SD and compared by T- or Chi-2 tests (*: p < 0.05).

RESULTS: There was no difference in age, sex-ratio, origin of the brain death, arterial pressure, heart rate or vasopressors requirements between the 2 groups of donors. HAS group donors received 1500 ± 943 ml of HAS. ALB infusion was 711 ± 822 ml in the HAS group vs 2452 ± 1094 in the ALB one (*). Four fine needle biopsies performed at the time of surgery in the HAS group revealed in all cases an osmotic nephrosis. Sex-ratio, age, nature of the nephropathy, ischemia times were not different among recipients.

Renal parameters of organs donors and kidney recipients [%].

Donors	V	Creat.	Azotemia	Reci- plants	V > 200	Lower Creat.
	ml.min-1	μ mol.l-1	mmol.l-1		ml/h	μ mol.l-1
HAS (19)	7.04 ± 6.3	131.5 ± 44	7.98 ± 4.8	HAS (26)	25 [96]	146 ± 67
ALB (21)	9.6 ± 6.5	113.9 ± 62	6.5 ± 4.8	ALB (28)	27 [96]	167 ± 126

CONCLUSION: During brain death organ donor resuscitation, HAS is efficient as ALB to maintain a good hemodynamic status. Despite, an osmotic nephrosis, V and Creat. are not different in donors and early renal function is not altered in kidney recipients. So, the use of HAS during pre-hospital resuscitation did not preclude organ donation and HAS could be perfused during donors resuscitation. Moreover, HAS costs are lower than 4 % ALB solutions.

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P129

HEMOFILTRATION DOES NOT IMPROVE SURVIVAL IN
PATIENTS WITH MULTIPLE ORGAN FAILURE

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One of the life threatening problems after polytrauma, major surgery or sepsis syndrome is the development of multiple organ failure (M.O.F.). Endotoxins, leucotrienes or other toxic middle molecules are believed to mediate this M.O.F. Clearance of this mediators by means of hemofiltration could be of advantage in preventing or treating M.O.F. Therefore we studied the survival rates of 41 patients with M.O.F. (2 or more organs failing, including renal failure) 32 patients (63 ± 16 yr) were treated with hemofiltration (HF) for $6,8 \pm 5,4$ days. 9 patients (63 ± 20 yr) were treated with hemodialysis (HD) for $3,3 \pm 4,2$ days. In the patients treated with HF APACHE II score was 20 ± 6 (vs 17 ± 8 in HD group), sepsis was present in 69% (vs 56% in HD group). ICU mortality was 63% in HF and 44% in HD group. Hospital mortality was 72% in HF group.

We conclude that hemofiltration does not improve survival rate in patients with M.O.F. Our data do not lend support to the theory that removal of endotoxins by hemofiltration may decrease incidence or outcome of M.O.F.

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SUCCESSFUL HEPARIN-FREE
HEMODIALYSIS (HFHD) OF PATIENTS AT
HIGH RISK OF HEMORRHAGE

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The risk of life-threatening hemorrhage in acute hemodialysis remains high because of the general requirement of heparinisation. The low in vitro thrombogenicity of Polycarbonate membrane and the recent reports of its good biocompatibility have led us to assess its use in I.C.U. patients at high risk of hemorrhage without heparin. We conducted a prospective study in which 51 dialysis were performed on 9 patients: post-operative(1), hemorrhagic syndrome(3), thrombopenia(3), hemolytic-uremic syndrome(2). Blood compartment was prerinised with 10000IU of heparin in 2000 ml of saline, fluid no injected to patient. Blood flow rate was maintained at 250 ml/min. The incidence of overall clotting was 2%. No hemorrhagic complications were observed. Dialysis were successfully accomplished in sight of that mean duration was 244 ± 20 minutes. Urea and creatinine interdialytic decrements were $48\% \pm 9\%$ & $42\% \pm 9\%$ respectively. The two important conditions for HFHD are the removal of all air from the dialyzer during the priming operation and the maintain of blood flow rate above 250ml/min. We conclude that HFHD is a safe and efficacious method in ICU patients at high risk of hemorrhage.

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THE ROLE OF ERYTHROPOIETIN IN THE DEVELOPMENT OF ANEMIA IN A ICU
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Most critically ill patients develop some degree of anemia that can be due to several factors, including perhaps some erythropoietin (EPO) deficiency. To test this latter hypothesis EPO levels were determined in 16 patients who stayed more than 7 days in our ICU. EPO dosages were performed with a photometric enzyme immuno-assay (Boehringer Mannheim Biochemica). Nine of the patients were male and seven female. Mean age was 50.8 years, mean Apache II score was 18 and mean ICU stay was 15 days. Ten patients showed a normal response of EPO corresponding to their degree of anemia (EPO 186 pg/ml for Hct 27.1%). Six patients showed a blunted EPO response (EPO 90 pg/ml for Hct 24.0%). Each of these six patients had sepsis and acute renal failure (ARF). In conclusion, we confirm that most ICU patients develop anemia. In patients with acute renal failure and sepsis a more severe anemia is seen, which could be caused by inhibition of EPO production. The release of cytokines, such as tumor necrosis factor might be implicated.

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PERIOPERATIVE RENAL FUNCTION IN LIVER TRANSPLANTATION

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The incidence of acute renal failure (ARF) after liver transplantation (OLT) may be as high as 94% [1]. Renal function (RF) may be impaired as a consequence of preexisting renal malfunction, acute post-OLT disease states and by nephrotoxic drugs. We therefore investigated prospectively RF of OLT recipients. Methods: In 30 patients (P) various indices of RF (creatinine clearance [C_{Cr}], as % of normal), fractional excretion of Na [FE_{Na}], urinary to plasma osmolality ratio [U/P_{Osm}], osmolar [Ex_{Osm}], Na [Ex_{Na}] and K [Ex_K] excretions, etc.) were determined pre-OLT, daily in the immediate post-OLT period during their stay in the intensive- and intermediate care units (median 11d, [range 6-66]) and 1 to 6 months post-OLT (late sample, 124d [30-224]). ARF was defined as $C_{Cr} < 20\%$ of normal. P were classified by post-OLT C_{Cr} ; these values were compared to pre-OLT C_{Cr} . Results: 16 P had normal C_{Cr} ($>80\%$) pre- as well as post-OLT (Table). The no. of P with normal C_{Cr} decreased from 22 (73%) pre- to 17 (57%) post-OLT with a net of 5 P shifting from $C_{Cr} > 80\%$ to $< 20\%$. For features of post-OLT RF in P with $C_{Cr} > 20\%$ see Figure (median, 25,75 percentiles, n=22). In 53% of P a reversal of the Ex_{Na}/Ex_K ratio occurred post-OLT. Discussion: Our data show no major impact of uncomplicated OLT on perioperative RF. Features of RF after OLT were: stable C_{Cr} , transiently increased FE_{Na} as a consequence of an increased sodium

load due to fluid resuscitation, high Ex_{Osm} (post-OLT catabolism), preserved tubular function (i.e. concentration ability, $U/P_{Osm} > 1.2$), and an inverse ratio of Ex_{Na}/Ex_K (aldosteronism due to corticosteroid immunosuppression). In contrast to other reports the incidence of ARF was low in our P (27% compared to 94% and 66%, respectively [1,2]). Glomerular (C_{Cr}) and tubular (FE_{Na} , U/P_{Osm}) function was preserved in most P. Meticulous monitoring of RF may be helpful in detecting renal impairment before ARF occurs. References: 1. Nephron (1990) 55:121. 2. Kidney Int (1987) 31:195.

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CLEARANCE OF UNFRACTIONATED AND LOW MOLECULAR WT HEPARIN DURING HAEMOFILTRATION

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Though not previously recorded, clearance into the ultrafiltrate of both unfractionated (UF1000) and low molecular weight (Fragmin) heparin would be expected during haemofiltration (HF) in view of their molecular weights (mean 13000 [range 5000-35000] and 5000 daltons [range 2000-8000] respectively) and the filter pore size (35000 μ). Constant infusions of either unfractionated heparin (5000 U/hr) (n=8) or Fragmin (3000 U/hr) (n=7) were thus administered into the arterial side of a Hospal AN69 haemofilter circuit in ICU patients undergoing continuous venovenous HF at a blood flow rate of 150 ml/min. Blood and ultrafiltrate samples were drawn at 1 and 2 hours for measurement of (i) heparin (by anti-Xa assay standardised with the appropriate International Standard) and (ii) anti-thrombin III.

		1hr blood	1hr filtrate	2hr blood	2 hr filtrate
anti-Xa	UF1000	0.27 $\pm$ 0.04	0.01 $\pm$ 0.01	0.30 $\pm$ 0.05	0.03 $\pm$ 0.02
	fragmin	0.34 $\pm$ 0.06	0.04 $\pm$ 0.03	0.38 $\pm$ 0.06	0.03 $\pm$ 0.03
ATIII	UF1000	0.47 $\pm$ 0.07	-	0.46 $\pm$ 0.08	-
	fragmin	0.56 $\pm$ 0.09	-	0.51 $\pm$ 0.12	-

Heparin levels in blood were at the lower end of the range necessary for therapeutic anticoagulation (0.3-0.8 IU/ml), however UF1000 and fragmin were both barely detectable in the ultrafiltrate. This may be due to either the negative charge of the heparin or, possibly, to binding. Plasma ATIII levels were well below the normal range of 0.8-1.2 IU/ml in all but three of the patients studied; as ATIII is necessary for heparin action the finding of these subnormal levels carries important implications for anticoagulant therapy in the critically ill patient.

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PUMP-DRIVEN CONTINUOUS VENOUS VENOUS HEMOFILTRATION IN SEPTIC CATABOLIC PATIENTS.

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Continuous arteriovenous hemofiltration (CAVH) is an alternative to conventional dialysis techniques in critically ill patients with renal failure. Nevertheless, its successful application is strongly dependent upon an adequate arterial driving pressure. The relationship between blood pressure and flow through the extracorporeal circuit and ultrafiltration rate is such that it is difficult to achieve clearances so as to maintain adequate plasma level of creatinine and urea in the septic haemodynamically unstable (i.e. requiring vasoactive therapy) and hypercatabolic patient without use of intermittent haemodialysis or haemodiafiltration. In order to improve clearances we routinely use Pump-Driven Continuous Venous Venous Hemofiltration (PDCVH). 18 patients (pts) suffering from generalized sepsis have been treated according a standard protocol: age was 59.1 years, SAPS 17.2. Pts were treated for an average period of 9.2 days obtaining a daily ultrafiltrate production of 21.4 liters. In all pts, though the high catabolism (basal nitrogen output > 0.3 gr/kg/day), there was a significant decrease of urea and creatinine blood concentration:

Urea pre-treatment 204.2 mg/dl Urea post-treatment 159.9 mg/dl

Creatinine pre 6.5 mg/dl Creatinine post 3.9 mg/dl

Clearance of urea (median of all the determinations pooled) was 12.8 ml/min with a sieving coefficient of 0.8. Daily values were independent from the age of the filter. The overall mortality was 55% (10/18) without differences between the two groups (Survivors vs Deceased) in age, SAPS, duration of treatment, daily production of ultrafiltrate, pre and post treatment plasma level of urea and creatinine. Over more than 4000 hours of treatment there were no significant complications and the technical drawbacks were easily coped with. In conclusion PDCVH is an effective and well tolerate technique of renal support even in hypercatabolic patients. Recent studies suggest that the high ultrafiltration volume obtained with this method may affect the final outcome if compared with CAVH, perhaps allowing higher elimination of mediators responsible for the development of subsequent multiple organ failure.

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CONTINUOUS VENO-VEINUS HEMODIAFILTRATION (CVVHD) WITH THE EQUALINE SYSTEM IN CARDIOSURGICAL PATIENTS

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This article is a short report of the results obtained in the treatment of Acute Renal Failure (ARF) in cardiosurgery patients through of Equaline System which permits, during the course of continuous veno-venous hemodiafiltration (CVVHD), an automatic replacement of fluid to the patient. This allows the maintenance of a perfect fluid balance and an adequate clearance capacity. In cardiosurgical patients with a very high degree of hemodynamic instability, hemofiltration is not advisable because, during the course of treatment, the hemodynamic can become worse and the removal of the liquids takes place mainly intravascular. The slow and continuous removal of liquids through the use of continuous ultrafiltration is more suitable for these patients but does not guarantee adequate clearance. So, it was decided to use continuous ultrafiltration through the Equaline System together with a dialysate flow through the filter. In the treatment of 5 patients suffering from ARF as a result of cardiogenic shock, we used a blood flow rate of 25ml/min and a dialysate flow of 1lt/h. In all 5 cases it was possible to observe a reduction in the Urea and Creatinine values after only 12 hours of treatment. After 5 days of treatment the Urea level had decrease to average values of 125 ± 28 mg/dl and Creatinine to 3.1 ± 0.9 mg/dl. No significant complications were observed and the method was effective in the maintenance of volemic balance as well as in the clearance of blood catabolites.

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PATTERNS IN THE SAND: RADIOGRAPHIC EVIDENCE FOR DYNAMIC EVENTS AFFECTING TRACHEAL TUBE BIOFILM

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Bacterial scatter from tracheal tube biofilm has been shown to occur during the inspiratory phase of mechanical ventilation, and a dynamic physical process has been proposed, as the mechanism underlying particle dissemination². It is possible that scatter of tracheal tube biofilm into the lower respiratory tract contributes to the subsequent development of nosocomial pneumonia.

In order to demonstrate evidence for the occurrence of dynamic phenomena *in vivo*, tracheal tubes were collected from 50 consecutively extubated adult intensive care patients for radiographic examination. The inner surface of each tube was dusted with Zinc powder to excess while still damp, and X-rayed using standard equipment and film. The negative image produced by biofilm was recorded against a MacGill curve template, and the thickness measured with micrometer callipers. A residual biofilm was present in 45(90%) tubes, with a greater proportion having biofilm at the lower end of the tube. In 23(46%) tubes, one or more ripple-like outlines were observed. In 37(74%) tubes the maximum thickness of biofilm exceeded the 0.5mm necessary to ensure the occurrence of gas-liquid interaction. These observations suggest that particle dissemination from the luminal biofilm could have occurred in the majority of tubes examined, and that two-phase flow occurred in almost half of them. The role of these phenomena in the pathogenesis of nosocomial pneumonia requires further investigation.

1 Inglis TJJ, Millar MR, Jones JG et al. J Clin Micro 1989;27:2014-2018.

2 Inglis TJJ, Jones JG, Newman SP. B J Hosp Med 1989;42:141-142.

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REDUCED OXYGEN CONSUMPTION (VO₂) DURING CONTINUOUS ARTERIO-VEINUS HEMOFILTRATION IN SEPTIC PATIENTS

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During continuous arterio-venous or veno-venous hemofiltration a significant reduction in the core temperature is frequently observed. We report in this study the metabolic and gas exchange effects and the mechanisms of this hypothermia.

Material and methods. 17 I.C.U patients requiring continuous hemofiltration for oliguric renal failure after septic shock were studied. Hemodynamic status was monitored by a Swan-Ganz catheter and an arterial line as a part of the routine management of septic shock. The central temperature was continuously monitored by the thermistor probe of the Swan-Ganz catheter. Measurements for gas exchange data were performed in stabilised patients before initiation of the C.A.V.H and at regular intervals for 48 hours. Eleven between the seventeen patients presented mild hypothermia from 37.4 ± 0.9 to 34.6 ± 0.8 . The gas exchange data before and during the hypothermic state are presented.

Results.

	before C.A.V.H	during Hypothermia	statistics
pH	7.20 ± 0.6	7.33 ± 0.1	
PaCO ₂ mmHg	36 ± 10	35 ± 9	
PaO ₂ mmHg	103 ± 37	140 ± 42	$p < 0.01$
PvO ₂ mmHg	35 ± 4	41 ± 5	$p < 0.01$
SvO ₂ %	65 ± 8	73 ± 6	$p < 0.01$
DO ₂ ml/min	851 ± 293	830 ± 251	
VO ₂ ml/min/m ²	141 ± 22	112 ± 22	$p < 0.01$
(a-v)DO ₂ ml/dl	4.6 ± 1.2	3.8 ± 0.8	$p < 0.01$
O.E.R. %	33 ± 7	27 ± 7	$p < 0.01$
QVA/Q _t %	18 ± 14	15 ± 10	

Conclusions. Hypothermia during C.A.V.H significantly decrease oxygen consumption, and increase PaO₂ by a PvO₂ effect. The principal factors leading to temperature reduction during C.A.V.H were 1) Sedation 2) The use of muscle relaxants if sedation was not effective to make the patients cooperative to the ventilator and 3) The high ultrafiltration rate (up to 1lt/hour) of the C.A.V.H and the inadequately warmed compensation fluids.

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CLINICAL APPROACH OF Na MASS TRANSFER IN CONTINUOUS HAEMOFILTRATION.

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Continuous venous-venous haemofiltration (CVVH) is an efficient method to treat critically ill patients in acute renal failure (ARF). With high volume CVVH (> 24 l/24 h), the convective sodium (Na) transfer is considerable according to a sieving coefficient of Na of 0.99 ± 0.02 . In some situations Na balance equilibrium is difficult to obtain.

In order to give some advice on Na mass transfer, we designed a prospective study to compare a theoretical model based on the monocompartmental kinetic osmotic space of Na (60 % of body weight), to biological and clinical parameters obtained in patients treated with CVVH.

Ten patients hospitalised in our unit and treated with CVVH were included in the study. All the patients had an ARF associated with multiple organ failure. SAPS score was 19.4 ± 4 . Patients weight was measured daily. Ultrafiltrate (UF) and the replaced haemofiltration fluid volume were measured and weighted hourly. All the supplied and loosed fluids were checked daily and Na mass was measured in all of it. Natremia and UF Na were measured twice a day.

18 CVVH sessions of 24 hours were studied. UF rate was 19 ± 6 l/24h. Mean Na mass remove by filtration was 2675 ± 477 mEq/24h. Mean Na mass value was 2728 ± 489 mEq/24h. for losses and 2547 ± 471 mEq/24h. for supplies. Mean Na mass transfer was -349.8 ± 445 mEq/24h.

Theoretical Na mass transfer was calculated by the following equation :

$NaMT = [Na_f \times (0.6 \times BW_f)] - [Na_i \times (0.6 \times BW_i)]$, as NaMT : Na mass transfer, Na_f and Na_i : final and initial natremia, BW_f and BW_i : final and initial body weight.

Final Na mass calculated was 4979 ± 1025 mEq, the initial one was 5113 ± 1065 mEq, with an average calculated Na mass transfer of -269 ± 362 mEq/24h. There was a closed correlation between Na mass transfer measured and Na mass calculated with R-squared at .857 ($p < 0.01$).

Clinician can forecast Na mass transfer for each patient treated with haemofiltration, in using the following parameters : initial natremia, the one hopped at the end of the session and the weight variation expected.

In conclusion, we validated a simple theoretical model based on monocompartmental kinetic osmotic space of Na. This model could be used in clinical situations to perform mandatory Na mass transfer in continuous haemofiltration.

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VASCULAR ACCESS FOR CONTINUOUS ARTERIO-VEINUS HEMO DIAFILTRATION (CAVHD)

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CAVHD and related techniques rely on vascular access to a large artery and a large vein with wide-bore catheters. The femoral vessels or a Scribner shunt are used most often. Bleeding, large retroperitoneal hematoma, arterio-venous fistula formation and infection are possible complications. We report our experience in 62 patients treated with CAVHD.

Type of catheter: in 39 patients conventional polyurethane 15 cm, 7 Fr cath; in 23 patients silicone 20 cm, 12 Fr cath (MEDCOMP, USA).

Site of access: 53 patients femoral vessels; 2 patients axillary artery and axillary vein; 5 patients axillary artery and subclavian vein; 2 patients Scribner shunts.

First time access failure: 1 patient;

Catheter replacement because of insufficient flow: 3 patients.

Bleeding: One patient removed his arterial catheter, leading to blood loss; One artery had to be surgically sutured after removal of the catheter. This patient appeared to be still heparinized.

Introduction-site infection: One patient.

Catheter-related sepsis: Not documented.

We conclude that vascular access is safe in CAVHD and leads to few complications.

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ACTIVATION OF THE COMPLEMENT SYSTEM IN BABOONS CHALLENGED WITH LIVE E.COLI: CORRELATION WITH MORTALITY AND EVIDENCE FOR A BIPHASIC ACTIVATION PATTERN

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We have studied differences in activation of the complement system in a baboon model for sepsis in which baboons were challenged with a lethal or sublethal dose of E.coli. In the lethal group (n=4) a pronounced activation was observed immediately after the start of the E.coli administration, which resulted in peak levels of the complement activation parameters, i.e. C3b/c, C4b/c and C5b-9, of 8, 5 and 12 times the baseline values, respectively. In contrast with the lethal group, only a modest increase of 1 to 2 times the baseline values of the complement activation parameters was observed in the sublethal group (n=10) during the first hours. However in samples obtained at 24 hours in the sublethal group a steep increase in C3b/c, C4b/c and C5b-9 of 6, 8 and 5 times the baseline values, respectively, was observed, which suggested a second phase of complement activation. This second phase of complement activation was due to an endogenous mechanism, since neither circulating micro-organisms nor endotoxin could be detected during this second phase of complement activation.

In experiments in which 3 baboons were challenged with a sublethal dose of E.coli and were sampled more frequently, this second increase in complement activation parameters was paralleled by the appearance of the acute phase reactant C-reactive protein, which suggest that complement activation is mediated by CRP dependent mechanism.

The pronounced differences in complement activation between both groups suggest that the complement system is involved in the pathogenesis of the lethal complications during sepsis.

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Miscellaneous I

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DEEP VEIN THROMBOSIS SECONDARY TO CENTRAL VENOUS CATHETER.

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Deep venous thrombosis (DVT) of the upper extremity has been considered an uncommon condition accounting for less than 2% of all DVT. The central venous catheter (CVC) is an important causal factor and its wide use in the ICU's can increase the incidence in these patients. Objective: The aim of this study is to know the incidence of the DVT secondary to CVC. Methods: We studied 15 patients who had single or multiple CVC for a minimum of 15 days. The age of the patients was 48.6±21.48 years. All received antithrombotic prophylaxis (enoxaparin 20 mg/day). All patients underwent physical examination looking for signs or symptoms of DVT. We performed superficial ECO-Doppler on femoral (F), axillary (A), subclavian (S) and jugular veins (J), and transesophageal ECO-Doppler on the superior vena cava (SVC) and right atrium (RA). When the above studies were positive pulmonary ventilation perfusion scanning was performed.

Results: 7 patients (46%) showed DVT in one or more of the veins above mentioned with ECO-Doppler. Clinical signs were present in only 3 cases. The DVT had the following distribution: 1 in RA, 4 in SVC, 2 in J, 5 in S, 1 on A and 1 in F. The affected veins of each patients is represented in the table. Factors causing DVT in these patients included: a) Duration of the catheterization: those patients with positive DVT had a duration of causal catheter of 15 ± 7 days and 45.8 ± days for the remainder of the catheters whether causative or not, compared with 21.5 ± days for the DVT negative group. b) Infection: 6 of the 7 patients with DVT+ (85%) presented with positive catheters cultures, compared to one (12%) in the DVT- group. All the infections were by Staphylococcus PC- and in one case additionally with Enterococcus. c) Parenteral Nutrition: 10 patients received PN, 6 (85%) of the DVT+ and 4 (50%) of the DVT- group. d) Antithrombin III: levels were less than normal in all patients with DVT+ (50.8 ± ng/ml). The perfusion scan demonstrated pulmonary defects not related with the ventilation scan or X-rays studies (suggestive of pulmonary embolism) in 3 of 7 cases with DVT+.

VENOUS THROMBOSIS						
Pat.	RA	SVC	J	S	A	F
1	x	x		x		
2		x	x	x		
3			x	x		
4		x		x		
5						x
6				x	x	
7		x				

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DETECTION OF DEEP VEIN THROMBOSIS (DVT) IN CRITICALLY ILL PATIENTS BY VEINUS ULTRASONIC DUPLEX SCANNING (VUDS). A PROSPECTIVE STUDY IN A MEDICAL ICU.

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Patients admitted to a medical ICU often have multiple risk factors for DVT including positive pressure ventilation, immobility, advanced age, sepsis... Unfortunately few data exist regarding the frequency of DVT in this population. The clinical diagnosis of DVT is difficult; venous ultrasonic duplex scanning is a non invasive reliable technique for diagnosis and exact localisation of the thrombosis, its site and the degree of obstruction. We prospectively used this technique to evaluate the incidence of asymptomatic DVT in all long term (> 8 days) hospitalized patients. A total of 100 patients were admitted to the study: 59 men, 41 women, mean age = 59.4 ± 13 years, SAPS = 11.8 ± 4, 90 patients under mechanical ventilation. Doppler flow measurements (Mira[®] 4-8 MHz) and duplex ultrasonography (Aloka[®], 5 MHz) were done once weekly. Patients received either standard heparin (15 cases), or low molecular weight heparin (58 cases). No prophylaxis was used in case of high risk of bleeding (27 cases). Deep vein thrombosis occurred in 20 patients (mean delay = 12.5 ± 8 days). There were 13 isolated calf veins thrombosis and 7 proximal DVT with or without calf veins thrombosis. A follow-up did not show clinical evidence of pulmonary embolism in any cases. Mortality was not higher in the DVT group (25% vs 27%).

Asymptomatic DVT are frequent in the ICU and early detection seems to be justified. A 20% occurrence in this asymptomatic patient population underscores the need for aggressive DVT prophylaxis.

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