Critical Care 1998, Volume 2 Suppl 1
http://ccforum.com/supplements/2/S1

CRITICAL CARE

MEETING ABSTRACTS Open Access

18th International Symposium on Intensive Care and Emergency Medicine

Brussels, Belgium. 17–20 March 1998

Published: 1 March 1998

These abstracts are available online at http://ccforum.com/supplements/2/S1

MEETING ABSTRACTS

P001

Hemodynamics in induced whole body hyperthermia

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Critical Care 1998, **2(Suppl 1):**P001

Background: Whole body hyperthermia induced by radiative systems has been used in therapy of malignant diseases for more than ten years. Von Ardenne and co-workers have developed the 'systemiche Krebs-Mehrschritt-Therapic' (sKMT), a combined regime including whole body hyperthermia of 42°C, induced hyperglycaemia and relative hyperoxaemia with additional application of chemotherapy. This concept has been employed in a phase I/II clinical study for patients with metastatic colorectal carcinoma at the Virchow-Klinikum since January 1997.
Methods: The sKMT concept was performed eleven times under intravenous general anaesthesia, avoiding volatile anaesthetics. Core temperatures of up to 42°C were reached stepwise by warming with infrared-A-radiation (IRATHERM 2000®). During the whole procedure blood glucose levels of 380–450 mg/dl were maintained as well as PaO_2 levels above 200 mmHg. Extensive invasive monitoring was performed in all patients including measurements with the REF-Ox-Pulmonary artery catheter with continuous measuring of mixed venous saturation (Baxter Explorer®) and invasive monitoring of arterial blood pressure. Data for calculation of hemodynamic and gas exchange parameters were collected four times, at temperatures of 37°C, 40°C, 41.8–42°C and 39°C, during measurements FiO_2 was 1.0 at all times. Fluids were given in order to keep central-venous and Wedge pressure within normal range during the whole procedure. Statistics were performed using the Wilcoxon Test.
Results: Statistically significant differences were found between heart rate, cardiac index and systemic vascular resistance comparing data at 37°C and 42°C. Heart rate and cardiac index increased to a maximum at 42°C ($P < 0.0001$) whereas systemic vascular resistance had its minimum at 42°C ($P < 0.0001$). Mean arterial pressure dropped with increasing temperature, differences were not significant. Calculation of stroke volume index and ventricular volumes showed only a slight decrease in endsystolic volumes with increasing temperature, the resulting differences in right ventricular ejection fraction were marginally significant ($P = 0.038$) comparing 42°C to baseline. Right ventricular stroke work index as well as mean pulmonary arterial pressure increased at 42°C ($P = 0.0115$ and $P = 0.0037$), pulmonary vascular resistance only dropped little compared to systemic vascular resistance, left ventricular stroke work index even dropped with increasing temperature, though showing no significant difference. Values for mixed venous oxygen saturation did not vary during therapy, pulmonary right-left shunt showed a temperature associated increase ($P = 0.0323$) to a maximum at 42°C.
Conclusion: Under the procedure of sKMT cardiac function in patients, who do not have any pre-existing cardiac impairment, can be maintained almost unchanged, ie with normal right and left ventricular pressure, despite an increase in right ventricular stroke work
Acknowledegment: Supported by Deutsche Krebshilfe.

P002

Induced hyperthermia causes significant changes in lymphocytes

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Critical Care 1998, **2(Suppl 1):**P002

Background: Changes in lymphocyte subpopulations are determined under several clinical conditions eg during activation of the immune system. Our aim was to analyze the influence of induced elevated body temperatures on lymphocytes in patients without infections or other physiological stimulators of the immune system. Therefore we examined blood of patients with metastatic colorectal carcinoma during whole body hyperthermia of 42°C caused by infrared-A-radiation. This is used as part of so called 'systemische Krebs-Mehrschritt-Therapie' (sKMT), which was started as a phase I/II clinical study at Virchow-Klinikum in 1997.
Methods: Lymphocyte subpopulations were investigated by flow-cytometry-analysis. Blood samples were obtained before beginning of therapy at 37°C, at 40°C, at the end of the plateau of 42°C and after therapy at 37°C again. Time between investigations was about 2 h. Subpopulations were natural killer cells, T-Cells, IL2-Receptor on T-Cells, T4-Cells and T8-Cells. Cell counts were compared by using a Wilcoxon rank sum test.
Results: The number of lymphocytes per nl decreased significantly from 37°C to 42°C (Fig. 1). This effect was mainly caused by a significant decrease of the absolute T4-Cell count and a slight decrease of the T8-Cell count with a resulting significant decrease of T-Cells. In addition, IL2-Receptor expression on T-Cells, as a marker for activation, decreased significantly. In contrast, the number of natural killer cells per nl

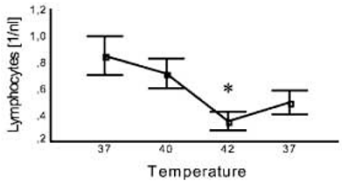

Fig.1: Number of Lymphocytes per nl (Mean-Values with SEM)

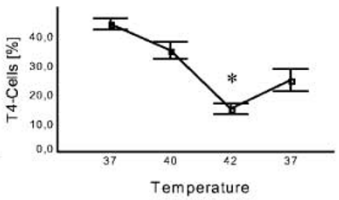

Fig.2: T4-Cells [% of Lymphocytes] (Mean-Values with SEM)

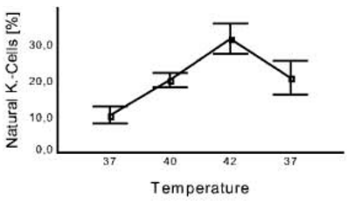

Fig.3: Natural killer cells [% of Lymphocytes] (Mean-Values with SEM)

Figures 1-3 (abstract P002)

increased. Looking for changes in relation between lymphocyte subpopulations, we found a significant percentual decrease of T4-Cells (Fig. 2), no percentual changes in T8-Cells but a significant percentual increase of natural killer cells (Fig. 3). Effects were reversible and at the last time-point at 37°C all examined parameters showed a tendency to the initial values.

Conclusions: Elevated body temperatures up to 42°C induce a change in lymphocytes which is similar to early responses of the immune system to other stress situations or host response. For example natural killer cells are known to increase in the early phase after severe trauma, whereas the number of T4-Cells decreases in these patients. Thus, isolated induced hyperthermia in absence of infections or other physiological stimulators of the immune system seems to cause a kind of host response. It seems remarkable, that these effects were reversible in a very short time-period after decrease of temperature.

Acknowledgement: Supported by Deutsche Krebshilfe.

P003

Relationship between reactive hemophagocytic syndrome (RHS) and multiple organ system failure (MOSF)

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Critical Care 1998, **2(Suppl 1):**P003

Objective: To report two cases which show that severe RHS can be reversible, can be a cause of cytopenia in the ICU, and can be associated with MOSF. In both cases, a bone marrow aspirate showed histiocytes, hypocellularity of all cell lines, and hemo- and erythrophagocytosis.

Case reports: 1) A 3 year-old boy with Mucha-Haberman syndrome was admitted to the PICU for septic shock (Staphylococcus epidermidis and Candida in blood), acute respiratory distress syndrome (ARDS), capillary leak, acute renal failure, liver dysfunction, MOSF and RHS. PRISM II score was 13. The pancytopenia worsened (WBC: 900 cells/mm^3; Hb: 59 g/l; Plt: 36000/mm^3), then resolved 2 months later. The patient required mechanical ventilation for 6 weeks. Length of stay in ICU was 2 months.

2) A previously healthy 4 year-old girl was admitted to the PICU for respiratory failure. PRISM II score was 23. She developed ARDS, cardiomyopathy with shock and complete atrio-ventricular block, capillary leak, liver dysfunction and RHS (WBC: 1900 cells/mm^3; Hb: 65 g/l; Plt: 58000/mm^3). Serology for respiratory syncitial virus was positive. The duration of RHS was 20 days; length of mechanical ventilation was 16 days, and length of stay in the PICU was 3 weeks.

Conclusion: Both patients recovered completely; thus severe cases of pediatric RHS can be reversible. These cases also show that RHS may be a significant cause of cytopenia in the PICU. Data in the literature and these cases suggest that RHS may be an integral part of MOSF: 1) RHS appeared and disappeared with MOSF; 2) RHS and MOSF share similar trigger events, such as infection or neoplasia; 3) increased level of cytokines (IL-6, IFN-alpha and IL-2 receptor, etc.) are present both in MOSF and RHS [1-3].

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P004

LPS does not induce changes in hepatocellular microtubule cytoskeleton

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Critical Care 1998, **2(Suppl 1):**P004

Introduction: Lipopolysaccharides (LPS) are known to be involved in the pathogenesis of septic shock and multiorgan failure. It has been demonstrated that LPS may cause changes in monocyte cytoskeleton and directly influence assemblation of isolated microtubuli. As liver failure is increasingly observed during septic shock we estimated the influence of LPS on microtubule cytoskeleton of cultivated hepatocytes and human blood monocytes.

Methods: HepG2 cells, murine hepatocytes, or human monocytes (positive control) were incubated with LPS FITC labelled or unlabelled (0.1–200 µg/ml) up to 48 h. After staining with antibodies to tubulin and tau proteins cells were analysed by fluorescence and laser scan confocal microscopy. Activation of MAP-kinases was investigated by Western Blot using phosphospecific antibodies.

Results: Immunofluorescence revealed that the cytoskeleton of hepatocytes was not affected by LPS. Furthermore, no phosphorylation of MAP-kinases was found after LPS-incubation. Mouse hepatocytes and HepG2 cells did not accumulate FITC labelled LPS. In contrast, human blood monocytes showed an accumulation of FITC-LPS, an activation of MAP-kinases and changes in microtubule cytoskeleton.

Conclusions: Our results might explain the frequently observed late onset of liver failure during sepsis-syndrom. Further studies on possible protective factors in hepatocytes and the complex co-operation between LPS and cytokines leading to hepatocellular damage are necessary.

Acknowledgement: Supported by Deutsche Forschungsgemeinschaft Re 653/5-1 and Thuringian Ministry of Science, Research and Culture F 3.1-908/7-143.

P005

HepG2 hepatocytes express IFN-γ, TNF-α, TGF-β, M-CSF, oncostatin-M, ICAM-1, IL-4, IL-5, IL-7, IL-10, IL-11, IL-12 and IL-6 receptor genes *in vitro*

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Critical Care 1998, **2(Suppl 1):**P005

Introduction: Pro- and antiinflammatory cytokines are known to be involved in the pathogenesis of septic shock and multiple organ dysfunction, including liver failure. Many lympho- and monokines may alter hepatocellular function. Liver parenchymal cells themselves, in contrast to mononuclears like Kupffer cells, are generally considered only targets but not producers of these important mediators.

Methods: In order to investigate whether hepatocellular cells are a potential source of various regulatory cytokines we have estimated the multiple cytokine gene expression in the culture of well differentiated human HepG2 hepatoma cells using RT-PCR.

Results: Our findings demonstrate that HepG2 cells express mRNAs for IFN-γ, TNF-α, TGF-β, M-CSF, oncostatin-M, ICAM-1, IL-4, IL-5, IL-7, IL-10, IL-11, IL-12 and IL-6R. At the same time the expression of IL-1, IL-2, IL-3, IL-6, CD40 ligand and IL-2R genes was not detected.
Conclusions: Hepatocytes are potential producers of a variety of cytokines, some of them being able to regulate hepatocellular functions directly, others are important regulators of leukocyte functions. Thus, on the one hand, hepatocytes may express autoregulatory cytokines and, on the other hand, influence the functions of other liver cells like Kupffer, Ito or endothelial cells. Due to their large amount, liver parenchymal cells could be an important source of systemically acting pro- and anti-inflammatory and other regulatory cytokines.
Acknowledgement: Supported in part by grants from the Deutsche Forschungsgemeinschaft (Re 653/5-1) and the Thuringian Ministry of Science, Research and Culture (B301-95026).

P006

Autoantibodies against oxidated low density lipoproteins (oLAb) and procalcitonin (PCT) as prognostic markers for patients suffering from sepsis and systemic inflammatory response syndrome (SIRS)

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Critical Care 1998, **2(Suppl 1):**P006

Objective: To investigate the role of lipidperoxidation and infection during acute sepsis we measured antoantibodies against oxidated LDL (oLAb) and procalcitonin (PCT) comparing the neopterin as a marker of macrophages activation and CRP as marker of inflammation.
Design: A prospective, descriptive cohort study.
Patients: 23 patients admitted to the ICU with verified sepsis (n=12, s=6) or SIRS (n=11, s = 6).
Measurements and results: The clinical severity of the disease was asessed using the APACHE II score over a period of 24 h after admission. Determination of serum levels of all parameters under study was performed on daily drawn serum samples. Surviving septic patients produced significantly increasing oLAbs (P < 0.001) as significantly decreasing PCT levels (P < 0.001). In contrast, in non-survivors oLAbs were decreasing (P < 0.05) and PCT levels were increasing (P < 0.05).
The identical effect was found for the SIRS group with the exception, that the significance of PCT in survivors was slightly lower (P < 0.05).
Conclusion: Despite both patient groups were rather small, we consider that the measurement of oLAb as well as PCT to be a useful prognostic marker concerning the outcome of sepsis as well as of SIRS patients.

P007

Endotoxin-induced adhesion of human red blood cells to vascular endothelium does not depend on the presence of leukocytes but is modified by different flow pattern

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Critical Care 1998, **2(Suppl 1):**P007

Introduction: Endotoxin-induced (ETX) adhesion of leucocytes to vascular endothelial cells is a well investigated phenomenon. However, little is known about the effects of endotoxin on erythrocyte-endothelial cell interactions . The objective of this study was to investigate the effects of ETX on adhesion of human red blood cells (RBC) to human vascular endothelial cells (HUVEC) in the presence or absence of leukocytes and under different conditions of flow.
Methods: Endothelial cells were obtained from human umbilical veins and cultured as first and second passage monolayers and then grown to complete confluency on cover slips. RBC were harvested from fresh blood donated by healthy volunteers, washed with isotonic NaCl and resuspended to a hematocrit of 30% in medium (M199, GIBCO, Canada). Group A (n = 7) served as a control, whereas in group B, C and D (n = 7 in each) both RBC and HUVECs were incubated with ETX (75 µg/ml) at 37°C for 2 h. In group E whole blood was incubated with ETX and thereafter RBC were isolated as described above. The HUVEC coated cover slips were placed in a flowing chamber and perfused with the RBC suspensions at a flow rate of 0.65 ml/min in group A, B and E and 1.3 ml/min in group C. In group D stop and go flow patterns found in the microcirculation of septic animals were mimicked by applying a flow rate of 0.65 ml/min with four stops (4–6 s) per minute. The flow chambers were arranged on a microscope and connected to a video recording system. In each experiment 15–20 sites of a defined area were recorded and analysed.
Results: The control group showed an adhesion of 71 ± 8 cells/mm^2. Incubation of HUVECs and RBC with ETX increased RBC adhesion in group B to 172 ± 25 cells/mm^2 (P < 0.05). Incubation of whole blood including leucocytes with ETX did not exhibit a different degree of adhesion compared to group B. When flow rate was elevated to 1.3 ml/min, the number of adherent RBC decreased to 89 ± 20/mm^2 comparable to the control group with a flow rate of 0.65 ml/min. In group D with intermittent stops of flow, RBC adhesion increased to 274 ± 35 cells/mm^2 (P < 0.05) compared to control, group B and group C.
Conclusion: Incubation of RBC and HUVECs with endotoxin promoted erythrocyte adhesion to human vascular endothelium. The presence of leukocytes during the endotoxin exposure did not affect the degree of adhesion. Elevating flow rate, however, reduced erythrocyte adhesion, while stop and go flow pattern favoured erythrocyte adhesion. These findings suggest that altered RBC may contribute to the microcirculatory injury observed in sepsis.

P008

Adhesion molecule, soluble adhesion molecule, and cytokine levels in patients with severe burns

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Critical Care 1998, **2(Suppl 1):**P008

Object: We measured endotoxins, inflammatory cytokines and soluble adhesion molecules in the blood of 17 severe burn patients to determine the involvement of these factors in the pathophysiology in burn patients.
Design: Prospective study.
Patients: Seventeen patients with burns with a total burn surface area of 20% or more and a burn index of 15% or more.
Measurement and main results: Endotoxin was measured by an endotoxin-specific assay. Tumor necrosis factor-α, interleukin 6 and interleukin 8 were measured by an enzyme-linked immunosorbent assay. Soluble adhesion molecules were also measured by an enzyme-linked immunosorbent assay. CD11a, CD11b, and CD18 were measured by a flow cytometry. Their levels were high in the non-surviving group, the septic shock group, and the multiple organ dysfunction syndrome group, suggesting the possibility of a close connection between them and the evolution of the pathophysiology in patients with burns complicated by infection (Table).
Conclusion: Soluble adhesion molecules were found to indirectly reflect the level of endothelial cell adhesion molecules, suggesting that inflammatory cytokines may also be involved as factors in their production.

Table (abstract P008). Comparisons of the factors in the sepsis group and the sepsis-free group

	Sepsis (-) (n=4)	Sepsis (+) (n=13)	P value
Endotoxin (pg/ml)	8.1 ± 10.1	12.5 ± 8.8	0.1630
TNF-α (pg/ml)	74.5 ± 58.7	638.1 ± 792.7	0.0151
IL-6 (pg/ml)	65.3 ± 112.4	754.9 ± 862.1	0.0346
IL-8 (pg/ml)	83.9 ± 11.7	280.9 ± 114.8	0.0168
sICAM-1 (ng/ml)	682.1 ± 291.3	924.6 ± 542.1	0.0362
sELAM-1 (ng/ml)	261.7 ± 23.0	342.1 ± 53.4	0.0101
sVCAM-1 (ng/ml)	1245.1 ± 422.6	3028.9 ± 1861.2	0.0438

P009

Circulating markers of endothelial activation in acetaminophen induced acute liver failure

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Critical Care 1998, **2(Suppl 1):**P009

Background: Once defined clinical criteria are fulfilled, survival following acetaminophen overdose is very poor without emergency liver transplantation. The early identification of patients developing multiple organ failure (MOF) is important for prompt listing for transplantation. MOF is associated with early elevations of the circulating markers of endothelial activation E-Selectin, VCAM-1 and ICAM-1 and Von Willebrand Factor (VWF). We determined their levels and those of Interleukin-6 (IL-6) on admission in acetaminophen overdose patients, to evaluate their use in the identification of those who would require transplantation.
Patients: Nine healthy controls and 20 patients were studied. Eleven patients became encephalopathic and seven patients either died or required emergency liver transplantation.
Methods: E-selectin, VCAM, ICAM, IL-6 and VWF were determined on admission using commercial ELISA. Statistical testing used Mann-Whitney U tests and Spearmans Rank correlation. Results were corrected for multiple testing.
Results: All molecules assayed were significantly higher in patients than controls ($P_c < 10^{-4}$). IL-6 alone was higher in non survivors than survivors [158 pg/ml (range 22–440) vs 32 pg/ml (3.5–177), $P_c < 0.05$]. Adhesion molecule levels were consistent with multiple organ failure of a non-septic aetiology. VWF was elevated in those patients who became encephalopathic : 371 U/dl (149–658) vs 178 U/dl (65–340), $P < 0.04$ and correlated strongly with mean arterial pressure ($r = 0.664$, $P < 0.005$).
Conclusions: ICAM, VCAM and E-selectin are poorly predictive of outcome in ALF, but suggest a non-septic aetiology of MOF. The pathogenesis of encephalopathy may involve endothelial activation and cardiovascular dysfunction. IL-6 appears the most useful early marker of a poor outcome in ALF.

P010

Circulating endothelial adhesion molecules in critically ill septic patients

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Critical Care 1998, **2(Suppl 1):**P010

Introduction: Recently it has been demonstrated the importance of the endothelium in the physiopathology of organ failure and death in experimental sepsis and soluble forms of adhesion molecules have been shown to be excellent markers of endothelial activation or even damage in this setting [1] But their definite role in clinical sepsis has not been clearly defined [2]. The objective of this study is to assess whether circulating concentrations of endothelial adhesion molecules [endothelial leukocyte adhesion molecule-1 (SLLAM-1) and intercellular adhesion molecule-1 (sICAM-1)] can be used to define, confirm or predict the outcome in critically ill septic patients.
Methods: Prospective, longitudinal, descriptive cohort study with no therapeutic interventions in which participated 63 patients admitted to the ICU with the clinical diagnosis of severe sepsis (21) or septic shock (42) [3] and 10 healthy adults that served as controls. Blood samples from and indwelling arterial catheter were collected from patients on days 1.3 and 7 after their admission to the ICU for measuring plasma concentrations of sELAM-1 and sICAM-1 (ELISA, R&D Systems). Additionally biological data (age, sex, APACHE II, blood leukocyte count, platelet count, coagulation, haemodynamic and blood gas variables, serum lactate levels, need of vassopressor support, culture results, SOFA score, individual organ dysfunction) and mortality were obtained. Statistical analysis was performed using Student t-test, Mann-Whitney U test. $P < 0.05$ was considered significant.
Results: Plasma levels of sELAM-1 and sICAM-1 on day 1 and 3 were significantly higher ($P < 0.001$) in septic patients than in controls. Patients with bacteremia had higher levels of ICAM-1 on day 1 ($P = 0.024$) and 3 ($P = 0.008$). Soluble levels of the molecules measured did not correlate with any other clinical or laboratory parameter at admission. With regard to outcome sELAM-1 on day 1 was significantly elevated in patients that developed coagulopathy and ICAM-1 on day 3 in those patients who developed shock ($P = 0.007$), acute renal failure ($P = 0.02$) or coagulopathy ($P = 0.05$). Both levels of sELAM-1 and ICAM-1 were similar in surviving and nonsurviving patients.
Conclusions: Plasma endothelial adhesion molecules concentrations are elevated in critically ill septic patients but their levels show a high degree of individual variation and have a poor global correlation with biological data and final outcome. sICAM-1 on day 3 might be useful for identifying the subgroup of patients who will develop multiorgan failure and therefore could benefit from a more agressive preventive or therapeutic approach.

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P011

Antibodies to ICAM-1 and PECAM-1 ameliorate pulmonary injury after intestinal ischemia-reperfusion in the rat

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Critical Care 1998, **2(Suppl 1):**P011

Full text: Intestinal ischemia-reperfusion (I/R) gives rise to acute lung injury characterized by neutrophil sequestration and microvascular injury. Important mediators of I/R-associated injury include neutrophils and platelet-activating factor (PAF). During conditions of inflammation neutrophils and endothelial cells show an increased expression of adhesion molecules. ICAM-1 on endothelial cells is needed for high affinity bonds between neutrophils and endothelial cells, necessary for the further transmigration of neutrophils, where PECAM-1 is involved.
In the present study, a significant increase in albumin leakage over the pulmonary capillaries, as well as increased pulmonary MPO (myeloperoxidase)-content was found in rats subjected to 30 min intestinal ischemia (by clamping the superior mesenteric artery) followed by 12 h reperfusion. Treatment with anti-ICAM-1 or anti-PECAM-1 monoclonal antibodies significantly reduced the otherwise occuring increase in both albumin leakage and pulmonary MPO-content in pancreatitis animals. There was also an increase in serum IL-1β levels after intestinal I/R, which could be prevented by use of antibodies to ICAM-1 and PECAM-1.
In conclusion we found that the acute lung injury seen after intestinal I/R in the rat to a large extent could be prevented by blocking the adhesion/transmigration process of pulmonary leukocytes.

P012

Lipid peroxidation parameters and antioxidant status of critically ill intensive care unit patients

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Critical Care 1998, **2(Suppl 1):**P012

Full text: Lipid peroxidation (LPO) is believed to play a crucial role in several disorders involving free radical action. Especially intensive care unit (ICU) patients suffer from situations, which lead to formation of free radicals and subsequent LPO, eg septicemia, multi organ failure or ischemic situations. Methods for the measurement of LPO products are usually restricted to specialists due to relatively complicated methodology. On the other hand, there is demand for routine methods to monitor LPO and/or antioxidative capacity of ICU patients. The scope of this study was to evaluate and compare some methods for the measurement of LPO products and

antioxidant capacity with special respect to therapeutic intervention and clinical outcome of the patients.
Ten consecutive ICU patients (2 female, 8 male) received daily antioxidant infusions including glutamine. Blood samples were drawn daily at 8:00 and 11:00 a.m. before onset of infusion therapy. After the end of infusion therapy, one sample was taken each day at 15:00 p.m. Each patient was monitored for 6 to 8 consecutive days. Plasma was obtained by centrifugation and was stored at -80°C until use. Malonic dialdehyde (MDA) was determined by HPLC and used as a reference method. Total antioxidant status (TAS, Randox, U.K.) was determined photometrically at 560 nm. Human antibodies against oxidised LDL (oLAb) were measured by ELISA (EliTec, Austria) in addition to our routine diagnostic program.
During the observation period, one patient (male, 39 years) died, while all others recovered. None of the three methods evaluated was clearly indicative for the fatal outcome, although trends could be observed. Out of more than 200 single determinations, less than 10% were within the normal range for MDA (<0.7 µmol/l)and TAS (1.3–1.77 mmol/l). Every third sample exceeded the normal range of MDA twofold (>1.4 µmol/l), and half of the samples gave antioxidant capacities of less than half of the normal range of TAS (<0.7 mmol/l). In samples taken after antioxidant therapy, there was a clear trend to higher TAS levels, but not high enough to strike the normal range. Concerning oLAb titres, compared with normal healthy subjects, we observed a significant trend towards lower titres, especially in septicemic patients.
These data convincingly support the hypothesis, that LPO is one very important factor in a great variety of disorders of ICU patients. Although none of the parameters evaluated was indicative for the fatal outcome of one patient, results obtained by these methods clearly showed the critical situation of these ICU patients and were to some extent indicative for therapeutical success. Due to their relative simplicity, TAS and oLAb can be adapted to routine laboratories with clinical chemistry and/or ELISA equipment. MDA measurement still requires a HPLC unit. From these results it is tempting to speculate upon importance of antioxidant therapies for the outcome of critically ill ICU patients, but further research is necessary to find clear and convincing solutions for that aspect.
Dedication: The authors dedicate this study to Prof. H. Esterbauer, who died in early 1997.

P013

CD64 upregulation on peripheral granulocytes is not a marker of sepsis and does not correlate with serum concentrations of granulocyte colony-stimulating factor (G-CSF) in postoperative/posttraumatic patients with severe sepsis

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Critical Care 1998, **2(Suppl 1):**P013

Purpose: To study whether the modulation of the expression of CD64 on the surface of neutrophils correlates with the inflammatory response and changes in serum concentrations of G-CSF in postoperative/posttraumatic patients with severe sepsis and septic shock.
Methods: Sixteen of these patients were studied upon admission to the intensive care unit (ICU) staying for more than 5 days. In these patients, a longitudinal analysis on the kinetics of leukocyte counts, the expression of CD64 and G-CSF serum concentrations was performed on a daily basis until discharge from the ICU. Surface expression was tested by flow cytometry using a Coulter Epics XL-MCL (Coulter Electronis, Krefeld, Germany). Results are expressed as a ratio between the mean channel value of the CD64-positive granulocyte fraction and the isotype control IgG_1, ie CD64/IgG_1.
Results: In all patients, CD64 was homogeneously expressed on all granulocytes. Six out of the 16 patients responded with an increase in CD64/IgG_1 > 2.5 following manifestation of an infectious focus. In the remaining 10 patients CD64/IgG_1 remained or declined below 2.5 and even below 1.5 despite bacterial infection, severe sepsis and septic shock. High expression of CD64-density (ratio > 2.5) occured incidentally with low serum concentrations of G-CSF (< 170 pg/ml) in individual patients and vice versa, i. e., low CD64 ratio < 1.5 and high G-CSF (up to 65,000 pg/ml). In a single patient with shock not due to infection, CD64/IgG_1 remained below 1.7, despite serum concentrations of G-CSF up to 2300 pg/ml. Serum concentrations of G-CSF did not correlate with the expression of CD64 (r = 0.02–0.61 for individual patients).
Conclusions: G-CSF has been proven a relevant hematopoietic factor to cope with acute inflammation and sepsis *in vivo*. CD64 expression has been suggested to indicate G-CSF serum activity and activation of neutrophils *in vivo*, and to serve as a marker of sepsis. The non-responsiveness of CD64 to G-CSF indicates that other factors must be involved and that active counterregulatory effects occur in patients with severe sepsis and septic shock. Thus, CD64 expression cannot serve as a longterm marker of sepsis.

P014

Selenium substitution in patients with severe systemic inflammatory response syndrome (SIRS)

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Critical Care 1998, **2(Suppl 1):**P014

Objective: To determine the effect of selenium substitution on morbidity and mortality in patients with systemic inflammatory response syndrome (SIRS).
Design: Controlled randomized prospective pilotstudy comparing patients with or without selenium substitution in an intensive care unit of an university hospital for internal medicine. 42 patients were included with SIRS due to infection and a minimal APACHE-II score of 15 points on the day of admission. The selenium substitution group (Se+) received sodiumselenite during 9 days (535 µg for 3 days, 285 µg for 3 days and 155 µg for 3 days) and thereafter 35 µg per day i.v. (Se+, n = 2), the control group (Se-) received 35 µg sodiumselenite throughout treatment period (Se-, n = 21).
Interventions: Morbidity and clinical outcome was monitored by scoring using the APACHE-III score, occurrence of acute renal failure, need and length of mechanical ventilation and hospital mortality. Blood samples on day 0, 3, 7 and 14 were analysed for serum selenium concentration and glutathion peroxidase activity.
Main results: The median APACHE-III score on admission, age, sex, underlying diseases, serum selenium levels and glutathion peroxidase activities on admission were identical in both groups. In Se+ patients serum selenium levels and glutathion peroxidase activity normalised within 3 days, whereas in controls both parameters remained low (P < 0.0001). APACHE-III score improved on days 7 and 14 in the Se+ group (P = 0.018). Hemofiltration of acute renal failure was necessary in 9 Se- compared to 3 Se+ patients (P = 0.035). Overall mortality in Se- group was 55 % versus 33.5 % in the Se+ group.
Conclusion: Selenium substitution in patients with SIRS improves clinical outcome and reduces the incidence of acute renal failure.

P015

Granulocyte colony-stimulating factor (G-CSF) enhances superoxide production in acute liver failure (ALF): an *in vivo* effect

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Critical Care 1998, **2(Suppl 1):**P015

Methods: The *in vitro* ability of G-CSF to improve neutrophil superoxide production has been previously demonstrated in ALF patients [1]. However, the *in vivo* effect on neutrophil function is unknown. Therefore G-CSF was given to three groups of ALF patients (n = 6) as a daily infusion at four different dosages (25, 50, 100 and 150 µg/m^2). Superoxide production was measured after fMLP stimulation, before and at 24 and 96 h.
Results: See table.
G-CSF significantly enhanced superoxide production at 96 h (P < 0.05). Furthermore, this effect was observed at doses below the standard therapeutic dose of 150 µg/m^2. Further studies are needed to determine the therapeutic value of G-CSF in the prevention and treatment of infection in ALF patients.

Table (abstract P015)

G-CSF	Hours after G-CSF infusion		
µg/m^2	0 h	24 h	96 h
25	221.4 (58.1)	267.9 (62.7)	382.7 (40.6)
50	308.1 (17.2)	339.3 (56.3)	592.0 (98.7)
100	231.5 (65.2)	225.9 (52.6)	317.5 (82.2)
150	217.4 (30.7)	357.0 (62.2)	358.4 (45.4)

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P016

Pulmonary injury after intestinal ischemia and reperfusion injury: effects of treatment with lexipafant, a PAF antagonist

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Critical Care 1998, **2(Suppl 1):**P016

Full text: Intestinal ischemia and reperfusion (I/R) can lead to the development of pulmonary injury characterized by increased leakage of macromolecules over pulmonary capillaries, and leukocyte sequestration. Important mediators of I/R-associated injury include polymorphonuclear granulocytes (PMNs) and platelet-activating factor (PAF). PMNs exposed to PAF demonstrate an increased expression of adhesion molecules, leading to increased PMN-endothelial cell interactions. Once adherent, PAF can further activate PMNs to increased respiratory burst activity and degranulation, leading to damage of the pulmonary endothelium. In the present study, we found an increased leakage of radiolabeled human serum albumin in the lungs of rats after 30 min intestinal ischemia (by clamping of the superior mesenteric artery) followed by 3 and 12 h reperfusion. The increased leakage could at least in part be prevented by lexipafant, a potent PAF-antagonist, administered intraperitoneally, after the onset of reperfusion. Pulmonary myeloperoxidase (MPO) content also increased after intestinal I/R, indicating PMN sequestration through the pulmonary endothelium. In conclusion, pulmonary injury in the rat, characterized by increased leakage of radiolabeled albumin over the endothelial barrier, correlated well with increased pulmonary MPO-content, implying the involvement of PMNs in the pathogenesis of remote organ injury after experimental intestinal I/R. Treatment with a PAF antagonist, lexipafant, decreased the severity of pulmonary damage. The potential clinical use of PAF-antagonists in I/R-associated pulmonary injury remains to be evaluated.

P017

Pentoxifylline in severe sepsis: a double-blind, randomized placebo-controlled study

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Full text: Pentoxifylline (POF) inhibits macrophage production of tumor necrosis factor alpha (TNF) as a central mediator in sepsis. To evaluate the therapeutic effect of POF in patients with sepsis a prospective, double-blind, placebo-controlled study in two centers (Lübeck, Kiel) was performed. 51 patients were included and randomized to receive POF continuously (1 mg/kg bw/h i.v.) or saline solution as placebo over 28 days maximally or until patients were discharged from ICU or died. Bioactivity of TNF and interleukin (IL)-6, MOF-score according to Goris as well as organ function were determined at diagnosis, daily from day 1 to 7, on day 10, 14, 17, 21, 24 and 28 after diagnosis of sepsis. There were no differences in patients characteristics at diagnosis concerning APACHE II score [17 ± 4 (mean ± SD)] for POF and 18 ± 5 points for placebo), MOF-score (10.5 vs 10.7) or organ function. At study entrance 23 of 27 patients in the POF-group and 21/24 in the placebo-group had septic shock. No adverse effects of POF-treatment were observed. The 28 day mortality rate was 30% (8/27) in POF treated patients and 33% (8/24) in the control group. Hospital mortality was 41% (11/27) and 54% (13/24). Serum concentrations of TNF and IL-6 were not significantly different throughout the evaluation. MOF-score was lower in POF treated patients after day 4 compared to placebo treated patients which reached significant differences on day 14 and 21 ($P < 0.05$, unpaired t-test). $PaO_2/FioO_2$-ratio was significantly improved in POF treated patients from day 10 (266 ± 132) to day 21 (346 ± 142) compared to the placebo group (201 ± 161 vs 221 ± 112, $P < 0.05$ and $P < 0.01$ on day 14 and 17). Pressure-adjusted heart rate (HR×CVP/MAP) was significantly improved from day 6 to day 10 ($P < 0.05$) in patients treated with POF compared to the control group. A multi-center trial is needed to evaluate the efficacy in improving organ function and outcome in severe sepsis.

P018

Treatment of severe sepsis in patients with highly elevated IL-6 levels with anti-TNF monoclonal antibody MAK 195F: The Ramses study

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Critical Care 1998, **2(Suppl 1):**P018

Full text: This prospective placebo-controlled double-blind clinical study investigated the efficacy of the monoclonal anti-TNF antibody MAK 195F (Afelimomab) compared to placebo in patients suffering from severe sepsis and septic shock with highly elevated IL-6 levels. Patients were stratified at entry into the trial by a semi-quantitative rapid stick test into those with IL-6 serum levels and below 1000 pg/ml serum. High IL-6 patients were randomised to receive either MAK 195F as 9 single doses for 1 mg/kg in 8 h intervals or placebo as additive treatment and followed for 28 days. Low IL-6 patients were not randomised and only followed for survival.
Altogether 944 patients were enrolled into the study before the trial was stopped prematurely. This early termination was based on the results of a planned interim analysis which releaved that it was very unlikely that the study would finally end up with a positive result when completed as planned. From those 944 patients 446 were stratified to be randomised, 224 received MAK 195F and 222 received placebo, 498 patients were not randomised. Mortality rates in the randomised patients was 57.7% in the placebo-treated group and 54.0% in the MAK-treated group. The mortality rate in the non-radomised patients was 39.6%. Whereas the mortality difference between the two randomised patient groups did not reach statistical significance, the difference between the randomised and non-randomised patients was highly statistically significant ($P < 0.001$).
In conclusion, this study demonstrated that the innovative IL-6 rapid stick used to stratify the study patients was a powerful tool to identify patients with a high mortality risk in sepsis. However, the study failed to proof the efficacy of MAK 195F to reduce mortality in septic patients with highly elevated IL-6 levels. A similar study is currently still ongoing in North-America.
Acknowledgement: This study was supported by Knoll AG, Ludwigshafen, Germany

P019

C1-Inhibitor substitution as ultima ratio therapy in septic shock: experience with 15 patients

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Critical Care 1998, **2(Suppl 1):**P019

Introduction: Plasma C1-Inhibitor (C1-INH) is the major inhibitor of both the classical pathway of complement system and contact activation. A relative deficiency of C1-INH has been proposed as an important contributor to the development of shock and organ failure [1,2]. Among others, our working group has published two cases of successful C1-INH substitution in septic patients recently [3].
Methods: In a retrospective study we investigated data of 15 patients with septic shock who received C1-INH concentrate as ultima ratio therapy. The mean substitutional dosage of C1-INH concentrate (Berinert HS', Centeon) was 10.300 units. Mean values for C1-INH activity, antigenic C1-INH level, fluid balance, hemodynamic and respiratory parameters were compared 24 h prior to 96 h after C1-INH administration.

Results: After substitutional therapy the antigenic C1-INH level increased significantly (from 159 to 228%) while the functional C1-INH activity did not change statistically. The daily fluid balance decreased from +2695 to -186 ml/24 h (P = 0.05), hemodynamic parameters were not affected. There was a good tendency towards higher arterial-to-inspired oxygen ratios (P = 0.55) after C1-INH administration.
Conclusion: Our data show significantly higher antigenic C1-INH levels after substitutional therapy but no difference in C1-INH functional activity. This may be due to complex formation of C1-INH with its target proteases. Prior to C1-INH administration the patients had positive fluid balances and impaired arterial-to-inspired oxygen ratios. If This is looked upon as an equivalent to capillary leakage these results encourage to perform a randomised controlled study on C1-INH substitution in septic patients.

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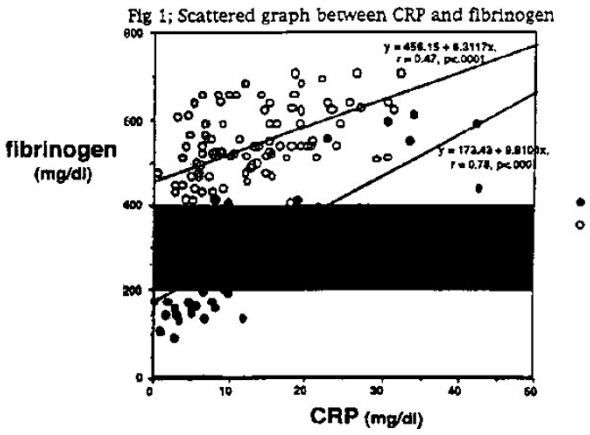

Figure 1 (abstract P021) Scattered graph between CRP and fibrinogen.

P020

Increased monocyte activation and tissue factor expression in patients with sepsis

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Background: Tissue factor (TF) is believed to play an important role in the initiation of intravascular coagulation. Accumulating evidence has been provided that TF expression in monocytes may determine disturbances in intravascular coagulation and outcome in sepsis. A direct proof of an increased monocyte TF activity and/or antigen in septic patients is still lacking.
Patients and methods: 47 patients treated in the Intensive Care Unit of an university hospital were included in the study. Sepsis and the degree of organ dysfunction were assessed according to the criteria of the ACCP/SCCM Consensus Conference and the SOFA score. Blood samples from an arterial catheter were anticoagulated with sodium citrate. Binding to monocytes of FITC-labelled monoclonal antibodies against TF and CD11b was determined by flowcytometry.
Results: Compared to non-septic patients (n = 20) monocytes of septic patients (n = 27) bound significantly higher amounts of anti- TF antibody (mean fluorescence intensity - MFI: 14.3 ± 3.3 vs. 18.9 ± 6.4; P < 0.01). The same was true for binding of the antibody against the activation-dependent antigen CD11b. MFI in non-septic patients amounted to 266 ± 72 and in septic patients 335 ± 86 (P < 0.005). Using a non-parametric analysis we found significant correlation between anti-TF and anti-CD11b binding (P < 0.03) as well as between SOFA Score and anti-CD11b or anti-TF binding (P < 0.03 and 0.02, respectively).
Conclusion: The results indicate that monocytes in septic patients are on a higher activation level and have higher amounts of TF antigen when compared to non-septic ICU patients. Thus, the study confirmed the proposed role of monocyte TF expression for sepsis-associated activation of coagulation.

P021

Significance of the changes in blood fibrinogen levels as an acute phase reactant in septic DIC

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Critical Care 1998, **2(Suppl 1):**P021

Background: Although treatment of DIC is said to be more effective when it is started at early stage, early diagnosis of DIC occurring in surgical infectious SIRS (Septic DIC) is difficult because in these cases decrease in blood fibrinogen levels rarely occurs and the magnitude of elevation of blood FDP is usually small. In the present study, we had observed the changes in blood fibrinogen production in the liver and also we investigated the correlation between the blood levels of other acute phase reactant and IL-6.
Patients and method: Blood was withdrawn from 18 septic DIC cases and 20 non-DIC infectious SIRS cases at 4 points (the day of DIC diagnosis, next day, the 3rd day and the 5th day). The blood samples are analyzed for IL-6, C-reactive protein (CRP) fibrinogen, Thrombin antithrombin III complex (TAT), α2-Plasmin inhibitor-plasmin complex (PIC) and D-Dimer.
Results: 1. There was a significant correlation between CRP and IL-6 (r = 0.73, P < 0.0001) in septic DIC cases. 2. Although fibrinogen did not significantly correlate with IL-6 (r = 0.027, P < 0.84), there was a significant correlation between CRP and fibrinogen (r = 0.55, P < 0.0001) in septic DIC cases. 3. We could also observe a significant correlation between CRP and fibrinogen (r = 0.78, P < 0.0001) in non-DIC infectious SIRS cases. 4. A scattered graph was made between CRP and fibrinogen in septic DIC cases and non-DIC infectious SIRS cases (Fig. 1). While blood fibrinogen in the half of septic DIC cases, its values were lower than those in non-DIC infectious SIRS cases when patient of both group had same CRP.
Discussion: From these data, we can predict fibrinogen level in correspondence with blood CRP in individual SIRS cases. When measured fibrinogen was lower than this level, we could identify the pathophysiological state in which fibrinogen was consumed (hypercoagulation). And this would lead to early diagnosis and evaluation of severity of the septic DIC.

P022

Coagulation and fibrinolysis after head injury

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Critical Care 1998, **2(Suppl 1):**P022

Introduction: It is believed that abnormal coagulation and fibrinolysis is a frequent complication in patients with head injury, and this abnormality is initiated by the released of thromboplastin (tissue factor) from damaged brain. But some authors [1,2] reported that the activation of coagulation and fibrinolysis after head injury is not the specific phenomenon comparing with the population of trauma victim. Recently, we have been able to measure some molecular markers of coagulation and fibrinolysis system in clinical setting. We compared coagulation and fibrinolysis activity of trauma and head injury patients using the molecular markers.
Materials and methods: Blood samples were collected in 1, 3 and 5 days after onset from 31 trauma patients (TR) (patients with

Table (abstract P022)

	TR	HI	CVD
numbers of pt.	31	12	27
day	2.7 ± 0.3	2.5 ± 0.6	3.3 ± 0.4
TAT	84.1 ± 13.8*	77.7 ± 31.2	28.7 ± 7.4*
PIC	3 ± 0.4	4.2 ± 2.1	2.7 ± 0.5
D dimer	20.8 ± 2.7*	19.1 ± 5.3	6.9 ± 1.1*
PAI-1	30.6 ± 3.1*	30.7 ± 5.4	17.3 ± 1.4*
tPAI-C	19.7 ± 1.8	20.3 ± 3.8	19.2 ± 1.8
cTM	29.9 ± 2.8	25.9 ± 2.4	28.2 ± 1.4
PCA	84.2 ± 3.0*	83.6 ± 5.5	99.5 ± 3.2*

(mean ± SE; *$P < 0.05$, TR vs CVD)

head-Abbreviated Injury Score (AIS) = 3 were excluded), 12 head injury (HI) patients (patients with other system AIS = 3 were excluded) and 27 cerebrovascular disease patients (CVD) (patients with intracranial hemorrhage or subarachnoid hemorrhage), and thrombin-antithrombin III complex (TAT), a 2 plasmin inhibitor plasmin complex (PIC), D-dimer, plasminogen activator inhibitor (PAI-1), tissue plasminogen activator (tPA)-PAI-I complex (tPAI-C), thrombomodulin (TM) and protein C activity (PCA) were measured.

Results: PCA and PAI- I on 1 day had good correlation with injury severity score (ISS). TAT, D-dimer and PAI-1 of TR were significantly ($P < 0.05$) higher than those of CVD, and PCA of TR were significantly lower than those of CVD, but there were no difference between TR and HI.

Conclusions: HI and TR had significantly activation of coagulation and fibrinolysis compared with CVD, but there were no evidence that HI had significantly activation of coagulation and fibrinolysis compared with TR.

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P023

Close relationship of PAI-1 (plasminogen activator inhibitor-1) with multiple organ dysfunction syndrome and abnormal glucose metabolism investigated by means of artificial pancreas

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Critical Care 1998, **2(Suppl 1):**P023

Background: There are many reports in recent years that the PAI-I is related to cardiovascular diseases and glucose intolerance especially in diabetic patients. But the role of role of PAI-1 to organ dysfunction and glucose in acutely ill patients is not clearly analysed. We invesigated the contribution of coagulopathy including abnormal PAI-1 level to organ dysfunction and to abnormal glucose metabolism in serious patients by means of the bedside type artificial pancreas (AP).

Materials and methods: Thirty-five serious patients with glucose intolerance, consisting of 25 males and 10 females aged from 23 years to 75 years, were investigated. Primary diseases were as follows: 12 patients with pneumonia, seven with abdominal diseases treated by surgery, six with acute pancreatitis, three with hepatobiliary disorders, two with diabetic foot, and five with other diseases. Analysed items were, 1) regarding multiple organ failure (MOF), MOFscore (calculated from the MOF criteria of Japanese Association for Critical Care Medicine), 2) regarding glucose metabolism, (a) M value (mg/kg per min: measured by the euglycemic hyperinsulinemic glucose clamp method with AP. The clamped blood glucose level was 80 mg/dl with the insulin infusion rate of 1.12 mU/kg per min) as an indicator of peripheral glucose tolerance, (b) MCRI (ml/kg per min: metabolic clearance rate of insulin: measured by the glucose clamp method) as an indicator of insulin metabolic rate, 3) regarding coagulation and fibrinolysis, (a) DIC (disseminated intravascular coagulation) score calculated from the DIC criteria of the Ministry of Health and Wealth of Japan, (b) PAI-I, (c) tPA-PAI (tissue plasminogen activator-PAI-1 complex), (d) FDP, (e) anti-thrombin III, (f) D-dimer, (g) PIC, (h) TAT, (i) plasminogen, (j) protein-C, 4) TM (thrombomodulin) as a parameter of endothelial cell injury, and 5) serum fat (free fatty acid (FFA), triglyceride, cholsterol). AP used was STG-22, made by NIKKISOH Corp. in Japan.

Results: There were correlations between the following parameters. 1) Between MOF and other parameters; positive correlation between DICscore and MOFscore ($y = 0.533x + 2.70$, $n = 26$, $r^2 = 0.705$), MOFscore and PAI-I ($y = 0.00996x + 0.588$, $n = 14$, $r^2 = 0.282$), MOFscore and tPA-PAI ($n = 15$, $r^2 = 0.239$), 2) between PAI-I or tPA-PAI and other parameters; (a) negative correlation between tPA-PAI and M value ($y = -17.4x + 98.9$, $n = 13$, $r^2 = 0.665$), b) positive correlation between PAI-I and MCRI ($y = 16.4x-108$, $n = 8$, $r^2 = 0.532$), tPA-PAI and MCRI ($n = 8$, $r^2 = 0354$), TM and PAI-1 ($y = 0.0155x + 2.55$, $n = 13$, $r^2 = 0.635$), TM and tPA-PAI ($n = 14$, $r^2 = 0.660$), FFA and PAI-1 ($y = 0.000490x + 0.144$, $n = 10$, $r^2 = 0.477$), FFA and tPA-PAI ($n = 11$, $r^2 = 0.429$). Other parameters but PAI-I and tPA-PAI related to coagulopathy showed no definite relationships with MOFscore, M value, MCRI, TM and FFA

Conclusion: Multiple organ dysfunction syndrome, glucose intolerance, and increased insulin metabolism were revealed to be closely related to increased PAI-I or tPA-PAI, which reflect decreased fibrinolysis. Injury of endothelium and increased serum FFA level were thought to be related to increased PAI-I and tPA-PAI, which may explain the progression of MOF partly. In addition, PAI-1 and tPA-PAI seemed to be sensitive marker of, and might be one of the risk factors of multiple organ dysfunction syndrome and nutritional metabolic disorder.

P024

Use of antithrombin III in cancer patients with sepsis complicated with disseminated intravascular coagulopathy

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Introduction: Mortality rate from sepsis is estimated to be 20% to 60% with disseminated intravascular coagulation (DIC) often accompanying sepsis. Replacement therapy with antithrombin III (ATIII) concentrate has been hypothesized to be a means for attenuating DIC, since ATIII is rapidly consumed during DIC. A reliable index of poor prognosis is an initial decrease of serum ATIII level. The purpose of this pilot study was to evaluate the effects of the administration of ATIII in patients sepsis complicated by DIC.

Materials: All adult patients admitted to the surgical intensive care unit at the University of Texas M.D. Anderson Cancer Center with clinical evidence of sepsis and DIC were eligible for inclusion. Exclusion criteria consisted of leukemia and treatment with heparin. Patients received 100 units/kg of ideal body weight of antithrombin III (Thrombate III®) at time zero, repeated 12 h later, and daily for three days. Serum ATIII levels were drawn prior to enrollment, prior to and after each dose, and for 2 days after the last dose. Levels were analyzed at the conclusion of the study. No other intervention was provided by the investigators. Patients were otherwise managed by their primary care providers and consultants as their clinical situation warranted.

Results: The study population included 4 women and 1 man with an average age of 59.6 years (33–84). Severity of illness was measured by a mean APACHE II of 21.8 (19–24) and a mean TISS of 55.6 (45–70) at the time of study enrollment. The ICU and hospital mortality rate were 80%, with one patient not surviving to complete the study regimen. Serum ATIII levels at the time of enrollment ranged from 22 to 78 MUI/ml, averaging 45.4 (normal 80–120). The one surviving patient had the highest ATIII level (78 MUI/ml) prior to study enrollment. A rise in ATIII levels after treatment was found in each patient, with all but one patient having levels normal or supranormal after the first dose of treatment. One patient, with the lowest pretreatment level (22 MUI/ml), had levels that remained below normal during most of treatment and was decreased (51 MUI/ml) at day 2 post treatment.

Conclusions: We have found a variable response in ATIII levels in patients with sepsis after ATIII treatment. Future studies involving ATIII replacement should include the use of ATIII levels to guide dosing regimens.

P025

Effect of antithrombin III on inflammatory immune response in patients with severe sepsis

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Critical Care 1998, **2(Suppl 1):**P025

Full text: Antithrombin III (AT III) is an important inhibitor of thrombin activity, as well as of many other proteases of the coagulation system. AT III administration showed beneficial effects on septic multiple organ dysfunction in clinical and experimental studies. It was the aim of this study to determine whether continuous long-term AT III supplementation alters the systemic inflammatory response in patients with severe sepsis. In a prospective study 29 surgical patients with severe sepsis were randomly assigned to receive either conventional intensive care treatment (n = 15, control group) or additional AT III supplementation with a plasma AT III activity >120% during a fourteen day study period (n = 14, AT III group). Plasma Interleukin (IL)-6 and IL-8, and the circulating adhesion molecules ICAM-1 and soluble E-selectin, as well as PMN elastase were determined daily by ELISA. Total leukocyte count and C-reactive protein (CRP) were measured daily and body temperature was registered. Compared to control patients, a downregulation of plasma IL-6, and, to a lesser degree, also of plasma IL-8 was observed in the AT III group ($P < 0.05$). AT III supplementation prevented the continuous increase in ICAM-1 plasma concentration observed in control patients and lead to a significant fall in serum soluble E-selectin and in CRP concentration ($P < 0.05$). This fall corresponded to a downregulation of body temperature over time ($P < 0.05$). There was no AT III effect on PMN elastase concentration or total leukocyte count. Our results show that long-term antithrombin III supplementation attenuates the systemic inflammatory response in patients with severe sepsis.

P026

Release of endothelin in an experimental model of shock and ARDS in sheep

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Critical Care 1998, **2(Suppl 1):**P026

Objectives: The Endothelins (ETs) are a class of 21 amino-acid peptides, which were first described in 1988 as vasoactive peptides produced in the endothelial cells of the porcine aorta. Meanwhile three different subtypes have been identified. ETs act as potential vasocontrictors in the cardiovascular system. In the lungs, ETs induce bronchospasm and via vasoconstriction pulmonary hypertension followed by severe edema formation. It is well known, that ETs are synthesized and present in the lung. Additionally a high number of ET-receptors has been identifed in the lung. Recent studies show elevated ET-plasma concentration in various diseases like cardiogenic shock, subarachnoidal bleeding, COPD, sepsis and trauma. This study was performed to evaluate the ET-plasma concentration after induced hypovolemic shock states and ARDS.
Methods: The experiment was performed in 14 anesthesized, and mechanically ventilated sheep (21–28 kg BW) during two different consecutive shock models (A: 3.5% BW ultrafiltrate withdrawal by hemofiltration; B: Blood withdrawal up to 3.5% of BW) and after lung lavage induced ARDS. A 4 F catheter was placed in the A. carotis to obtain blood pressure. Cardiac output was determinated by a 7.5 F fiberoptic thermodilution catheter placed into the main pulmonary artery. Blood samples from the A. carotis (CAR) and the A. pulmonalis (PUL) and urine samples were taken at baseline, 15 min after hemofiltration, 15 min after blood withdrawal and 5, 20, 60 min after lung lavage. ET-concentrations were measured by RIA (Nichols, Bad Homburg, FRG). Transpulmonary flux was calculated by the equation: (ET - concentration [A. pulmonalis] - [A. carotis])/cardiac output. Statistical analysis was performed using Wilcoxon sign rank test.
Results: A significant increase of plasma-ET concentrations from baseline levels in the A. carotis and A. pulmonalis (CAR 7.89 ± 3.9 µg/ml; PUL 8.22 ± 4.1 µg/ml) was observed during hypovolemia with ultrafiltration (CAR 14.9 ± 7.8 µg/ml, $P < 0.01$; PUL 15.4 ± 7.1 µg/ml, $P < 0.01$), and during hypovolemia with blood-withdrawal (CAR 14.4 ± 6.6 µg/ml, $P < 0.01$; PUL 13.6 ± 6.4 µg/ml, $P < 0.01$), and 60 min after ARDS (CAR 10.6 ± 5.0 µg/ml, $P < 0.05$). No significant difference was found between plasma-ET concentration in CAR and PUL at any state. Urine-ET concentration showed a slight, but not significant increase after ARDS, but no alterations in hypovolemic states. Flux calculation did not indicate significant changes.
Conclusion: The presented data show a significant increase in plasma-ET concentration after induced hypovolemic shock. It can be speculated that the potential vasoconstrictory effects of ETs act as a paracrine regulator of vascular tone. In contrast to other studies we could not find a significant change in the early state of induced ARDS. In a saline lavage model desquamation of bronchial and bronchialar epithelium, hyaline membranes and accumulations of pyknotic cells in peterminal airspaces can be observed. These pathological changes may explain the lack of an early response due to partial destruction of endothelium cells.

P027

Effect of interleukin-6 and interleukin-10 on nitric oxide production by endothelial cells

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Critical Care 1998, **2(Suppl 1):**P027

Introduction: Nitric oxide (NO) is synthesised from conversion of L-arginine to citrulline by NO-synthase (NOS). NO mediates vascular dilation, muscle relaxation and platelet aggregation. Constitutive NOS (cNOS) exists in endothelial cells but not in vascular smooth muscle. Among others the cytokines IL-6 and IL-10 can be measured in high concentrations during sepsis. IL-10 has an inhibitory effect on the NO synthesis in LPS stimulated macrophages by inhibiting NOS. Recently, IL-10 have been reported to have a stimulatory effect on the NO production by endothelial cells in human saphenous veins in a concentration dependent way.
Aim: To investigate the *in vitro* effect of IL-10 and IL-6 on NO production by endothelial cells in human saphenous veins.
Methods: Human saphenous veins from patients undergoing CPB were used. The vessels were suspended in phosphate buffered saline (PBS) with the endothelial side up. The tip of the amperometic probe was positioned 10 µm above the cell surface. Concentrations of the NO gas in the PBS solution were measured in real time with a DUO 18 computer data acquisition.
Results: The vessels were exposed to IL-10 (10^{-8} M), IL-6 (10^{-6} M) anti-IL-6 ($l0^{-6}$ M) alone or in combination. IL-10 increased the NO production by the endothelial cells. IL-6 on its own did not affect the NO production. When IL-6 was added minutes following the IL-10 administration, it diminished the IL-10 induced NO release. Anti-IL-6 did not have any influence on the NO production, but the IL-6 inhibition of IL-10 stimulated NO release, was blocked when anti IL-6 was added.
Conclusion: These results show that IL-10 stimulate NO release from endothelial cells. Addition of IL-6 can attenuate the effect of IL-10 on endothelial cells.

P028

Effects of nitric oxide (NO) on platelets in neonates

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Critical Care 1998, **2(Suppl 1):**P028

Full text: Nitric oxide (NO) is known to play a crucial role in primary hemostasis due to its platelet-inhibitory properties. To investigate the effects of NO on neonatal platelets, umbilical cord blood from 10 healthy term neonates was obtained immediately after birth. Blood samples from both the mothers and non-pregnant female blood donors (n = 10) were analyzed in parallel as controls. Citrated platelet rich plasma was incubated with the NO-donor SIN-1 (10 µM), an active metabolite of molsidomine, prior to activation with 10 µM adenosine-diphosphate (ADP) or 0.05 U/ml human α-thrombin (both ED_{50}), or with agonists or buffer only. Platelet activation

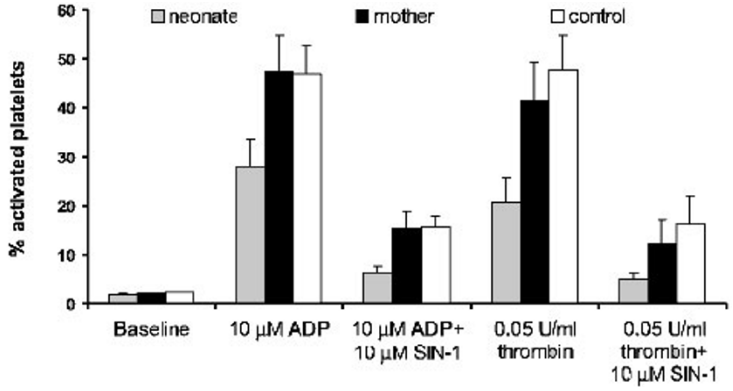

Figure (abstract P028) Effects of SIN-1 on GPIIb-IIIa activation in platelets from cord blood (neonate), mother and female control, activated with ADP or thrombin.

was analyzed in a two-color flow cytometry assay using phycoerythrine (PE) or fluoresceine-isothiocyanate (FITC) conjugated monoclonal antibodies directed against glycoprotein-(GP)-Ib (CD42b) and activated fibrinogen receptor GPIIb-IIIa (PAC-1), respectively. No significant differences for PAC-1 binding to resting platelets (baseline) was observed between neonate, mother or control, indicating absence of pregnancy- or delivery-induced activation of circulating platelets (see figure). No significant differences of platelet response to ADP or thrombin were found between controls and mothers, indicating normal platelet response of the mother. Compared to both the mother and control, neonatal GPIIb-IIIa activation was significantly ($P < 0.05$) depressed, ie newborn platelets revealed hyporeactivity to ADP and thrombin. NO significantly ($P = 0.001$) inhibited GPIIb-IIIa activation in all groups, however, percentual downregulation of GPIIb-IIIa-exposure was not significantly different in newborns, mothers, or controls (ca. 70 ± 5%). This demonstrates depressed response of neonatal platelets to agonists, but normal reaction to platelet inhibitory compounds such as NO. Since newborn platelets are starting from a lower level of activation, NO nearly diminished platelet activation. This might be of clinical relevance, since hemorrhagic complications remain a serious problem in critically ill term neonates, or even more in premature newborns. Several studies showed reduced platelet function in both healthy volunteers and patients with adult respiratory distress syndrome (ARDS) during inhalation of gaseous NO. NO-inhalation is well established in the pediatric ICU for treatment of infant respiratory distress syndrome (IRDS) or persistent pulmonary hypertension. The presented data indicate that inhalation of NO might be an additional risk-factor for bleeding complications in critically ill neonates.

Acknowledgement: Supported by Deutsche Forschungsgemeinschaft DFG Fa 139/4-2

P029

Nitric oxide (NO) metabolite levels are not increased during hypotensive periods in human sepsis

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Critical Care 1998, **2(Suppl 1):**P029

Purpose: Excess NO production has been proposed to cause the hemodynamic derangements of septic shock. This study was undertaken to determine whether serum NO metabolite levels correlate with hemodynamic changes in human sepsis.

Methods: A 12-month prospective study of surgical ICU patients with SIRS, sepsis, severe sepsis or septic shock was undertaken. Serum NO_2/NO_3 levels were determined by chemiluminescence from blood drawn during blood culture acquisition or hypotension (SBP <90 mmHg), then daily for 7 days or until ICU discharge or death. The following were collected: vital signs, pulmonary artery catheter data, white blood cell count (WBC) and arterial base deficit (BD). T-test analysis compared NO_2/NO_3 levels in hypotensive and normotensive patients. Pearson correlation coefficients were determined for NO_2/NO_3 and the variables above. Data are mean ± SEM; $P < 0.05$ defined significance.

Results: NO_2/NO_3 levels were 12.2 ± 3.8 pmol/µl in 13 hypotensive vs 12.7 ± 2.0 in 9 normotensive patients (NS). Correlation coefficients (r^2) are depicted:

Conclusions: NO metabolite levels are not different in hypotensive and normotensive septic patients. There is poor correlation between NO metabolite levels and physiologic changes in human sepsis. Further study regarding the role of NO as the principal vasodilator in sepsis is warranted.

Table (abstract P029)

	SBP	P	CI	SVO_2	SVR	WBC	BD
NO_2/NO_3	0.04	0.01	0.10	0.16	0.05	0.09	0.04

P030

Serum TNF alpha and IL-8 levels in difficult weaning patients

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Critical Care 1998, **2(Suppl 1):**P030

Introduction: Metabolic status and severity of illness play important role in developing ventilatory dependency during long term ventilatory support in critically ill patients. The aim of the study was to evaluate TNFα and IL-8 serum levels during weaning from long term ventilatory support.

Methods: After institutional approval 26 critically ill patients were prospectively studied during ventilatory support and weaning. All patients were weaned according to standard weaning protocol. Blood samples were drawn daily and collected until analysis. Apache II score, ventilatory days and 'weaning' days were recorded. After successful weaning patients were divided in two groups according to the length of weaning (W): group S (W ≤ 3 days, $n = 6$), group L (W ≤ 3 days, $n = 20$). TNFα and IL-8 serum levels were selected and measured at the time of admission (T1), on the last day of full ventilatory support (T2), on the day when weaning was started (T3) and on the first day after 24 h of spontaneous ventilation (T4). Values are expressed as a mean ± SD, *t*-test or Mann Whitney Rank Sum test where appropriate were used for statistical analysis (Sigma Stat Statistical Software, Jandel Co., USA), $P < 0.05$ was considered statistically significant.

Results: Total ventilatory and weaning days were 24.1 ± 11, resp. 7.5 ± 3 in group L and 10.7 ± 4.6 resp. 2.6 ± 1.7 in group S. Selected results of TNFα (in pg/ml) and IL-8 (in pg/ml) are presented in the table.

Table (abstract P030)

		T1	T2	T3	T4
Group S	TNFα	10.8 ± 5.59	10.6 ± 9.52	6.42 ± 7.11	0*
Group L	TNFα	11.7 ± 7.67	12.6 ± 5.6	7.8 ± 5.9	7.15 ± 6.04*
Group S	IL-8	55.2 ± 33.3	65.8 ± 37.2	47.3 ± 42.0	6.32 ± 10.8*
Group L	IL-8	205.2 ± 356.8	89.9 ± 101.6	73.8 ± 100.4	38.7 ± 27.6*

*$P < 0.05$

Discussion: Serum TNFα and IL-8 levels were persistent in patients with prolonged ventilatory support. This suggests that these mediators may also be involved in ventilatory failure leading to difficult weaning after long term mechanical ventilation.
Acknowledgement: Supported by grant IGA MZ CR 3674-3.

P031

Matrix metalloproteinase-1, soluble Fas ligand, and soluble Fas antigen levels in patients with multiple organ dysfunction syndrome

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Critical Care 1998, **2(Suppl 1):**P031

Full text: Fas L induces apoptosis by binding to Fas. It is reported that the extracellular matrix degrading enzyme, metalloproteinase, is involved in conversion from membrane Fas L to soluble Fas (sFas).
In this study, the involvement of matrix metalloproteinase-1 (MMP-1), soluble Fas ligand (sFasL), and soluble Fas antigen (sFas) in apoptosis at the onset of multiple organ dysfunction syndrome (MODS) was examined. The subjects were 52 patients. Blood sampling was continued from the time before or at the onset of MODS up to its recovery or death. MMP-1, the tissue inhibitor of metalloproteinase-1 (TIMP-1), MMP-1/TIMP-1 complex, sFas L, sFas, tumor necrosis factor-α (TNF-α), TNF receptor I (TNFR I), TNFR II, nitrite/nitrate (NOx), transforming growth factor β (TGF-β), and endotoxin were measured.
With the increase in dysfunctional organs, sFas, TNF-α, and NOx increased, and showed significantly higher levels in those that died than in the survivors. Their levels were significantly correlated with the MMP-1 level, and the MMP-1 level was negatively correlated with the TGF-β level. At the onset of MODS, the sFas, TNF-α, and NOx levels were high, suggesting that apoptosis occurred. It was also suggested that MMP-1 was involved in sFas and TNF-α production, and TGF-β suppressed MMP-1 production.

P032

Endothelium activation during prolonged extra-corporeal circulation

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Critical Care 1998, **2(Suppl 1):**P032

Objectives: The aim of this study was to monitor the plasma levels of soluble adhesion molecules in patients undergoing cardiac surgery in extracorporeal circulation (EC). We investigated the relationships between the levels of adhesins released during the prolonged extracorporeal circulation and postoperative morbidity.
Study design: We assessed 10 patients (NYHA class II or III) undergoing elective cardiac surgery with flat-sheet membrane oxygenation. The procedures were: coronary artery bypass grafting, cardiac valve implantation or both. The duration of CPB was 135–246 min, core temperature 28–31°C. The patient statuses were assessed daily with SOFA and Marshall MODS scores. The soluble vascular cell adhesion molecule (sVCAM-1), soluble intercellular adhesion molecule (sICAM-1), soluble endothelial leukocyte adhesion molecule (sELAM-1), lactate levels and WBC were measured before induction of anaesthesia, during EC, one and two days after operation.
Materials and methods: Arterial blood samples were collected on heparin. Plasma was immediately obtained by centrifugation and then frozen at -70°C until the assay was performed. Activity of sVCAM-1, sICAM-1 and sELAM-1 was measured using enzyme- linked immunoabsorbent assays (ELISA).
Results: The plasma concentrations of sVCAM-1 were significantly higher during the entire study (mean 954.38, 818.60, 1291.09, 1264.09 ng/ml). In four patients who developed postoperative multiple organ dysfunction failure the sVCAM-1 were significantly higher than in those with uneventful recovery. sICAM-1 levels after operation were above the normal range (mean 272.88, 236.97, 294.64, 410.52 ng/ml). There was no significant differences in plasma sELAM-1 levels during the whole time of observation (mean 43.07, 29.45, 48.57, 49.18 ng/ml before anaesthesia, during surgery, on day 2 and 3, respectively). sICAM-1 levels after operation were above the normal range (mean 272.88, 236.97, 294.64, 410.52 ng/ml).
Conclusions: Extracorporeal circulation with membrane oxygenation is followed by a significant endothelium response and release of soluble adhesion molecules into the bloodstream. There is the correlation between the markedly increasing level of sVCAM-1 and sICAM-1 and the appearance of postoperative complications.

P033

Systemic inflammatory response syndrome (SIRS) without systemic inflammation

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Background: Criteria of SIRS, developed to detect early systemic inflammation (SI), are sensitive enough to include also patients (pts) without SI. To address this problem, we developed composite systemic inflammation score (CSIS) based on phagocyte activation markers to evaluate degree of SI in acutely ill pts with SIRs.
Patients and methods: 100 pts at medical emergency were included. CD11b expression levels on neutrophils (PMNs) and monocytes (MO) were determined by flow cytometry, serum levels of IL-6, IL-1β, and TNF-α by ELISA, and of C-reactive protein (CRP) by immunoturbidimetry. To calculate CSIS, IL-6, IL-1β, TNF-α, CRP and CD1 expression levels were each scored 0 to 4 points; maximum CSIS is 20 points.
Results: 61 pts had SIRS2, 14 SIRS3, 2SIRS4, 20 sepsis, 2 severe sepsis, and 1 septic shock. Drug intoxication (17 pts) and acute myocardial infarction (15 pts) were most common diagnoses. CD11b expression increased in order : SIRS2 = SIRS3 < Sepsis; CRP in order: SIRS2 < SIRS3 < Sepsis, and IL-6 and IL-1β both in order: SIRS2 < SIRS3 < Sepsis. 13.8% of pts had CSIS 0 indicating virtually absence of SI. CSIS of SIRS2 pts (median 1.5; range 0–8) was lower than that of SIRS3 pts (3.5; 0–9, $P = 0.013$) and that of Sepsis pts (5; 3–10, $P < 0.001$); also SIRS3 differed from Sepsis ($P = 0.0018$). Among 81 pts with CSIS = 1, proportions of pts with increased IL-6, CRP, CD11b, IL-1β, and TNF-α were 79.0%, 72.8%, 61.7%, 25.9% and 2.5%, respectively.
Conclusions: Quantifying phagocyte CD11b expression and circulating IL-6 and CRP concurrently provides a means to identify patient who meets SIRS criteria but lacks SI.

P034

Measurement of circulating ICAM-1 in patients with acute lung injury on ventilators in intensive care unit

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Critical Care 1998, **2(Suppl 1):**P034

Full text: Serum levels of circulating inter cellular adhesion molecule-1 (ICAM-1) were measured by usign a sandwich-type Enzyme Linked Immunosorbent Assay (ELISA) kit (R&D System Inc). cICAM-1 was detected in the serum of fifteen normal healthy volunteers with an age range of 20 to 56 years, who had an average level of 172.4 ng/ml and a range of 92.59 ng/ml to 305.32 ng/ml. A significant elevation of cICAM-1 levels was observed ($P < 0.0006$) in patients with acute lung injury as compared with the normal. The trends of the patients' cICAM-1 were determined by sequential measurements during their stay in ICU. Seven patients

demonstrated a rising trend of serum cICAM-1. The remaining patient showed a falling trend, with a marked elevation (>1300 ng/ml) of cICAM-1 level on the day of admission into ICU. The cICAM-1 levels of the eight patients were correlated with two clinical parameters: ratio of arterial oxygenation to inspired oxygen fraction (PF ratio), and pressure adjusted heart rate. Despite a poor correlation of cICAM-1 levels with the PF ratio, cICAM-1 levels were elevated to at least 400 ± 20 ng/ml, when the PF ratio was low (<300). The infection pattern in these patients were also analyzed by bacteriological investigations done on clinical samples. The measurements of cICAM-1 levels may be important in understanding the pathophysiology of critically ill patients with acute lung injury. Further studies on the immunological mechanism and modulation of the injurious inflammatory response may benefit critically ill patients with the development of effective immunotherapy.

P035

Human peripheral blood mononuclear cells express mRNA for procalcitonin; modulation by lipopolysaccharides and sepsis related cytokines

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Critical Care 1998, **2(Suppl 1):**P035

Introduction: Procalcitonin (PCT), the precursor of calcitonin, is produced under physiological conditions in the thyroid. It was recently identified as a marker of severe especially bacterial infection. Elevated PCT levels have been demonstrated in septic patients also after thyroidektomy. Therefore other sites of PCT expression have to be considered.
Methods: Possible PCT mRNA expression in peripheral blood mononuclear cells (MNC) from healthy humans was assessed by reverse transcriptase polymerase chain reaction (RT-PCR) using a novel primer set (B.R.A.H.M.S, Berlin). Levels of PCT mRNA expression were estimated in control and cultures of MNC stimulated by lipopolysaccharides (LPS) and sepsis related cytokines. Restriction mapping was performed to verify the specificity of PCR primers for human PCT by digestion of PCR amplified thyroid medullary carcinoma cDNA.
Results: RT-PCR analysis demonstrated that MNC express mRNA for PCT and that LPS as well as various cytokines may modulate this expression. In the cultures stimulated with LPS from E. coli B4 and Salmonella abortus equi the final RT-PCR product for PCT mRNA was elevated up to 200% to 2300% in comparison with 100% in control culture. Pronounced effects were also observed for IL-lβ, 100–1800%; IL-6, 200-3500%; TNF-α, 200-9000%; IL-2, 250–1500%. IL-10 had no effect on the expression of mRNA for PCT.
Conclusions: We demonstrate for the first time that PCT is expressed in MNC. This expression is modulated by bacterial LPS and sepsis related cytokines. Therefore MNC may be one of the sources for elevated plasma PCT levels in septic patients.

P036

Procalcitonin, cytokines and C-reactive protein in systemic inflammatory response

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Critical Care 1998, **2(Suppl 1):**P036

Background: Procalcitonin (PCT) is a biochemical marker with a high specificity for bacterial and mycotic etiology of inflammation. Its production is selectively induced by endotoxin-cytokines mechanism.
Aim of study: To verify differential diagnostic value of PCT in inflammation of different etiology and intensity and to test practical use of PCT estimation.
Methods: In a prospective pilot study, 14 patients with various main diagnoses admitted to a medical ward entered the study. Serum levels of PCT, interleukin 6 (IL-6), C-reactive protein (CRP), body temperature and APACHE-II score were estimated in 12 h intervals within 6 days. Results were statistically evaluated by linear correlation analysis.
Results: 1. Patients with bacterial sepsis showed highest levels of PCT. Elevated levels of PCT were also present in patients with systemic autoimmune diseases. Patients with viral etiology of inflammatory process and those with no inflammatory process had normal levels of PCT.
2. Significant correlation was found between PCT and IL-6 (r^2 = 0.6568), and PCT and CRP (r^2 = 0.3714) in patients with bacterial sepsis. Correlation of CRP and IL-6 levels was less significant (r^2 = 0.1968).
3. No correlation between PCT and number of leukocytes, body temperature, lactate, and sedimentation of erythrocytes was observed neither in septic nor in non-septic individuals.
Discussion: Estimation of serum procalcitonin level in septic patients seems to be a reliable and easy-to-do test which corresponds with IL-6. As laboratory estimation of cytokines is relatively difficult and expensive, procalcitonin can be a good variant.

P037

Procalcitonin in paediatric sepsis

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Critical Care 1998, **2(Suppl 1):**P037

Objective: To document the relationships between procalcitonin (PCT), C-reactive protein (CRP) and leucocyte count (WCC) in children with sepsis, and to compare their diagnostic value in septic shock.
Methods: PCT, CRP and WCC were measured on admission to the PICU in 146 children, median age 18 months (range 0.1-202), mortality 22/146 (15%). PCT was measured by immunoluminometric assay (BRAHMS Diagnostika, Berlin, Germany). Patients were categorized a priori according to clinical and laboratory data as having either septic shock (n = 51) [1], localized bacterial infection (n = 33), viral infection (n = 14) or as non-infected controls (n = 48). Data were analysed by Kruskal-Wallis ANOVA and Dunn's test for multiple comparisons.
Results: PCT was significantly higher in septic patients compared to localized infection, viral infection and controls respectively (all P < 0.001). Receiver operating curve analysis indicates PCT > 20 ng/ml as the best discriminator of septic shock with positive and negative predictive values of 87% and 89%. In contrast, CRP > 35 mg/l had positive and negative predictive values of 65% and 83%.
Conclusion: Procalcitonin is a better discriminator of systemic from localized bacterial infection than either CRP or leucocyte count.
Reference

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P038

Urinary procalcitonin associated with a microbiologically diagnosed pneumonitis: preliminary results

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Critical Care 1998, **2(Suppl 1):**P038

Full text: Procalcitonin (PCT), the prohormone of calcitonin, is a 116 amino-acid protein stimulated by bacterial inflammation and produced by neuroendocrine cells of different organs, included the lung. Elevated serum levels of PCT have been found in several diseases such as sepsis syndromes, inhalation burn injury, infectious pneumonitis. PCT has been measured in body fluids other than serum in only few papers and with conflicting results. The aim of the present study was to verify whether PCT levels measured in the serum, urine, and bronchoalveolar lavage (BAL) fluid could be a marker of pulmonary infection, diagnosed by a positive cultural bacterial exam in the bronchial washing (BW).
Until now, 10 patients with pulmonary diseases were studied. Four of them had a radiologically diagnosed pneumonitis, 3 had a non-small cell lung cancer (NSCLC), 3 had other non-infective lung diseases. All the patients underwent a flexible fiberoptic bronchoscopy (FOB) with BAL

Table (abstract P037)

	Septic	*P*	Local	*P*	Viral	P	Control
PCT	91.6 (22-323)	<0.001	7.2 (2-17)	NS	0.4 (0-0.8)	NS	0 (0-1.4)
CRP	86 (29-113)	NS	27 (10-94)	NS	10 (7-29)	NS	9 (7-16)
WCC	12.9 (5.7-18)	NS	9.7 (6.7-17.4)	NS	6.9 (4.5-10)	NS	13.5 (7.8-16.4)

PCT (ng/ml), CRP (mg/l) and WCC ($\times 10^9$/l), median (interquartile range)

and BW. The quantitative determination of PCT was performed in the serum, urine and BAL fluid by the immunoluminometric assay (ILMA) using the LUMItest PCT kit (BRAHMS Diagnostica, Berlin, Germany).
PCT was not detectable in BAL fluids of all the patients. A positive determination of PCT was obtained in a total of 4 patients : in 2 of them in urine, in 1 patient in both urine and serum, and in 1 patient in serum. A trend towards a significant association between smoking habit and urinary PCT was found (PCT = 0 in non-smokers, 0.73 ± 1.27 ng/ml in ex-smokers, 1.77 ± 2.06 ng/ml in smokers). Urinary PCT was lower in patients with a radiologically diagnosed pneumonitis than in patients with NSCLC (0.95 ± 1.90 vs 1.83 ± 1.68 ng/ml, respectively). However a positive coltural exam for bacteria in BW was found in only 1 out of 4 patients with a radiologically diagnosed pneumonitis and in 2 out of 3 patients with NSCLC. Condidering the 3 patients with a positive coltural exam for bacteria in BW, a trend towards a significant higher urinary PCT values was found in these patients in comparison with the 7 patients with a negative coltural exam (1.83 ± 1.68 vs 0.54 ± 1.43 ng/ml, respectively). The 4 patients with a positive determination of PCT in urine and/or serum had a significant higher number of total cells in the BAL fluid in comparison with the remaining 6 patients (218 000 ± 155 000 vs 60 000 ± 30 000 respectively, $P = 0.01$).
In conclusion, these preliminary results seem to indicate that an increased level of urinary PCT is associated with the presence of pulmonary infection also complicating other lung diseases such as NSCLC and demonstrated by a positive coltural exam for bacteria in BW. Urinary PCT reflects the severity of alveolitis which usually derives from pulmonary infection. Taking into account the smoking habit of the patient, urinary PCT could be a simple and non-invasive marker useful in the follow-up of patients with a microbiologically diagnosed pneumonitis.

P039

Procalcitonin (PCT) for monitoring ICU patients with severe polytrauma and early SIRS: results of a prospective study

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Critical Care 1998, **2(Suppl 1):**P039

Introduction: PCT has been described by a number of authors for its use in monitoring severely ill patients. An increase of serum PCT concentration is usually found in a systemic response of the organism eg in severe sepsis or septic shock. Yet the exact patho-physiological mechanisms or possible function of PCT remain unclear. In this open prospective study we used PCT for the monitoring of intensive care unit (ICU) patients with severe polytrauma and early systemic inflammatory response syndrome (SIRS) in clinical routine.
Methods: PCT was measured using a commercial immunoluminometric assay (LUMItest ProCT by BRAHMS Diagnostica GmbH, Berlin, Germany). The assay was adapted to a Liamat system (Byk Sangtec). All 26 patients had a mean ISS (Injury Severity Score) of >50 and fulfilled the criteria for SIRS (systemic inflammatory response syndrome). There were 4 patients with septic episodes and 4 patients with manifestation of an ARDS. In addition, IL6 and CRP levels were measured. Blood samples for laboratory analysis were taken daily.
Results: If not indicated otherwise numbers are given as median (25th–75th percentile). We did 145 PCT measurements in 26 patients which we observed for an average of 14 days after admission. Overall we found a PCT of 0.5 µg/l (0.2–2.6 µg/l). Evaluating the data of patient without sepsis, we found the highest PCT values in patients with severe SIRS and at least 2 major organ systems involved, especially when severe pelvic trauma was sustained. A Kruskal Wallis analysis revealed significant differences in the median PCT concentrations in these 3 groups. SIRS only: 0.2 µg/l (0.1–0.55 µg/l), severe SIRS: 5.8 µg/l (1.4–34.2 µg/l), Sepsis: 0.5 µg/l (0.3–3.5 µg/l).
Conclusions: Aim of our study was to investigate the value of PCT in monitoring of critically ill trauma patients in an evidence based procedure. We confirmed the data of other authors regarding the PCT levels in SIRS. However, we found that patients with major trauma especially the combination of pelvic and chest trauma developed PCT levels that in previous studies were found in severe bacterial sepsis only.

P040

Postoperative plasma concentrations of procalcitonin after different types of surgery

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Critical Care 1998, **2(Suppl 1):**P040

Introduction: Procalcitonin (PCT) is an inflammatory induced protein indicating severe bacterial infection or systemic inflammation in

Table 1 (abstract P040) Maximal postoperative PCT plasma concentrations (µg/l) of patients with a regular postoperative course during a 5 day observation period

Type of surgery	median	75% perc.	90% perc.	maximal concentr.
Non-abdominal surgery* (n=37)	0.38	0.55	1.06	2.5
Cholecystectomy (n=11)	0.49	0.60	0.62	0.62
Resection of intestine** (n=20)	1.50	2.49	3.00	5.13
Major abdom. and retroperitoneal s.*** (n=12)	0.54	1.57	5.53	5.76
Cardiac and thoracic surgery (n=37)	0.61	1.24	1.96	4.96

*hip-replacement, peripheral vascular surgery, thyroidectomy, hernia surgery; **resection of colon, sigma, rectum, gastrectomy; ***esophagectomy, Whipple's operation, aortic aneurysm; perc., percentile

critically ill patients. To use PCT for diagnosis of infection or systemic inflammation also in the postoperative period, PCT should not substantially be induced by the surgical trauma in patients with a regular postoperative course. We thus measured PCT and CRP plasma concentrations after different types of surgery in patients with a regular postoperative course.
Methods: Postoperative plasma concentrations of PCT and CRP were prospectively measured preoperative and 5 days postoperative in 117 patients with a regular postoperative course and no signs of infection or inflammation after different types of surgery (Table 1).
Results: Postoperative induction of PCT largely depends on the type of surgery. Intestinal surgery and major abdominal operations more often increase PCT, whereas after primarily aseptic surgery PCT is normal in the majority of patients (Table 1). CRP concentrations were increased after all types of surgery (data not shown).
Conclusions: Postoperative moderately increased PCT plasma concentrations may be expected also without infection or inflammation in some patients after certain types of surgery. Since PCT concentrations are significantly more elevated during sepsis and severe bacterial infections, PCT might indicate infection or inflammation also postoperative. The significance of PCT for diagnosis of postoperative infections however should be evaluated by further investigations.

P041

Enhanced preoperative C-reactive protein plasma levels predict postoperative infections in patients undergoing cardiac surgery

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Critical Care 1998, **2(Suppl 1):**P041

Introduction: Some patients undergoing cardiac surgery show enhanced levels of C-reactive protein (CRP) before surgery. Recently, postoperatively enhanced CRP levels have been related to postoperative infections. The question therefore arises whether preoperatively enhanced CRP levels are a risk factor for postoperative infections in patients undergoing cardiac surgery.
Measurements and results: CRP was measured in 863 patients undergoing cardiac surgery with cardiopulmonary bypass. CPR levels were determined on daily intervals from the day before surgery till day 6 after surgery. Furthermore, we documented infectious diseases related data. Patients developing an infection during the postoperative course had significantly higher CRP levels at the day before surgery, 17.7 ± 4 mg/l vs. 7.8 ± 0.7 mg/l. Furthermore, CRP levels in patients developing an infection were significantly higher at day 1, 4 and still at day 6 after surgery. The incidence of postoperative infections was significantly higher in patients with enhanced preoperative CRP levels than in those with normal preoperative CRP levels (upper quartile vs. lower three quartiles), 25.0% vs. 11.2% respectively. Furthermore, the length of postoperative hospital stay was significantly longer in patients with enhanced preoperative CRP levels than in those with normal preoperative CRP levels, 9.6 ± 0.8 vs 7.6 ± 0.3 days. Multivariate analysis including the variables enhanced preoperative CRP, and CPB duration, age, gender, and diabetes mellitus demonstrated that preoperatively enhanced CRP wast the most important independent variable predicting postoperative infection (OR, 2.7; 95% CI, 1.6 to 4.3).
Conclusion: This study shows for the first time that preoperative measurement of CRP may offer a useful, predictive marker in risk stratification for postoperative infections in patients scheduled for cardiac surgery.

P042

In vitro production by whole blood of pro- and anti-inflammatory cytokines in neonates with transposition of the great arteries having undergone arterial switch operation

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Critical Care 1998, **2(Suppl 1):**P042

Background: Cardiac operations induce a systemic inflammatory reaction which could influence reactivity of immune competent cells in the days or weeks following the operative procedure and thus postoperative infectious morbidity.
Objectives: To test the hypothesis of whether pro- and anti-inflammatory cytokine synthesis is modified in neonates having undergone cardiac operation.
Methods: 15 neonates with transposition of the great arteries were investigated before as well as 5 and 14 days after arterial switch operation. Mean age at operation was 6 days. Whole blood (1 ml) was stimulated *in vitro* with bacterial endotoxin (LPS) (1 ng/ml) and the concentrations of the pro-inflammatory cytokines TNFα and IL8 and of the natural anti-inflammatory cytokine IL10 were measured in the cell culture supernatant.
Results: As compared with the control culture, there was a significant production of TNFα, IL8 and IL10 before as well as 5 and 14 days after the operation. In comparison with the preoperative results, TNFα and IL8-production decreased significantly 5 days after the operation ($P < 0.02$ and < 0.05, respectively) whereas IL10-synthesis remained unchanged. There was no significant difference between cytokine production before and 14 days after the operation.
Conclusions: Our results demonstrate that neonates having undergone cardiac operation display transient postoperative inhibition of the reactivity of immune competent cells with decreased production of pro-inflammatory cytokines. In contrast, the production of the natural anti-inflammatory cytokine IL10 remains postoperatively unaltered and could be in turn, at least in part, involved in the postoperative inhibition of TNFα and IL8 synthesis.

P043

Postoperative morbidity following cardiopulmonary bypass may be attributed to endotoxemia

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Critical Care 1998, **2(Suppl 1):**P043

Introduction: Increased concentrations of endotoxin (ET) have been measured in the plasma of patients undergoing cardiopulmonary bypass (CPB), however the significance of the increase is uncertain. Using a new rapid, reliable, whole blood method for ET detection, we sought to determine the prevalence of endotoxemia in a group of patients undergoing CPB, and describe the relationship between endotoxemia and postoperative morbidity.
Design: Prospective, observational trial in a Canadian tertiary medical centre.
Subjects: Twenty-seven patients undergoing coronary artery bypass graft surgery (CABG) or valvular heart surgery.
Methods: Whole blood samples (1 ml) were drawn at arterial line insertion, immediately postoperative, and at 24 h. Known pre-operative risk factors were assessed and subjects were assigned a mortality risk score [1]. MOD [2] scores and APACHE II scores were calculated at 24 h or at discharge from CVICU.

Results: Fourteen patients had CABG, 8 had mitral valve repair, 5 had aortic valve repair. Two patients died >48 h postoperatively. 22/27 patients (81%) had preoperative ET levels >50 pg/ml. All 5 pre-op ET negative patients had levels >50 pg/ml following surgery. There was no correlation between pre-op ET levels and indication for surgery, degree of left ventricular function or preoperative mortality risk score. Postoperative mean ET levels were significantly different from baseline levels (195.2 ± 224.0 vs 399.7 ± 282.8 pg/ml [P = 0.003]). Using univariate linear regression analysis, postoperative ET levels were associated with increased MOD score at 24 h (P < 0.05) and prolonged hospital stay (P < 0.05).

Conclusion: We found that patients undergoing cardiac surgery and CPB have high mean baseline ET levels. ET levels significantly increased following CPB and were associated with measures of increased morbidity such as MODS and hospital length of stay. Measuring ET using a rapid reliable assay, identifies a group of patients where perioperative treatment with an anti-endotoxin strategy, or alterations in perfusion related factors may be beneficial.

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P044

Influence of temperature on leukocyte kinetics during cardiopulmonary bypass and postoperative organ damage: an experimental study

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Critical Care 1998, **2(Suppl 1):**P044

Objectives: To Study the influence of core temperature during cardiopulmonary bypass (CPB) on leukocyte kinetics and perioperative organ damage.

Methods: Eighteen young pigs (weight 40 kg) were randomly assigned to a temperature (T°) group during CPB: normothermia (group 1, T° = 37°C, n = 6), mild hypothermia (group 2, T° = 28°C, n = 6) and deep hypothermia (group 3, T° = 20°C, n = 6). CPB was conducted with full flow in group 1 (2.7 l/m^2/min) and with reduced flow in group 2 and 3 (60% and 50% of full flow, respectively), for a duration of 120 min. Aorta was cross-clamped for 60 min and cardioplegia achieved with a single dose of 4°C cold Bretschneider solution. Leukocyte count was determined before, during and after CPB.

At the end of the experimentation (6 h after CPB) tissue probes of heart, lung, liver, kidney and intestine were taken for histological examination.

Results: In all groups, there was a significant fall of total leucocyte count at induction of CPB, without any intergroup difference (leukocytes=7800 ± 1150 cells/ml). Leukocyte count continued to decrease till clamping of the aorta in group 2 (4980 ± 513 cells/ml) and further till myocardial reperfusion in group 3 (3880 ± 625 cells/ml). In contrast, in group 1, leukocyte count increased significantly before myocardial ischemia and further at myocardial reperfusion (10 700 ± 803 and 14 100 ± 1960 cells/ml, respectively) (intergroup difference: P < 0.005 and < 0.001, respectively). Group 1 pigs had the highest transcoronary leukocyte gradient before clamping of the aorta (850 ± 454 cells/ml vs 150 ± 117 cells/ml in group 2 and 150 ± 159 cells/ml in group 3). At the end of CPB, there was no difference in leukocyte count between groups.

Results of the histological examination show that the most important tissue damage in terms of interstitial oedema and leukostasis in heart, lung, liver and intestine but not kidney was seen in group 1 followed by group 3 while the least important damage was present in group 2.

Conclusions: In our experimental series, CPB conducted under normothermia was associated with higher circulating leukocyte levels and higher intramyocardial leukostasis when compared with CPB conducted under mild or deep hypothermia. Mild hypothermia (28°C) but not normothermia or deep hypothermia (20°C) is associated with lower postoperative organ damage.

P045

Correction for haemodilution is necessary for properly interpreting laboratory results obtained perioperatively in open-heart surgery

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Critical Care 1998, **2(Suppl 1):**P045

Introduction: Extracorporeal circulation (ECC) induces an oxidative burst of free radicals. Free radical activity can be assessed, among others, by measuring plasma lipofuscin levels, lipofuscin being a product of lipid peroxydation by free radical activity. Thus, theoretically a rise in lipofuscin levels can be expected during ECC.

Haemodilution, using non-blood primes for extracorporeal circuits during open-heart surgery, is standard practice. Usually moderate haemodilution, with haematocrites in the range of 0.20-0.25, is aimed at. In blood coagulation studies the potential effects hereof on study results are taken into account, but whether this is necessary in other studies as well, is still controversial.

We investigated the effect of correcting for haemodilution by comparing corrected with uncorrected sets of results of perioperative plasma levels of lipofuscin in order to examine the effect of this practice on the interpretation of our results.

Methods and material: In nineteen consecutive patients undergoing elective, uncomplicated coronary-artery bypass grafting (creatinine clearance >50 ml/min, age <80 years, no hypotension (mean arterial pressure <60 mmHg for over 1 h), no congestive heart failure (NYHA III-IV), and no clinical evidence of infection) plasma lipofuscin levels are measured by spectrophotometry as units of quinine sulphate (pg/ml). Samples are taken A) 10 min prior to anaesthesia, B) 2 min after aortic clamp release, C) at admission to the ICU, D) 4, and E) 8 h postoperatively. Correction for haemodilution is calculated using the formula : 1-HtB/1-HtA. Mean lipofuscin levels at specified time points are compared with the mean preoperative initial value (paired t-test).

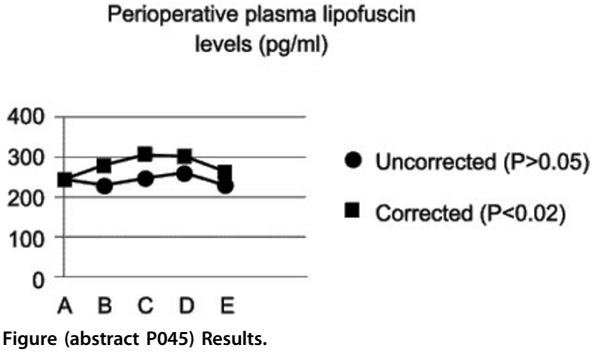

Figure (abstract P045) Results.

Discussion: Uncorrected plasma lipofuscin levels show no rise during open-heart surgery, whereas corrected values, which are all statistically significantly higher in comparison to the initial preoperative value, do. This is in agreement with the theoretically expected, and thus offers the opportunity for correct interpretation.
The above underscores the importance of correcting for haemodilution. It is essential for a proper interpretation of perioperative laboratory results and consequent understanding of the pathophysiology of ECC in open-heart surgery.

P046

Myocardial cell damage related to arterial switch operation in neonates and the role of pro-inflammatory, cytokines

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Critical Care 1998, **2(Suppl 1):**P046

Objectives: To investigate the role of myocardial depressant pro-inflammatory cytokines on myocardial cell damage related to arterial switch operation (ASO) in neonates.
Methods: 35 neonates (mean age 7 days) with transposition of the great arteries undergoing ASO were prospectively studied. ASO was performed using combined low-flow cardiopulmonary bypass (CPB) and cardiocirculatory arrest (CCA) under deep hypothermia. Patients with myocardial hypocontractility at the end of the procedure or 4 and 24 h postoperatively (po), as observed at echocardiography, were defined as having myocardial dysfunction (MD). Troponin-T (Tropo-T) and the creatine kinase isoform CKMB served as markers for myocardial cell damage during and after ASO. Interleukine (IL)-6 (a myocardial depressant cytokine) and IL-8 (involved in ischemia-reperfusion damages) served as marker for the systemic inflammatory reaction related to ASO.
Results: Five patients showed MD after ASO, all patients survived. Age at ASO, duration of CPB, CCA or aortic clamping were not different in patients with and without MD. In all patients, plasma levels of Tropo-T increased significantly during CPB ($P < 0.0001$). At the end of ASO, patients with MD had significantly higher values of Tropo-T than patients without MD ($P < 0.002$). In contrast to Tropo-T, levels of CKMB did not increase during CPB and were not different in patients with and without MD. IL6 and IL8 increased significantly in all patients during CPB ($P < 0.001$, respectively). Patients with MD had significantly higher IL6 and IL8 values 4 h po than patients without MD ($P < 0.001$, respectively). Tropo-T- and IL6 values measured 4 h after ASO were significantly correlated to each other ($P < 0.05$).
Conclusions: Our results demonstrate myocardial cell damage (as shown by Tropo-T liberation) and systemic inflammatory reaction (as shown by IL6- and IL8-production) related to ASO performed with combined low-flow CPB and CCA under deep hypothermia in neonates. Patients with MD have more important myocardial cell damage and higher magnitude of systemic inflammatory reaction than have patients without this complication. IL6 and IL8 both are possibly directly involved in the damage to the myocardial cell in this setting.

P047

A new model for evaluation of thrombosis and ischaemia/reperfusion injury

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Introduction: Experimental studies on ischaemia/reperfusion injury have traditionally focused on the isolated effect following simple occlusion of the nutrient artery. In myocardial infarction the reperfusion injury is further complicated by the presence of a thrombogenic area in the coronary artery that may cause repetitive episodes of re-occlusion and embolization.
Methods: In eight pigs a thrombogenic area was created in the left anterior descending artery (LAD) by exposure of adventitia into the lumen. The LAD was occluded proximal to the lesion for 50 min, followed by 4 h of reperfusion. Troponin-T (TNT), creatine kinase (CK), and collagen-induced platelet aggregation (CPA) were measured 4 times during the experiment Indium-labeled platelets were given 30 min prior to harvesting of the hearts.
Results: The infarct size/area at risk was 40 (35–63)% in the present study. TNT and CK increased significantly to 1.7 (0.6–3.5) µg/l ($P < 0.001$) and 1480 (1105–2249) U/l ($P < 0.02$), respectively. Infarct size correlated significantly with TNT-3h (ρ=0.85, $P < 0.002$), but not with CK-3h. Platelet aggregation decreased by 34% ($P < 0.05$) 15 min of reperfusion, but returned to base-line. Platelet accumulation in the left ventricle was significantly higher in area at risk [194 (157–206)%] compared to area not at risk (100%), and to the right ventricle [137 (120–142)%]; ($P < 0.05$).
Conclusion: In the present study Troponin-T showed a better correlation with infarct size than CK. A decreased reactivity of circulating platelets was observed after reperfusion and significantly more platelets were found in the area at risk. These results indicate that activated platelets become entrapped in the myocardium and may aggravate the reperfusion injury.

P048

Treatment of hypercoagulation state in acute myocardial infarction

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Critical Care 1998, **2(Suppl 1):**P048

Full text: It is known that thrombolysis does not always prevent the development of early repeated thrombosis of coronary vessels. We have developed a method of extracorporeal thermal plasmamodification — thermoplasmasorbtion (TPS), which allows to reach significant decrease of its coagulation state (complete removal of fibrinogen, reduction of activity of the external and internal coagulation factors) and decrease of blood viscosity. Is shown, that reinfusion of modificated plasma reduces platelet and red blood cells aggregation. 40 patients with myocardial infarction in acute period underwent the analysis. The TPS was applied to 20 patients (group 1) and 20 underwent conservative treatment (group 2). During clinical supervision more expressive positive dynamics changes were noted in all the patients of group 1: stenocardic cupping already in the 1st day of treatment, hemodynamic stabilization, absence of thrombotic and other complications. The improvement of clinical state of the patients of this group was proved by system and central hemodynamic rate: increase of end diastolic volume, decrease of systole frequencies, increase of ejection fraction with stable head ejection. In our opinion the given changes testify to the improvement of heart work with inclusion of a rate thermal plasmosorbtion in complex treatment of acute myocardial infarction.

P049

Artificial blood as a way to treat acute myocardial infarction

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Introduction: Artificial blood–perfluorochemical emulsion Perftoran is a way to improve oxygenation of the heart during periods of hypoxia and ischemia. This study was performed to determine the efficacy of an intravenous infusion of Perftoran for patients with acute myocardial infarction.
Methods: Forty patients, males not older then 60 with first acute myocardial infarction (AMI) were observed, 20 to receive Perftoran in the first 6 h of AMI (1st group) and 20 to receive no Perftoran (2nd group), along with 20 mg of intravenous nitroglycerin given over 8 h. Minimal effective dosage of Perftoran 4–5 ml/kg intravenous was used, infusion rate was 20–40 drops per minute. We investigated composite clinical outcomes, ECG changes, infarct size, creatine kinase activity, hemodynamic parameters, acid-base status, blood gases, oxygen supply and consumption.

Results: On the first and following days of AMI the repeated episodes of chest pain were observed in 81% cases in the second group and in 57% cases in the first group ($P < 0.001$). The patients of the first group also had positive ECG changes on the second day of the AMI: Development of terminal T-wave inversion, ST-segment normalization and 2 patients had Q-wave reduction. In Perftoran-treated patients non-damaged volume of left ventricle (in % from the first damage) was 25.06 ± 5.40 ($P < 0.05$) compared with traditional-treated parients, 6.60 ± 2.31%. By the 3rd-5th days of AMI in the first group there was observed an increase of arterial-venous O_2 content difference, O_2 delivery and 2 and more times than in the 2nd group.
Conclusions: The use of Perftoran in patients with AMI performs a positive effect on clinical characteristics of AMI, leads to reduce infarct size and decrease of ischemia in affected area.

P050

Morbidity in the SICU after transmyocardial laser revascularization

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Background: Transmyocardial laser revascularization (TMLR) is a modern technique of myocardial revascularization in patients with symptomatic coronary artery disease that is refractory to maximal medical therapy and who are unsuitable candidates for conventional methods of myocardial revascularization [1-3]. There are no studies showing the clinical events of the early postoperative period.
Objectives: To report the morbidity appeared in the surgical intensive care unit (SICU) after TMLR.
Methods: Description of the postoperative evolution in the SICU of patients who underwent TMLR between March and October 1997. Postoperative complications, clinical trendmarks and length of stay were recorded. Data are presented as mean values (range).
Results: TMLR was performed in eight patients, four men and four women, age 62 years (51-74), angina class 4. Cardiac events were: low cardiac output, 5; acute myocardial infarction, 1. Symptomatic angina, 1 and silent ischemia, 1. One patient received mechanical ventilation during 17 days because severe acute lung injury with a lung injury score (LIS) of 2.6; extubation was performed in the remaining 9.5 h (4-24) after admittance in the SICU, with a maximal LIS of 1.08 (0.5-2). Postoperative chest tubes drainage ranged between 280 and 1890 ml. Thrombocytopenia was a constant finding. No other complications were found and no patient died. The patient with prolonged mechanical ventilation stayed in the SICU 27 days; length of stay was 3.7 days (1-6) in the remaining.
Conclusions: Morbidity in the SICU after TMLP seems to be focused in the cardiovascular, respiratory and hematological systems. These preliminary findings need to be confirmed with other similar studies.
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P051

Intra-operative events do not predict perioperative myocardial infarction

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Critical Care 1998, **2(Suppl 1):**P051

Full text: Perioperative myocardial infarction (PMI) is infrequent, but has high mortality rate. Therefore, a diagnostic work up to rule out PMI is usually performed when cardiac or hemodynamic events occur during major operations. We performed this prospective study to determine whether or not these intra operative events accurately predicted the development of PMI. We hypothesized that they did. We studied patients who underwent major surgical procedures and a subsequent diagnostic work up to rule out PMI while they were in the recovery room. PMI work up included physical assessment, countinuous ECG monitoring, and three 12 lead ECG and cardiac enzymes performed every 8 h. Data collection included patient demographics, diagnoses, pre-existing cardiac risk factors, type and duration of anesthesia and surgery, intra operative cardiac and hemodynamic events, results of PMI work up, incidence of PMI and patient outcome. Fifty-eight patients entered the study, 28 males and 30 females. Their mean age was 61.8 years. Preexisting cardiac conditions included angina in 5 patients, previous MI in another 5, coronary artery bypass in 5, diabetes in 31, atherosclerotic arterial disease in 26, smoking in 35 and hypertension in 42. The mean anesthesia and operative times were 332.8 and 237.9 min, respectively. Intra operative events included hypotension in 20 patients, tachycardia in 15, hemorrhage in 6, ECG changes in 3, hypertension in 8 and physician concern for PMI risk in 6. Only one of 58 patients (1.7%) developed PMI.
Conclusion: Intra operative cardiac events alone are not very specific predictors of perioperative myocardial infarction.

P052

Painless acute myocardial infarction and diabetes mellitus

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Critical Care 1998, **2(Suppl 1):**P052

Full text: With diabetes mellitus, painless acute myocardial infarctus (PAMI) is a well-known clinical phenomen. Possible explanations include microangiopathy, diabetic neuropathy and abnormalities in myocardial metabolism in humans (hyperinsulinemia, hyperglycemia and insulin resistance).
Various studies show that with diabetes mellitus approximately 25–50% of AMI presents with only slight pain or without pain. For emergency prehospital services this feature plays an extremely important differential diagnostic role.
This is a presentation of our clinical experiences from January 1995 to September 1997. During this period, we dealt with 69 (28 female and 41 male) cases of AMI with patients suffering from diabetes.
All the patients had previously been registered at the regional diabetes center and had undergone treatment: 22 (31.8%) with insulin therapy and 47 (68.2%) with oral antidiabetes medicine. The average age of the patients was 51.3 ± 5.8 years.
All the patients underwent the ECG and enzyme analysis of AMI and preinterventional blood glucose levels. Thirty-two patients had no cardiac pain, only non-specific symptomatology (nausea, vomiting, dyspnea, perspiration, tiredness, palpitations, non-specific precordial sensations) or a dominating clinical picture of hyperglycemia (ketoacidosis) or hypoglycemia. For 4 patients we were not able to obtain relevant anamnestic/heteroanamnestic data.
Hyperglycemia (15.3–31.5 mmol/l; 20.61 ± 4.08) was verified in 43 patients (62.3%), of them 5 cases with coma (ketoacidosis).
Hypoglycemia (0.8–2.0 mmol/l; 1.47 ± 0.43) was registered in 11 patients (15.1%), of them 2 cases with coma.
Euglycemia (3.52–6.37 mmol/l; 5.28 ± 0.82) was registered in 15 patients (22.6%).
Conclusion: PAMI must to be excluded in the treatment of an emergency patient for whom there is an anamnestic or heteroanamnestic record of diabetes. Treatment of ketoacidosis should be carried out promptly, because of the high mortality rate with already developed ketoacidosis-coma and AMI. It is vital that the differential diagnosis is carried out promptly and accurately to ensure accurate and prompt therapeutic treatment

P053

A new system for quantitative determination of troponin T and myoglobin in the emergency room and in the intensive care unit

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Critical Care 1998, **2(Suppl 1):**P053

Full text: We present here the results of a multicentre evaluation of a small system (Cardiac reader) for the rapid and quantitative

determination of troponin T (CARDIAC T Quantitative test) and myoglobin (CARDIAC M test) in heparinized venous whole blood (150 µl). The measuring unit of the Cardiac reader contains a CCD camera that optically reads the signal and the control line of the respective immunochemical test strips. The tests have a reaction time of 10 or 14 min. The quantitative measuring range for the troponin T determination on the Cardiac reader is 0.1 to 3 µg/l and 30 to 700 µg/l for CARDIAC M.

The within-series imprecision was very acceptable for CARDIAC T Quantitative (CV 10 to 15%) and good for CARDIAC M (CV 5 to 10%). Compared with the Enzymun-Test Troponin T, the results obtained with CARDIAC T Quantitative show a high correlation (n = 40; r = 0.967; y = -0.006 + 1.093x). The method comparison between CARDIAC M and Tinaquant® Myoglobin shows that both assays agree well (n = 82; r = -0.959; y = 3.6 + 0.976x).

To assess the clinical efficiency, CARDIAC T Quantitative results of all five study centres (481 samples of patients with suspected acute coronary syndromes) were evaluated in a nine-field comparison table versus Enzymun-Test Troponin T. More than 90% clinical concordance were achieved with only 4 results that were clinically grossly discordant (0.8%); the corresponding Enzymun-Test Troponin T results were moreover directly at the cut-off point (0.10 mg/l). Sensitivity and specificity relative to Enzymun-Test Troponin T were 97 and 96%, respectively.

With the Cardiac reader reliable quantitative results can be easily obtained for both cardiac markers and entered into the hospital data system. Consequently, the Cardiac reader is especially suitable for use in emergency rooms and coronary care units.

P054

Intravenous magnesium reduces infarct size following an ischaemia/reperfusion injury combined with a thrombogenic lesion in the LAD

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Critical Care 1998, **2(Suppl 1):**P054

Introduction: Experimental studies have demonstrated that magnesium (Mg) therapy can protect the ischemic myocardium and modulate reperfusion injury. In myocardial infarction the reperfusion injury is further complicated by the presence of a thrombogenic area in the affected coronary artery that may lead to repetitive reocclusion and embolisation.

Methods: We investigated the effect of Mg on infarct size in a randomised, blinded study in pigs inflicted with a thrombogenic lesion in the left anterior descending artery (LAD) and mechanical occlusion of the vessel proximal to the lesion. Coronary occlusion was maintained for 50 min followed by 4 h reperfusion. Magnesium sulphate (6 mmol/30 min followed by 3 mmol/h) or saline was given at 20 min of coronary occlusion and continued for 4 h. ^{111}Indium-labeled platelets were given 30 min prior to harvesting of the hearts. Troponin-T (TNT) was measured at base-line and 3 h into reperfusion.

Results: The infarct size/area at risk (IS/AR) ratio in the placebo group was 40 (35–63)% (n = 8) compared with 16 (9–40)% (n = 6) in the Mg treated animals (P < 0.05). Platelet accumulation in AR was reduced with 15% in the Mg treated animals [placebo-group: 194 (157–205)% vs Mg-group: 166(131–213)%; NS]. Cellular leakage of TNT increased significantly in both groups and was at 3 h highest in the placebo group: 1.7 (0.6–3.5 µg/l compared to 0.3 (0.1–1.5) µg/l in the Mg-treated animals (NS).

Conclusion: The present study demonstrates that iv Mg infusion is able to reduce infarct size with more than 50% in this model where an ischaemia/reperfusion injury was combined with endothelial damage in the nutrient artery. The reduction in infarct size may be due to complementary actions on platelets and a cellular protection of the myocardium.

P055

Remifentanil in cardiac anesthesia: influence on postoperative ICU course

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Critical Care 1998, **2(Suppl 1):**P055

Introduction: Remifentanil (R) a new short-acting opioid, has been introduced in cardiac total intravenous anesthesia to solve the problems connected with the adminstration of long-acting opioids. Aim of our study was to evaluate the efficacy of R in optimizing mechanical ventilation and ICU stay after cardiac surgery.

Methods: We studied 30 consecutive pts, EF >40% scheduled for elective coronary surgery. Pts were randomized in two different groups: Group R (16 pts) receiving remifentanil, and group F treated with moderate dose fentanyl (14 pts). Induction of anesthesia was performed in both groups with fentanyl 15 µg/kg per min, vecuronium 0.15 mg/kg and thiopentone 0.5–1 mg/kg. In group R anesthesia was then maintained with continuous infusion of propofol 1–3 mg/kg per h and remifentanil 0.5–1 µg/kg per min running throughout the surgical procedure. In group F the maintenance was obtained with propofol 1–3 mg/kg per h and fenatyl 5–7 µg/kg per h running throughout the surgical procedure too. Propofol was continued at dose 0.5–1 mg/kg per h in the ICU until 30 min previous extubation in all pts. In adjunction pts of group R received remifentanil 0.1–0.2 µg/kg per min until extubation. In both groups we evaluated the duration of mechanical ventilation and of ICU stay. All data were analysed with t-test (P < 0.05).

Results: Mean time of mechanical ventilation was 4 ± 1.3 h in group F vs 9 ± 15 h in group R (P < 0.05). In group R mean ICU stay was shorter than group F: 18 h vs 27 h (P < 0.05). Global ICU cost charge/pt was $930 in group R vs $1390 in group F, according to DRG coefficients.

Discussion: Our experience suggests that remifentanil, combined with propofol, can improve early extubation and reduce ICU stay in uncomplicated CABG pts with good EF, so leading to a trend in cost reduction.

P056

Continuous infusion of propofol for sedation of pediatric patients following open-heart surgery

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Critical Care 1998, **2(Suppl 1):**P056

Introduction: The aim of this study was to prospectively evaluate safety and efficacy of propofol infusion as an alternative sedative agent in children with open-heart surgery.

Methods: Twenty-nine pediatric patients with complex congenital lesions, aged between 4 and 48 months, who underwent open-heart surgery, received propofol infusion as sedation after midazolam infusion was ineffective. The effective sedative dose of propofol was between 1.5 and 7.0 mg/kg per h (median 3 mg/kg per h). Measurement of heart rate (HR) electrocardiogram (ECG), blood pressure (BP), arterial blood gas (ABG) including pH, bicarbonate (HCO_3), partial carbon dioxide pressure (PCO_2), and blood oxygen saturation (PO_2); and blood chemistry including liver function tests (LFTs), triglycerides (TG), and total bilirubin (TB), were all done prior to and during propofol therapy.

Table (abstract P056)

Parameter	Change in median values	P values
HR (beats/min)	-10	0.009
BP (mmHg)	-2	0.001
Triglyceride (mmol/l)	0.2	0.001

Results: After 10–288 h of propofol infusion (median 74 h), no statistically significant differences were found in the parameters measured except a decrease in median HR with attendant decrease in BP, and an increase in median TG.
Conclusion: Continuous sedation with propofol is a safe and effective, alternative agent for sedation of infants and children after surgical repair of compex congenital heart disease.

P057

Gamma-hydroxybutyrate: an 'old' and very interesting drug: new perspectives?

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Critical Care 1998, **2(Suppl 1):**P057

Background and goal of study: Due to the unique property of lacking cardiovasculary and respiratory depressive effects, GHB is a very interesting alternative for sedation of critically ill patients.
Materials and methods: An epileptogenic effect described in some animals after high doses of GHB has not been seen in 20 patients analysed with on-line EEG under bolus-application and 20 min afterwards. We also show that the long duration of the effect of a single or repetitive dose of GHB can in fact be reversed by the application of Physostigmine.
Results and discussions: No signs of cerebral hyperexcitability were found in 20 patients receiving an anesthetic dosage of GHB. The problem of sodium-overload should not be an argument any longer as soon as the newly developed, sodium-free drug is available. The third argument against this drug, meaning the long and individually not calculable time of effect, does also not seem to be a good argument against it's use, since anaesthesia from GHB can be antagonized quickly by the application of physostigmine.
Conclusions: GHB is a very interesting drug for anaesthesia and sedation on ICU due to its missing depressive cardiovasculary and respiratory effects and many more aspects. So people should not allow themselves not to use that drug on their patients for the three most usually uttered reasons being sodium overload, cerebral convulsions and long and uncalculable time of action. All these arguments seem untrue.

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P058

Rapid and safe intubation with rocuronium bromide in critically ill patients

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Critical Care 1998, **2(Suppl 1):**P058

Background: Critically ill patients need sometimes orotraqueal intubation and mechanical ventilation. A muscle relaxant with rapid onset time, producing good intubation conditions is required. Succinylcholine provides this goal, but it has several undesirable side effects. Rocuronium bromide is a new muscle relaxant with an onset time shorter than other because its low potency, allowing orotracheal intubation at 60–90 s, being free of cardiovascular and other side effects.
Objectives: The aim of this study is to assess in a prospective manner onset time, and intubation conditions at 60 s, and side effects after a dose of rocuronium bromide.
Methods: Patients aged 18–70 years admitted to the ICU who required mechanical ventilation, were included in this study. Neuromuscular disease was an exclusion criterian. After fentanyl 1 μg/kg and etomidate 0.2 mg/kg, patients received a bolus dose of 0.6 mg/kg of rocuronium bromide. Heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and mean arterial pressure (MAP) were monitored before and after administration of bolus dose. Neuromuscular response was monitored with a peripheral nerve stimulator with two electrodes on the wrist. Train of four (TOF) was the mode chosen for stimulation and the number of responses at the thumb was recorded by tactile evaluation. Intubation conditions were assessed following previous published scores, in excellent, good, poor and impossible. Data are presented as mean values; statistical analysis was made by Wilcoxon test, considering $P \leq 0.05$ as significance level.
Results: Eight patients, mean age 54.5 years, three man and five women, were included in the study, all of them requiring mechanical ventilation because respiratory failure. Onset time of bolus dose of rocuronium bromide was 3.2 min; maximal degree of blockade was 80% in one patient and 100% in the remaining; and clinical duration was 24.2 min. Intubation conditions were excellent in six patients and good two ones. There were not significant changes in HR, SAP, DAP and MAP after rocuronium regarding control values and no other types of side effects appeared.
Conclusions: Rocuronium bromide allows rapid and safe intubation under suitable conditions in critically ill patients, without haemodynamic changes.

P059

The use of continuous epidural anaesthesia in intensive care units in Poland

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Critical Care 1998, **2(Suppl 1):**P059

Introduction: The aim of the study was to estimate the range of use of epidural anaesthesia in Intensive Care Units. Our study is a part of a large questionnaire surveillance study aimed at estimation of the widespread of regional anaesthesia in Poland.
Methods: The questionnaire was sent to 376 hospitals for adults, of a patients bed quantity of 250 and more, or specialised in orthopaedics, thoracic surgery, heart surgery or gynaecology and obstetrics. Head of Department of Anaesthesiology was asked to answer over 75 questions regarding the use of regional anaesthesia in his hospital. In regard of epidural anaesthesia in Intensive Care questions included : the presence of epidural anaesthesia, duration of catheter persist, use of catheter tunnelization technique, and the most frequent indications for epidural anaesthesia application in Intensive Care Unit. General questions included: the percentage of regional anaesthesia in all procedures, and for how long time they perform regional anaesthesia.
Results: We have obtained 118 responses (31.36%), 13 from university hospitals, 70 from regional hospitals, 17 from district hospitals, and 18 from specialised centres. Regional anaesthesia made from 3.6% to 83.3% (median value 21.4%) of all anaesthetic procedures. Application of epidural anaesthesia in ICU was confirmed in 64 hospitals (54.24% respondents), in 10 hospitals the epidural anaesthesia was not performed at all, in 28 there wasn't any Intensive Care Unit. The main indications reported were: acute pancreatitis, postoperative pain treatment, chest trauma and severe trauma. Occasionally epidural anaesthesia was used in myocardial infarction, asthma, vascular changes in lower extremities and in cancer patients. The mean time of use of catheter was 7 days. Tunnelization of the catheter was widely used in ICU practice.
Conclusions: Epidural anaesthesia has a place in Intensive Care practice in Poland. The use of this technique is restricted by hospital habits and costs. It is used mainly in acute pancreatitis, postoperative pain treatment and trauma.

P060

Electrocardiographic abnormalities in patients with cerebrovascular disease

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Critical Care 1998, **2(Suppl 1):**P060

Full text: Cerebral damage is frequently accompanied by ECG changes that consist mostly in repolarization disturbance in patients without coronary artery disease. Repolarization changes consist of sometimes dramatic ST segment elevations and inverted T waves in patients with normal hearts. These alterations resemble those of ischemic heart disease and may cause diagnostic mistakes.
We selected and studied 23 patients, 14 men and 9 women, mean age 63 ± 4 years, with recent stroke. Each patient underwent standard ECG, cardiac enzymes, M-mode and 2-D echocardiography and Doppler. On ECG, all patients presented inverted T waves and no alterations of ST segment. Cardiac enzymes were in the normal range and echocardiogram showed no wall motion abnormalities. Only 13 patients underwent coronary arteriography and all had normal coronary arteriograms.
Our findings confirm previous reports that associate acute cerebral accidents and repolarization abnormalities.
There is little information regarding a relationship between specific stroke location and disturbances in repolarization in humans, but there is substantial evidence that 'catecholamine storm', characterized by copious release of norepinephrine from cardiac β-1 receptor sites, during acute cerebral accidents is responsible for myocardial damage reflected in sub-endocardial injury.

P061

Sepsis: cause of late deterioration of intracranial pressure in patients with severe traumatic brain injury?

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Critical Care 1998, **2(Suppl 1):**P061

Introduction: Increased intracranial pressure (ICP) in patients with severe traumatic brain injury without findings of CT scan deterioration is frequently observed late during the course of treatment. The aim of this study was to evaluate the possible relationship between the late increase of ICP in head injured patients and the development of sepsis during their course on ICU.
Methods: 22 consecutive patients (median age 18) admitted to the ICU with severe traumatic brain injury (GCS < 8) and maintained according to a standard treatment protocol were retrospectively studied and divided into three groups. Group I (n = 6) were patients who developed no intracranial hypertension during their ICU stay, group II (n = 9) were patients with early intracranial hypertension and group III (n = 7) were patients who developed ICP deterioration on the 5th day or later after admission. Age, sex, initial GCS, incidence of secondary insults during first 24 hours after the injury, CT finding on admission, incidence of sepsis during the ICU stay, coincidence of sepsis with ICP deterioration, modified SOFA score (without neurological component) on the 2nd and 7th day of ICU stay, day of ICP deterioration and mortality in the groups were recorded. Fisher's exact test, t-test, and one way ANOVA test were used for statistical analysis (SigmaStat Statistical Software, Jandel Co., USA), P < 0.05 was considered statistically significant.
Results: No differences in age, sex, initial GCS, modified SOFA score on the 2nd day and incidence of secondary insults during first 24 h after the injury among groups were observed The overall incidence of sepsis was 33% (7/22 patients) and mortality rate was 22.2% (5/22 patients). The late intracranial hypertension was more frequently associated with the development of sepsis in group III (coincidence of sepsis and ICP deterioration in 1/9 patients in group II and 5/7 patients in group III, P = 0.035). Subsequent analysis in group III showed tendency to ICP deterioration in patients with sepsis compared to patients without sepsis (5/6 septic patients developed ICP deterioration compared to 2/5 nonseptic patients with ICP deterioration) but the difference did not reach statistical significance (P = 0.165).
Discussion: Frequent coincidence of late ICP deterioration and sepsis in patients with severe traumatic brain injury was observed. Late ICP deterioration could be in some cases the result of sepsis induced changes in vascular reactivity due to overproduction of NO and other vasodilatatory mediators.
Acknowledgement: Partially supported by grant IGA MZ CR 3672-3.

P062

Determinants of natriuretic peptides in early septic shock

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Critical Care 1998, **2(Suppl 1):**P062

Background and objectives: Circulating natriuretic peptides (atrial natriuretic peptide, brain natriurelic peptide) are sensitive indicators of the severity of heart failure. Comparable high plasma levels of natriuretic peptides has been found in severe heart failure (NYHA III-IV) and patients with septic shock (*Am Heart J* 1993, **126**:466–468). Impaired heart function, changes of cardiopulmonary hemodynamics and proinflammatory cytokines, ie interleukin-6 (IL-6) or tumor-necrosis-factor-α (TNF-α) might contribute to the modulation of natriuretic peptide release (*Am Heart J* 1997, **79**:1128–1131). Therefore, we studied the interrelation between IL-6, soluble TNF-receptors (TNF-R-p55, TNF-R-p75), atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) as well as heart function, cardiopulmonary and systemic hemodynamics in patients at the first two days following the diagnosis of septic shock.
Methods: Patients without acute renal failure (ARF) fullfilling criteria of septic shock (APACHE 28.4 ± 16.9; ELEBUTE 19.2 ± 4.2; n = 17). Determination of IL-6, TNF-R-p55, TNF-R-p75, ANP and BNP in plasma as well as cardiac index (CI), mean arterial pressure (MAP), right atrial pressure (RA), heart rate (HR), systemic vascular resistance (SVR) and mean pulmonary arterial pressure (PAP). Mean ± SD; r^2 = Pearsons correlation coefficient.
Results: IL-6 was significantly correlated to ANP (P < 0.01). During the first 2 days following diagnosis, IL-6 and ANP concordingly decreased (4033 ± 5657 vs 1978 ± 4751 pg/ml and 28.3 ± 16.6 vs 23.3 ± 15.1 pg/ml, respectively). BNP remained unchanged (12.4 ± 15.7 vs 12.8 ± 17.2 pg/ml), on both days inversely correlated to CI (P < 0.05). Accordingly, no significant differences of CI (4.5 ± 0.9 vs. 4.5 ± 1.0 l/min/m^2) or SVR (533.6 ± 136.9 vs 595.7 ± 210.2 dyn × s × cm-^{5}) could be determined. The fall of ANP from day 1 to 2 was independent of changes in RA (11.2 ± 4.2 vs. 11.8 ± 3.5 mmHg), HR (136.8 ± 27.2 vs. 142.4 vs. 62.6 bpm) or PAP (27.0 ± 6.6 vs 28.3 ± 4.6 mmHg). There was no significant change from day 1 to 2 of TNF-R-p55 (7.6 ± 3.5 vs 8.3 ± 6.0 pg/ml) and TNF-R-75 (11.0 ± 6.2 vs 12.9 ± 8.6 pg/ml). On day 2, ANP and BNP significantly correlated to CI (r^2 = -0.682 and r^2 = -0.574, respectively; P < 0.05), while CI inversely depend on SVR (r^2 = -0.801; P < 0.05). No significant negative correlation could be calculated between ANP, BNP and SVR or MAP.
Conclusions: Patients in early septic shock without ARF showed a directly correlated, concordant decrease of IL-6 and ANP independent of changes in RA, HR, PAP or CI. Vasodilative BNP release was inversely correlated to CI. Thus, interleukin-6 and left ventricular heart function might play a different role in the regulation of ANP- and BNP release in early septic shock.

P063

Prolonged hypernatremia safely controls elevated intracranial pressure in pediatric head injury patients

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Critical Care 1998, **2(Suppl 1):**P063

Introduction: The standard treatment of elevated intracranial pressure (ICP) includes the administration of hyperosmotic solutions. Osmolar diuretics

may lead to intravascular dehydration, hypotension, pre-renal azotemia and reduction of cerebral blood flow. Hypertonic saline solutions effectively reduce raised intracranial pressure in animals and humans without producing intravascular dehydration. We evaluated the degree of intracranial pressure control induced by the administration of 3% hypertonic saline (508 mOsms/l NaCl) in pediatric patients after traumatic brain injury.
Methods: We retrospectively reviewed the charts of 68 children who suffered traumatic brain injury with intracranial hypertension (ICP >20 mmHg). These patients received the conventional modalities for the treatment of intracranial hypertension including elevation of head (15°), pain control, hyperventilation, mannitol and sodium thiopentothal administration. In addition, they received continuous 3% saline infusions to reduce intracranial pressure below 20 mmHg. Hypertonic saline infusions were continuous and ranged between 2–7 days depending upon the patient's requirement for control of raised intracranial pressure.
Results: The mean dose of 3% saline was 17.23 ± 5 ml/kg/day. The highest, lowest and average serum sodium was 182, 140 and 158 ± 28 mEq/l respectively. The mean daily dose of mannitol was 2 ± 0.65 gm/kg/day. The highest, lowest and average serum osmolarity was 380, 276 and 316 ± 39 mOsm/l respectively. The mean serum creatinine was 0.7 ± 0.3 mg/dl. The intracranial pressure averaged 20 mmHg 92% of the time, 20–30 mmHg 7% and greater than 30 mmHg 1% of the time during the first seven days post injury. Ten (15%) of 68 patients expired. However only two (3%) children died of uncontrolled intracranial hypertension.
Conclusions: We conclude that administration of 3% hypertonic saline to pediatric brain injured patients with elevated intracranial pressure in conjunction with standard treatment modalities results in effective control of intracranial pressure. Hypernatremia and hyperosmolarity are safely tolerated in brain injured pediatric patients.

P064

Disorders of the effective osmolality in central nervous system injury

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Critical Care 1998, **2(Suppl 1):**P064

Full text: Disorders of the effective osmolality regulation are frequent in the cerebral affections that originate from trauma, vascular disease, imflamation or tumors. Hypo-osmolality and hyponatremia are presented in two different states: Inappropriate Vaseopressin Secretion Syndrome (IAHDS) and Cerebral Salt Wasting Syndrome (CSWS). Quick differential diagnose is important because the treatment of both syndromes is essentially different. Typical cause of hypernatremia is central diabetes insipidus (DI). The group of available calculated renal function parameters is applied in the differential diagnosis of these syndromes. They are creatinine clearance, excretion fraction of water and sodium, electrolyte clearance and electrolyte free water clearance. Investigation of ADH and natriuretic pepride could be even misleading. Pathophysiologic consequence of the state given by inappropriate elevation of one hormone can be the elevation of the second one.
The mentioned topic is documented with the four selected patients from the ICU. The syndromes were diagnosed using the computer program evaluating renal functions by means of 13 routinely monitored values and 12 output parameters.
Authors present brief clinical courses, biochemical results and calculated renal function parameters by one patient with the IADHS, by one with DI, by one with CSWS passing over to DI and by one with DI passing to IADHS. The importance of complex access to evaluation of renal functional parameters is stressed. These are influenced by actual therapy, eg by diuretics or osmotherapy.
Conclusions: Mentioned four cases are the example of the effective use of the currently investigated values in the diagnosis and monitoring of the effective osmolality disorders in cerebral affections.

Table (abstract P065) Perfusion pressure decrease (kPa) after a ANP administration (mean values ± SD)

Group	30-32 min	45-47 min	60-62 min	75-77 min
I Preeclampsia	1.01 ± 0.17	1.49 ± 0.22	1.99 ± 0.23	2.33 ± 0.39
II Normal pregnancy	0.94 ± 0.2	1.22 ± 0.19	1.43 ± 0.26	1.79 ± 0.24

P065

Perfusion pressure changes after ANP administration in preeclampsia: *in vitro* study

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Critical Care 1998, **2(Suppl 1):**P065

Introduction: Regulation of the blood flow in human placental tissue by changes of the vascular resistance is very particular, because of lack of sympathetic innervation in placental vessels [1]. The number of guanylate-coupled receptors in placental (issues, corresponding to ANP-receptors, has been found to be greater in preeclampsia, than in normal pregnancy [2]. The aim of the study was to investigate the influence of various doses of atrial natriuretic peptide (ANP) on perfusion pressure in preeclampsia.
Methods: Heparinized placentas (n = 14) obtained after preeclamp tic (n = 7; 1st group) and normal (n = 7; 2nd group, control) pregnancies delivered at term by cesarean sections were perfused *in vitro* using modified Cedard manner. Perfusion pressure, measured continuously, was the main parameter of the vascular status changes. The placental vessels were submaximally preconstricted by continuous infusion of the nitric-oxide synthase inhibitor N-?)-nitro-L-arginine (NOLA; 100 µmol/l, 10 min). Over 120 min depending on the period of experiment (30, 45, 60, 75 min) human synthetic aANP were administered (25, 50, 100, 200 nmol/l, 2 min increments).
Results: Mean value of perfusion pressure increase after NOLA infusion was 5.63 kPa (± SD 0,36), the differences between groups I and II did not reach statistical significance.
Conclusion: The responsiveness of the fetoplacental vasculature to the ANP given in higher doses (100, 200 nmol/l, 2 min increments) is increased in preeclampsia (P < 0.05).
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P066

Management of subarachnoid hemorrhage patients: is early surgery better than delayed?

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Critical Care 1998, **2(Suppl 1):**P066

Full text: There is no general consensus with regard to management of subarachnoid hemorrhage (SAH) patients. Early surgery has been advocated in order to minimize the rebleed risk, however it is more hazardous than delayed surgery, because the brain is tight and swollen, and the risk of vasospasm and infarction is increased.
The purpose of this retrospective study is to present our experiences in management of SAH patients. Between 1990–1995, 196 (59.4%) female and 134 (40.6%) male patients were admitted to our unit due to sudden onset of a headache. Subarachnoid hemorrhage was proven by CT scan and/or lumbar puncture and in 161 (48.8%) patients, three-vessels angiography showed one or more aneurysms. The conservatively treated group of SAH patients was statistically older than surgically treated group (P = 0.002). There was no statistically significant difference regarding age between male and female patients in both treated groups. Average

timing of aneurysm surgery was 73.9 ± 75.5 h after the onset of bleeding (range: 4–550 h).
All but 20 patients (all conservatively treated) received nimodipine to prevent or treat vasospasm. In 14 (4.2%) patients vasospasm was seen on angiograms and 34 (21.1%) patients developed clinically significant vasospasm postoperatively between days 3–5. Mortality rate in conservatively treated group was 23.1%, and in surgically treated group 5%.
We conclude that early surgery (between days 1–3) is better, however it is more hazardous due to higher risk of vasospasm. Rebleed was the major problem in conservatively treated group of SAH patients, but over all outcome was better.

P067

Low albuminemia on vasospasm following subarachinoid hemorrhage (SAH)

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Critical Care 1998, **2(Suppl 1):**P067

Introduction: The aim of this study was to determine the mechanism of low albuminemia on vasospasm following subarachnoid hemorrhage (SAH).
Patients and methods: We evaluated the changes in serum and urinary NAG, and renin-angiotensin substances (RAS) [plasma renin activity (PRA), angiotensin I and II] on day 1, 3, 7 and 14 following SAH. The subjects were 43 patients with SAH, who were classified as Group 1 [vasospasm (+)] and Group 2 [vasospasm (-)] according to the angiography findings between days 5 to 7 after the clipping operation. We performed hypervolemic and hypertensive therapy from day 3 to prevent vasospasm.
Results: We observed a significant decrease in serum albumin, and an increase in urine albumin and NAG in both groups from day 3, and a significantly higher amount of urinary albumin and NAG in Group 1 in comparison with data in Group 2. We also observed a significant increase of PRA and angiotensin I in both groups from day 3, and a significantly higher amount was observed in Group 1 than in Group 2. A significant increase in angiotensin II was observed in both groups on day 3, but we did not observe any significant difference between the two groups. All the RAS data was within the normal range.
Conclusions: An increase in renal concentrations of NAG is recognized as renal tubular dysfunction in vasospasm Group 1. We concluded that higher concentrations of urinary albumin related to renal tubular dysfunction is one of the causes of low albuminemia on vasospasm.

P068

Monitoring of hypervolemic hemodilution and hypertensive (HHH) therapy in subarachnoid hemorrhage (SAH) patients with pulmonary artery catheter (PAC)

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Background: Cerebral arterial vasospasm continues to be a major complication of aneurysmal SAH. Prophylactic HHH therapy may be beneficial reducing delayed ischemia after early aneurysm clipping. Minimal standards of monitoring are not well defined.
The aim of our study was to evaluate the contribution of PAC and cranscranial Doppler (TCD) monitoring during HHH-therapy in patients with SAH after early operative intervention.
Methods: We observed 37 ICU patients with SAH during HHH therapy. All patients received hypervolemic hemodilution therapy aiming for a hematocrit of 33–38%, 10–12 mmHg central venous pressure (or 15–18 mmHg pulmonary wedge pressure), and 160–200 mmHg systolic arterial pressure during the risk period for vasospasm. We evaluated clinical findings, PAC values and mean flow velocity (MFV) on both middle cerebral arteries (MCA).
Results: Outcome correlated with clinical state on admission (Fisher-exact test, $P < 0.05$). A constantly elevated systemic vascular resistance (SVR) was associated with a good outcome while declining SVR during clinical course with a poor outcome (analysis of variance for repeated measurements, $P < 0.05$). A successful HHH therapy according to the above hemodynamic criteria did not reduce occurrence of vasospasm (Fisher-exact test). In patients without vasospasm (MFV ≤ 140 cm/s, $n = 16$), we were able to develop a multiple regression model that explained 44% of variance of MFV by consideration of SVRI and hematocrit.
Conclusion: SVRI monitoring and manipulation using PAC during HHH therapy may affect outcome positively. An association of MFV with SVRI and hematocrit could be demonstrated.

P069

Diagnostics and treatment algorythms of acute brain injury period

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Critical Care 1998, **2(Suppl 1):**P069

Full text: On the basis experience in 137 patients treatment we elaborated working classification of acute brain injury period which made it possible to compose diagnostic and intensive care algorithms. The classification is based upon the determination of main pathophysiological processes characterizing the duration of the acute injury period and takes into account stress reaction, primary reperfusion, cerebral edema, recurring reperfusion, adaptation as well as the display of the processes upon the evaluation of patient state severity (compensated, subcompensated, decompensated, terminal).
Patient state of severity was evaluated on the basis of remaining capacities of the vitally important patient organs and systems (central nervous system according to Glasgo coma scale, vegetative nervous system state — cardiointervalography, cardiovascular system, respiratory system, homeostasis systems — by Appache II scale). The classifications we present takes into account the dynamic complex pathophysiological processes taking place in patient organism, and gives an opportunity of fast change in main accents of intensive care. Diagnostics and treatment algorithms on the basis of the present classification with the other modern methods of surgical treatment allowed to improve the posttreatment outcomes, to reduce early (till 10 days) lethality in the acute brain injury period by 8%.

P070

Cranial computed tomography in the emergency evaluation of adult patients without a recent history of head trauma: a prospective analysis

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Critical Care 1998, **2(Suppl 1):**P070

Objectives: To examine the pattern of nontrauma cranial CT use in an urban ED, to identify the rate of significant CT abnormalities in headache, and to develop criteria for restricting the ordering of CT scans.
Methods: A prospective, observational study of a case series of adults who underwent cranial CT scanning for non-traumatic headache was performed at the ED of an urban teaching hospital with an annual census of 55 000. Clinically significant CT scans were defined as: 1) acute stroke, 2) CNS malignancy, 3) acute hydrocephalus, 4) intracranial bleeding or 5) intracranial infection. X2 recursive partioning was used to derive a decision rule to restrict ordering of CT scans.
Results: Only 12 (4%) of 291 CT scans revealed clinically significant abnormalities. The presence of headache with vomiting was 100% sensitive (95%CI: 74–100%) and 49% specific (95%CI: 43–56%) in

detecting clinically significant CT scans. This set of features had positive and negative values of 8%(95%CI: 4–13%) and 100% (95% CI: 97–100%), respectively.

Conclusion: Clinically significant CT abnormalities were uncommon in the headache patients population, suggesting that current criteria for ordering nontrauma cranial CT scans may be too liberal. In this study, a set of clinical criteria was derived that may be useful at separating patients into high- and low-risk categories for clinically significant cranial CT abnormalities. Before these results are applied clinically, these criteria should be validated in larger, prospective studies.

P071

Cerebral blood flow velocities in hypoxemic patients

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Full text: According to the literature, in normocapnic hypoxia cerebral blood flow (CBF) increases in order to maintain a steady oxygen (O_2) delivery as well as to prevent a significant drop in cerebral venous O_2 tension. The aim of the present study is to investigate transcranial Doppler (TCD) velocitometric patterns in hypoxemic patients. CBF velocity was evaluated before and after inhalation of an O_2 enriched mixture in order to detect differences in O_2 delivery when chronic hypoxia was corrected. Eight patients (mean age 71.4 ± 2.2 yrs) with respiratory failure (RF) (hypoxemia without hypercapnia), were studied before starting a long-term oxygen therapy. None had a history of cardiovascular and/or hematologic diseases. A group of 8 healthy subjects, matched for age and gender, were also studied as reference group. Both patients with RF and normal subjects underwent a CBF velocity measurement, in supine position, by using TCD (Quantascope, Toshiba T2100, Vital Science, Amsterdam, The Netherlands) both in basal conditions (while breathing room air) and during the inhalation of an O_2 enriched mixture through a Venturi mask for at least 30 min. Heart rate was recorded and arterial blood gases were measured with a emogasanalyzer ABL-330 (Radiometer, Copenhagen) before the assessment of CBF velocity both in basal conditions and during the inhalation of the O_2 enriched mixture. A significant increase of PaO_2 and SaO_2 during the inhalation of the O_2 enriched mixture in comparison with basal conditions was found both in patients with RF (PaO_2: 54.1 vs 84.9 mmHg, $P = 0.004$; SaO_2: 86.6 vs 95.8%, $P = 0.003$) and in normal subjects (PaO_2: 82.9 vs 112.2 mmHg, $P = 0.0004$; SaO_2: 95.6 vs 97.8%, $P = 0.003$). The CBF velocities decreased in both groups (32.2 vs 27.9 cm/s, $P = 0.011$ in RF patients; 29.8 vs 19.9 cm/s, $P = 0.0003$, in normal subjects). However, the reduction of CBF velocities was lower in RF patients in comparison with the normal subjects (-4.3 ± 3.5 vs -10 ± 4.4 cm/s, respectively, $P = 0.012$).

In conclusion, the lower decrease of the CBF velocities in RF patients during the inhalation of an O_2 enriched mixture seems to indicate that chronic hypoxia induces a quite maximal vasodilatation to protect CBF and, thus, to maintain an adequate O_2 delivery to the brain.

P072

Use of single photon emission computed tomography (SPECT) in the follow-up of carbon monoxide poisoned patients treated with HBO therapy: a case report

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Full text: It is widely known that carbon monoxide (CO) has the toxic effects of tissue hypoxia and produces acute neurologic deficits and a severe neurologic reaction may be delayed for days or week after anoxic exposure. The prediction of outcome during the acute stages or the latest period is difficult in most cases because of variations in age, previous state of health, duration and severity of exposure, individual susceptibility and manner of treatment.

The initial laboratory findings do not provide any prognostic clues and attempts at further predicting the clinical outcome of acute CO poisoning by means of brain CT scan or other tests have remained unsuccessful. SPECT provides tomographic images of cerebral perfusion and it has been used in clinical practice.

We experienced two cases of CO poisoning in which SPECT was performed 1 month later from acute poisoning; they had different outcome and the clinical situation was directly related to SPECT imaging results.

The patients were a mother and her son, age 55 and 25 years, who were accidentally poisoned by a domestic bath heater. They were found unconscious at home and their GCS (Glasgow Coma Score) upon their arrival in the hospital was 3. Both patients were referred to our facility and improved greatly after HBO treatment (90 min at 2.8 ATA and 30 min at 1.9 ATA); the younger was almost totally awake and the older took a little bit longer period for regaining consciousness. The MRI in both cases showed edema and necrosis in both pallidi globi. Clinically, the younger recovered fully and the older had mild neurologic sequelae as ataxic walking and light dizziness, the last one disappeared in few days. They were treated for a total of 20 sessions of HBO at 2 ATA for 60 min.

The SPECT brain imaging was totally negative for the younger and showed a bilateral decrease of blood flow in the subcortical motor nuclei in the older patient.

We can conclude that SPECT imaging is more sensitive and more directly related with the clinical picture of the patient than MRI and we are strongly convinced to use this diagnostic test in all cases of severe carbon monoxide poisoning.

P073

The effects of diaspirin crosslinked hemoglobin (DCLHb) on oxygenation, perfusion and resuscitation: preclinical experience

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Full text: Preclinical studies of DCLHb, a highly solution of stabilized human hemoglobin tetramers, in animals with normovolemic hemorrhagic shock have demonstrated its ability to quickly restore mean arterial blood pressure, base deficit, and subcutaneous and mucosal pO_2 to baseline levels or higher. In addition, DCLHb has been shown to be capable of preserving normal gut architecture, decreasing bacterial translocation, increasing blood flow to key tissues and organs, and decreasing mortality in some models.

Administration of DCLHb to hemorrhaged animals may serve to create a small shift in blood flow from the muscle, resulting in a large increase in flow to vital organs. This shift may have a significant beneficial effect in certain indications, such as shock, and result in maintenance of vital organ perfusion. A further study of DCLHb as a low-volume resuscitation agent in severe hypovolemic, hemorrhagic shock in pigs demonstrated the agent's ability to improve gut microvascular oxygenation. In this study, palladium porphyrine phosphorescence was used as a marker of microvascular pO_2, the results indicated that DCLHb restores microvascular oxygenation to pre-hemorrhagic levels.

The studies outlined above and others have shown the ability of DCLHb to maintain vital organ perfusion consistently. This property of DCLHb may be explained in part by examining its pharmacological characteristics. For example, DCLHb has a pressor effect, involving a number of different autocrine systems in the body, including interactions with nitric oxide, endothelin, and the α-adrenergic system. DCLHb appears to work through multiple endogenous systems and mechanisms, each of which probably interact.

In summary, studies in animal models of hemorrhagic shock indicate the DCLHb has oxygen-carrying capabilities similar to fresh blood and has the potential to treat blood loss and ischemic situations, such as hemorrhagic shock, in humans. Trials are underway to investigate the safety and efficacy of DCLHb in such patient populations.

P074

Intraoperative administration of Hextend® versus 6% Hetastrach in saline for the treatment of hypovolemia during major surgery: preliminary results of a randomized clinical trial

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Critical Care 1998, **2(Suppl 1):**P074

Introduction: Hextend® is a new 6% hydroxyethyl starch (mean molecular weight 550 Kd) in a balanced and buffered electrolyte and glucose solution intended for use as a plasma expander. In animal models Hextend® appears to offer significant advantages over currently available alternatives (e.g Hespan®) in terms of acid/base/electrolyte/glucose balance and survival. Hextend can potentially serve as an economical, sterile, physiologically-balanced replacement for blood volume lost subsequent to trauma related bleeding. It may also be used to induce mild to moderate hypothermia in order to prolong survival time during transport to a critical care center. We report here the preliminary results of the on-going phase III study of Hextend®.
Methods: Following Institutional Review Board approval and informed patient consent, patients undergoing major elective surgery were enrolled at The Mount Sinai Medical Center (NY, NY) and Duke University Medical Center (Durham, NC) in a prospective, randomized, blinded clinical trial. Lactated ringers crystalloid was used as a maintenance fluid intraoperatively as follows: 7 ml/kg prior to induction of general anesthesia followed by an infusion of 5 ml/kg/h. Intraoperative hypovolemia was treated with 250 ml doses of either Hextend® or 6% hetastarch in saline. Where appropriate data (unaudited) are presented as median, mean ± SD, and range.
Results: Data from 117 patients are presented. Procedure types were major urologic (37.6%), major general (42.7%), major gynecologic (17.9%), and major orthopedic (1.7%). Postoperative length of stay (days) was 6, 7 ± 5,1–34. Duration of anesthesia (minutes) was 307, 315 ± 126, 90–780. Estimated blood loss (ml) was 800, 1161 ± 1331, 20–7300. The amount of study fluid administered (6% hetastarch of either type) was 1250, 1510 ± 1016, 0–5000. 38.5% of patients received the study fluid in excess of 20 ml/kg. No serious and unexpected adverse events related to the study fluid were observed in the study cohort.
Conclusions: Hextend® is a novel plasma volume expander presented in a balanced and buffered electrolyte and glucose solution. Data analysis and unblinding from this clinical trial will be completed soon and will be presented at this conference.

P075

Hypertensive reaction to a certain batch of albumin 5%: a case report

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Critical Care 1998, **2(Suppl 1):**P075

Case report: A 39-year-old female patient underwent maxillo-facial surgery for resection of a tumor adjacent to the mandible. General anesthesia was induced and maintained with propofol and sufentanil. After two thirds of the mandible and the tumor had been resected, and a reconstruction of the mandible by means of a vascularized fibular graft and a musculocutaneus graft from the wrist was taking place, an unexpected blood pressure reaction after an infusion of albumin 5% solution (HSA 5) occured. Up to this point cristalloids (5500 ml), colloids (HES 10%; 1000 ml), 8 units of PRCs and 4 units of FFP had been infused due to presurgical anemia and a blood loss of 2000 ml. An infusion of HSA 5 (Behringwerke-Centeon; Marburg; Germany; batch-no.: 254031) was started. After a few minutes, the arterial blood pressure (aBP) increased from 123/80 to 163/99 mmHg with a concomitant fall of heart rate (HR). The albumin infusion was stopped. No injections of local anesthetics containing vasopressors were carried out by the surgeons and no inotropic drugs were infused. After aBP and HR had returned to base line values, the HSA 5 infusion was started again and, after 50 ml had been infused, aBP increased again from 118/76 to 162/96 mmHg. The albumin solution was stopped and substituted by two other units of HSA 5 (batch-no.: 263021) of the same manufacturer, which were infused without any substantial effect on blood pressure. Therefore a fourth unit of HSA 5 from the batch (no.: 254031), which initially had lead to the aBP-abnormalities stated above, was started; aBP increased again from 103/64 to 166/91 mmHg. The infusion was cancelled, the remaining solutions were stored for analyses, the patient was transferred to the ICU and recovered uneventfully.
Discussion: These unexpected cardiovascular reactions lead us to report an 'adverse drug effect' to the manufacturer, whose analyses revealed no bacterial or chemical contaminations. He stated, that this hypertensive reaction may be classified as 'slight', that increases of aBP after infusion of human albumin would be well known, and that detecting such an effect only after a certain batch of HSA 5, might be ascribed to the variability in reactions to biological products. A survey of the literature on this topic was not conclusive [1]. With respect to the fact, that such effects might be overseen (especially in emergency situations) we recommend to monitor patients receiving albumin preparations closely.
Reference

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P076

The use of lithium dilution for measuring cardiac output and shunt fraction in patients during venovenous extracorporeal membrane oxygenation: a feasibility study in a flow model

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Critical Care 1998, **2(Suppl 1):**P076

Background: Increasing numbers of adult and pediatric patients are being treated with venovenous ECMO using double lumen catheters. One of the major limitations of these catheters is the recirculation of arterialised blood back into the ECMO circuit, rather than passing through the right heart and pulmonary circulation. This shunt fraction may amount to 50% of the total flow of the ECMO circuit and the management of these patients has been hindered by the absence of a simple clinical method for measuring cardiac output and this shunt fraction. We have previously described a method of measuring cardiac output in which lithium chloride is injected intravenously and its plasma

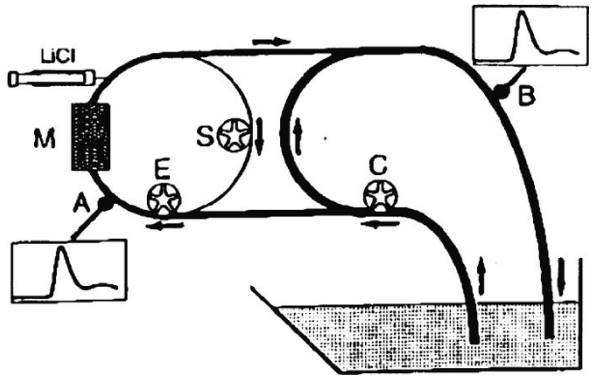

Figure 1 (abstract P076) Diagram of the flow model. Pump C representing the cardiac output was set up to draw 3 l/min from the 50 l bucket of saline. Some of this flow passed via the ECMO pump (E) through the membrane oxygenator (M) and then either recirculated through the ECMO circuit via the shunt pump (S) or returned to the bucket. LiCl injections were made just downstream of the oxygenator and dilution curves were recorded simultaneously by the sensors A and B.

Table (abstract P076). Results for the 9 injections (l/min)

Pump C	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Calculated 'cardiac output'	3.0	3.1	3.2	2.8	3.2	3.1	3.0	2.9	2.6
Pump E	0.52	0.52	0.52	1.01	1.01	1.01	2.0	2.0	2.0
Pump S	0.06	0.12	0.25	0.12	0.25	0.5	0.25	0.5	1.0
Calculated shunt flow	0.07	0.14	0.26	0.15	0.25	0.53	0.32	0.57	1.1

concentration-time curve measured in arterial blood using a lithium-selective electrode [1].

Methods: The patient circulation and ECMO circuit were represented by a flow model (Fig. 1). Pump C was set at 3 1/min throughout. Pump E (ECMO) and S (shunt) were varied to provide 3 shunt fractions, (approximately 12, 25, 50%) at each of 3 ECMO flow rates (approximately 0.5, 1.0 and 2.0 l/min). Following a bolus injection of lithium chloride (0.15 mmol), its dilution curves were recorded simultaneously by sensors A and B (see Fig. 1). The flows through pump S and pump C were calculated from the 9 pairs of lithium dilution curves and compared to the actual flows delivered.

Results: This method would be suitable for adult and pediatric patients (in whom a smaller dose of lithium would be given). Although cardiac output could be measured during ECMO if the lithium was injected into the pulmonary artery, the proposed method avoids pulmonary artery catheterisation and allows shunt flows to be calculated.

Reference

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P077

Cardiac output estimation with transesophageal Doppler

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Critical Care 1998, **2(Suppl 1):**P077

Background: Transesophageal Doppler monitoring provides continuous, non invasive monitoring of cardiac output by measurement of aortic flow velocities. The first transesophageal monitors developed for clinical use performed inconsistently in anesthetized patients and thus failed to gain wide clinical acceptance [1,2]. A second generation of transesophageal Doppler improved performance compared to the first generation, even if it was still unsuitable to accurately measure absolute cardiac output values [3].

Material and methods: A new developed transesophageal Doppler device for cardiac output estimation (COdopp) monitoring (ODM II, Abbott, USA), which displays aortic blood flow velocity in real time, was prospectively evaluated in 7 critically ill patients. One patient was a COPD with an acute heart failure, the second was abdominal aortic aneurysm post-operative with multiple organ failure, the third a politrauma, and the last a comatose patient affected by an intracerebral hemorrhage. The aim of the study was to assess the reliability and accuracy of this Doppler device, in comparison with the thermodilution method. A 7.5-Fr pulmonary catheter (Abbott, USA) was inserted via left succlavian vein in the 4 patients, and, after hemodynamic stabilization, a Doppler probe was positioned in esophagus, following Doppler signals of discending aorta. To estimate cardiac output, diameter of aorta was automatically calculated from a nomogram based on patient characteristic, including sex, age, height and weight. As reference standard, thermodiluition CO measurements (COtd) were obtained using iced temperature injectate and a dedicated, calibrated computer (Horizon 2000, Mennen). During a 5-min period where the mean arterial pressure variation was less than ± 5 mmHg, repeated simultaneous COtd and COdopp measurements were obtained and defined an epoch. An epoch was accepted for analysis when three CO values with less than 15% variation, largest to smallest, were obtained for each method of CO determination.

Results: 51 couplets of data were obtained. Hearth rate range was 56-124. Cardiac output range measured by thermodiluition was 3.4-11.5 while CO range measured by Doppler was 3.6-11.2. Linear regression was good (COdopp = COtd × 0.9155 ± 0.7334; $r = 0.9745$ and $P < 0.0001$; $r^2 = 0.9496$). Bland and Aitman test [4] showed an acceptable difference of the two standard deviation range of 1.56 l/min (bias = 0.141176 ± 0.389449 l/min [SD]).

Conclusion: Compared with previous results these data improved the reliability of the new transesophageal Doppler to measure absolute value of cardiac output. Further studies are needed to confirm the accuracy of this new transesophageal Doppler device in hemodynamically instable patient.

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P078

Femoral artery catheterisation for cardiac output measurement using the femoral artery thermodilution technique does not compromise limb perfusion

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Critical Care 1998, **2(Suppl 1):**P078

Background: Measurement of cardiac output and extra-vascular lung water in patients with Acute Respiratory Distress Syndrome receiving vasopressors involves femoral artery catheterisation through a 4.5-Fr sheath, with potential risk of vascular compromise to the limb. Scanning laser Doppler flowmetry is a new non-invasive technique for assessing tissue blood flow, making up to 250 point measurements of perfusion per second as a laser is scanned over a surface, creating a grey scale photographic and a colour perfusion. We have used this technique to assess pedal skin perfusion following Femoral artery catheterisation in addition to standard clinical evaluation.

Method: 10 intubated, ventilated and sedated patients without clinical evidence of peripheral arterial disease were randomised to right or left leg

Table (abstract P078)

Perfusion Units (PUs)	Pre mobilisation	Immediately post-insertion	24 h post-insertion
Insertion	230.5	205.7	217.1
legs	(21.5-592)	(19.3-621.7)	(29.6-467.9)
Non-insertion	218.1	188.8	219.9
legs	(19.3-586)	(19-601.8)	(29.7-410.5)
Insertion minus	12.46	16.8	-2.9
non-insertion legs	(-67.2 to 17.5)	(-41 to 142)	(-22.7 to 198)

catheterisation (Pulsiocath 2024L, Pulsion, Munich, Germany). 9 were receiving vasopressors (Noradrenaline 0.03–0.48 µg/kg/min, Adrenaline 0.09–0.8 µg/kg per min). Room temperature was constant and both legs were uncovered for 15 min equilibration. Measurements were made before and after insertion, and at 24 h. Laser Doppler scans (Moor LDI, Moor Instruments Ltd, Axminster, Devon, UK) of the plantar aspect of the feet, and systemic mean arterial and maximum calf occlusion pressures were recorded. The sole of the foot was outlined from the photographic image, allowing calculation of mean perfusion units (PUs) from the corresponding perfusion image (>17 000 individual perfusion measurements).
Results: Mean systemic and occlusion pressures, and skin perfusion were unchanged between legs, and between measurement time points, following insertion of the catheters. Mean biases prior to, immediately after and 24 h following catheterisation were 12.46, 16.35 and 2,85 PUs (95% confidence intervals -36.2 to 61.1, -17.9 to 50.6 and -48.7 to 54.4 PUs) respectively. The limits of agreement were -132.5 to 157.4, -85.3 to 119 and 156.7 to 151 PUs.
Conclusions: Femoral artery catheterisation for double-indicator dilution measurements does not reduce calf occlusion pressures or foot skin perfusion in patients receiving vasopressor drugs. Scanning laser Doppler flowmetry is easily used to assess changes in foot perfusion and the effect of interventions that may reduce blood flow to the skin of the foot.

P079

Measurement of cardiac output in infants less than 10 kg: accuracy of femoral artery thermodilution as compared to direct Fick

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Critical Care 1998, **2(Suppl 1):**P079

Introduction: Femoral artery thermodilution (FATD) has proven a useful technique for the measurement of cardiac output (CO) in children as it avoids the problems associated with pulmonary artery catheterisarion by placing the thermistor in the femoral artery. We wished to evaluate the accuracy of FATD using a commercially available device (COLD Z-021, Pulsion, Munich) amongst infants less than 10 kg.
Methods: 20 ventilated infants were studied following cardiac surgery, median weight 4.7 kg (range 2.5–10 kg). Absence of anatomical shunt was confirmed with Doppler Echocardiography. When haemodynamically stable, a 1.3 Fr thermistor was placed into the femoral artery via a percutaneously placed 22 gauge cannula. Five consecutive FATD measurements were made using iced 5% Dextrose solution (1.5 ml + 0.15 ml/kg body weight) given via a central venous cannula, then averaged. Over the same time period CO was also measured utilising the Fick principle, with O_2 consumption measured by a metabolic monitor (Deltatrac, Datex, Helsinki). Cuffed endotracheal tubes were used if air leaks of >5% of inspiratory tidal volume were present. Arterial and mixed venous O_2 contents were calculated using co-oximetry.
Results: There were no line related complications. Mean Fick CO was 0.77 l/min (range 0.32 to 2.21) mean FATD CO was 0.76 l/min (range 0.28 to 2.05). The mean bias was 0.009 l/min (95% confidence interval -0.03 to 0.05) with limits of agreement (mean bias ± 1.96 sd) of -0.15 to 0.17 l/min. The mean FATD coefficient of variation was 5.6%.
Conclusions: FATD is a safe, reproducible, clinically acceptable technique for bedside CO measurement in ventilated infants.

P080

Time course evolution of ventilatory response to inspiratory unloading in patients

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Critical Care 1998, **2(Suppl 1):**P080

Introduction: Inspiratory unloading decreases ventilatory drive and work of breathing in patients undergoing mechanical ventilation. We examined the time course of this effect in patients receiving permanent ventilatory support, provided by pressure support ventilation (PSV), or intermittent ventilatory support, provided by biphasic positive airway pressure (BIPAP).
Methods: Two sets of measurements were taken from 8 COPD patients durign the period of weaning from mechanical ventilation: First, during spontaneous breathing, then during the first 15 respiratory cycles following the onset of PSV; second, during BIPAP set in such a manner that one spontaneous breath took place between two pressure-assisted breaths. The following variables were measured: VT, PO.1, mean transdiaphragmatic pressure (Pdi), inspiratory work (Wi), and diaphragmatic electrical activity (EMG-di).
Results: The first breath following the onset of PSV was associated with an increase in VT and a drop in Pdi and Wi performed per liter, with unchanged values of PO.l, Wi performed per breath, and EMG-di. The same phenomena were observed for the assisted breath of BIPAP as compared to the preceding spontaneous breath. During the subsequent breaths of PSV; PO.l Wi, and EMG-di decreased progressively up to the sixth to eighth breath, and VT returned to pre-PSV values.
Conclusion: The decrease in ventilatory drive associated with PSV takes place from the first breath onwards, but requires 6 to 8 breaths to be fully achieved. This transient period could explain the characteristics of the pressure-assisted breaths intermixed with spontaneous breaths during BIPAP ventilation: an increased VT for an unchanged work per breath, suggesting an enhanced inspiratory efficiency.

P081

Interactive ventilation: first experience with patient controlled weaning by using a Siemens-SV 300 Automode® ventilator

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Critical Care 1998, **2(Suppl 1):**P081

Introduction: The new Siemens SV-300 A ventilator switches automatically between control and support mode of ventilation. At the first sign of respiratory effort, the ventilator allows the patient to breathe spontaneously with a preset pressure or volume support. In case of apnea, the ventilator automatically changes to a preset volume or pressure control mode. In our study the combination of pressure control and pressure support mode was used. 20 patients (pts) who underwent brain tumor surgery were randomized either to the Automode®-Group (*n* = 10, age 24–76 years, mean 49.7) or to the conventional weaning procedure with manually regulated SIMV-mode (Manual Mode, *n* = 10, age 22–70, mean 47.9) immediately after entering the ICU. Time from entering the study to extubation (weaning time) was measured. PCO_2-Levels during the weaning period were measured for each patient in fixed time intervals. The number of manipulations on the respirator during the whole weaning period was counted for each patient.
Aim of the study: Identification of malfunctions, cases of apnea and comparison of average weaning time, pCO_2 levels and number of manipulations necessary during the weaning period.

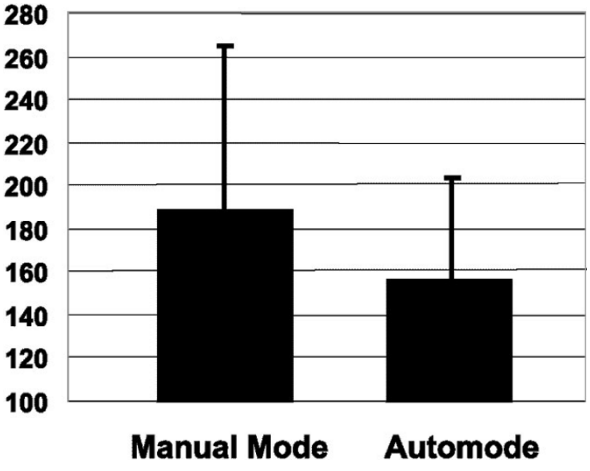

Figure 1 (abstract P081) Average weaning time (minutes, 10 pts each group with STD).

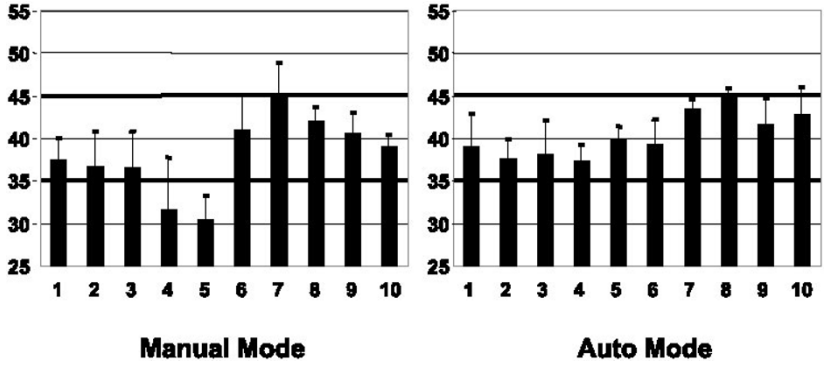

Figure 2 (abstract P081) Mean pCO_2-levels during weaning period (mmHg with STD for each patient).

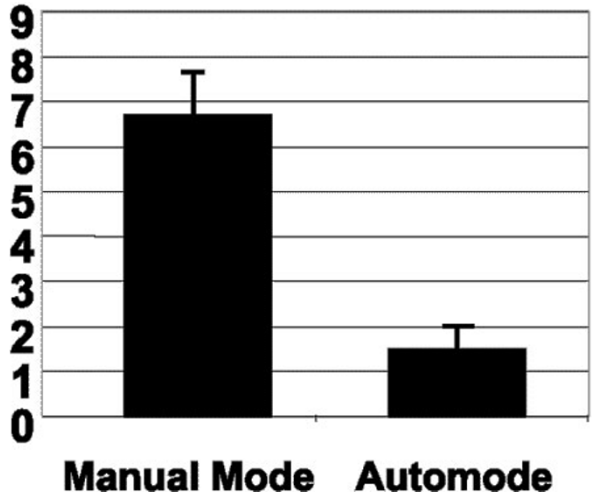

Figure 3 (abstract P081) Average number of manipulations.

Results: In the Automode®-Group no malfunctions or cases of apnea were observed. Average weaning time was shorter in the Automode®-Group (Fig. 1), pCO_2-levels seemed to be more stable (Fig. 2). The number of manipulations on the respirator were significantly lower in the Automode®-Group (Fig. 3).

Conclusions: With the new Automode®-option weaning seems to be more comfortable for the patient and the staff taking care. Automode® is an approach to adapt the machine to the patient and not the patient to the machine. Spontaneous ventilation is possible at an early point and at every time during the whole weaning process. PCO_2 levels seem to be more stable as a sign of a better adaptation to the patients ventilatory needs. Shortening of the total weaning time seems to be possible. Significant reduction of alarm beeps and consecutively less manipulations on the respirator (no apnea alarm, no struggling with SIMV-mode) reduce stress for the nursing staff.

P082

Mechanical ventilation effects on distal organs: preliminary reports

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Critical Care 1998, **2(Suppl 1):**P082

Full text: In order to test systemic effects of mechanical ventilation, we studied organs 'distal' to the lung by means of an *in-vivo* animal model. A total of 22 Sprague Dawley rats were anesthetized, curarized and mechanically ventilated (Harvard Rodent, mod. 683). Once total lung capacity was estimated (8 rats), a total of 7+7 rats were randomized to receive tidal volume of 25% and 75% of inspiratory capacity (CI), respectively. Ventilation strategies were: a) 25%CI (9.8 ± 0.7 ml/kg), respiratory rate (RR) 57.8 ± 5.9 bpm, positive end expiratory pressure (PEEP) 4.29 ± 0.64 cmH_2O, mean airway pressure (Paw_m) 6.96 ± 0.61 cmH_2O, peak inspiratory airway pressure (Paw_p) 13.4 ± 2.12; b) 75%CI (31.3 ± 3 ml/kg), RR 18.3 ± 3.3, PEEP zero, Paw_m 6.13 ± 0.53, Paw_p 28.7 ± 2.43. Arterial pressure (invasively monitored), paO_2 pH_a, and $paCO_2$ were not statistically different between groups throughout the experiment. After 1 h of ventilation animals were sacrificed, liver and kidney isolated and fixed in 4% formalin, cut and H&H stained for optic microscopy. Organs from rats ventilated with 75%CI were consistently different from those ventilated with edema, and liver more homogeneously edematous. From a morphometric assay conducted on 5+5 rats, 75%CI liver resulted represented by more empty zone (index of edema) as compared to 25% CI liver (18.17 ± 5.02 vs 11.89 ± 2.69, respectively; $P < 0.001$). We conclude that rats ventilated for an hour with a tidal volume equal to 75%CI are characterized by different liver and kidney morphology from those of rats ventilated with 25%CI, at the same (Paw_m), arterial pressure, acid-base status and oxygenation.

P083

Aspiration of airway dead space (ASPIDS) in mechanically ventilated patients

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Critical Care 1998, **2(Suppl 1):**P083

Introduction: Alveolar ventilation can be improved and CO_2 clearance enhanced by reducing dead space. We studied a system for the aspiration of gas from the airway dead space (Vd_{aw}) denoted ASPIDS. During ASPIDS, in the late expiration, CO_2 rich gas is aspirated from the distal end of the tracheal tube; simultaneously fresh gas is injected in the inspiratory line. Our hypothesis was that CO_2-laden gas in the Vd_{aw} could be eliminated and, keeping alveolar ventilation constant, a reduction in minute ventilation (MV) and airway pressure (Paw) achieved.

Materials and Methods: Six patients (4m/2f, mean age 56 ± 23 years) mechanically ventilated for cerebral pathologies (Crs: 78 ± 20 ml/cmH_2O) with a computer controlled Servo Ventilator 900C (basal ventilation: MV: 7.7 l/min; RR: 12.7; Ti: 33%; Tpaus: 5%; PEEP: 5 cmH_2O), were studied. The computer controls 2 solenoid valves for aspiration and injection. The aim was to keep $PaCO_2$ constant during ASPIDS while decreasing MV. ASPIDS was expected to clear from CO_2 the volume of connecting tubings (ie 150 ml). Consequently, MV was decreased, during ASPIDS, of 150 × RR (ie 1900 ml). Data collected after 20 min of ASPIDS were compared with baseline ventilation using a T test. The following parameters were recorded: HR, mABP, MV, Paw_{peak}, VCO_2, blood gases.

Table (abstract P083)

	MV (L)	Paw_{peak} (cmH_2O)	VCO_2	$PaCO_2$ (mmHg)	PaO_2 (mmHg)	HR	mABP (mmHg)
Baseline	7.7	24.4	171.3	36.2	103.0	94.3	67.2
ASPIDS	5.8*	16.2*	176.0	36.0	100.1	89.2	68.7

Results: Patients were stable during ASPIDS. PEEP level was maintained and no PEEPi developed. No side effects were observed.
Conclusions: From our preliminary results, ASPIDS appears to be a new safe and promising method that improves the efficiency of ventilation, decreases the pressure required, and reduces the potential for lung injury during mechanical ventilation.

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P084

Intratracheal gas insuflation (ITG) and biphasic positive airway pressure (BIPAP): an integrated strategy in acute respiratory distress syndrome

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Critical Care 1998, **2(Suppl 1):**P084

Introduction: TGI can reverse undesired effects of Permissive Hypercarbia acting primarily to reverse and control high $PaCO_2$ and low pH values. During ventilation aided by TGI the gas flow, introduced by a catheter positioned 1 inch above carina dilutes the CO_2 in the proximal anatomic dead space. The continuous flow however, in conventional pressure control modes, can be additive to the inspired Vt value, leading to a fast progressive hyperinflation and high airway pressures with a prohibitive risk for volu/barotrauma. This unwanted effect may be neutralized by the use of BIPAP (Drager Evita I-II) as a pure Pressure Control Mode that compensates the additional flow required to the TGI technique.
Methods: 5 ARDS (Lung Injury Score ≥2.5) patients on mechanical ventilatory support (MVS) with severe respiratory acidosis were enrolled. These patients had arterial pH levels ≤7.25 after all possible adjustments of the ventilatory parameters aiming to reverse the CO_2 values keeping low volumes and airway pressures. BIPAP was instituted and serial arterial blood gases were drawn at time 0, 30, 60, 90, 120 min, and 24 h after beginning BIPAP and TGI with a 7–9 l/min flow (same FIO_2 than the ventilator) through a 1 mm internal diameter catheter and conector (SIMS-PORTEX). The data was submitted to variance statistical analysis adjusted for repeated measures.
Results: A mean reduction of 8.6 mmHg (9.8%) of $PaCO_2$ after 30 min and 42.6 mmHg (46.8%) after 24 h was observed. The pH significantly increased after 60 min, after 90 min the mean pH value had risen 0.124 units. The PAO_2/FIO_2 ratio increased as well.
Conclusions: The combination of these two new and not very well known techniques, TGI and BIPAP, were useful in avoiding the adverse effects of high pressures and volumes to counteract the effects of high arterial CO_2 levels in patients with limited cardio-circulatory status and acute or chronic lung and cerebral diseases. In this small sample, considering the influence of time in the reduction of $PACO_2$ and in the increase of pH values, the best moment to verify the response of TGI is beyond 60 min.

P085

Temperature loss from gases in the ETT exposed to ambient

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Critical Care 1998, **2(Suppl 1):**P085

Introduction: It is essential to heat and humidify gases delivered to mechanically ventilated patients in order to maintain airway function. Humidifiers will control the gas temperature along the breathing circuit up to the temperature probe at the Y-piece. Beyond this point the gases will cool as they pass through an unheated length of circuit. In order to deliver optimally conditioned gases (ie core temperature and 100% RH) to the patient this temperature loss, and concomitant humidity loss, must be compensated for.
Method: Gas temperatures in the breathing circuits of 5 adult ICU patients undergoing mechanical ventilation, were monitored.Vt=0.75 ml (SD=0.04) and RR=11.4 bpm (1.5). The humidity and temperature of the inspired gases were controlled to 30°C, 34°C, 37°C, 40°C at 100%RH in sequence, by a heated humidifier with heated wire circuit (Fisher & Paykel MR730). The ambient temperature was 25°C with still air. The unheated length of breathing circuit on each patient was 10.8 cm (0.2) of endotracheal tube (ETT) protruding from the teeth, and 2 cm of suction

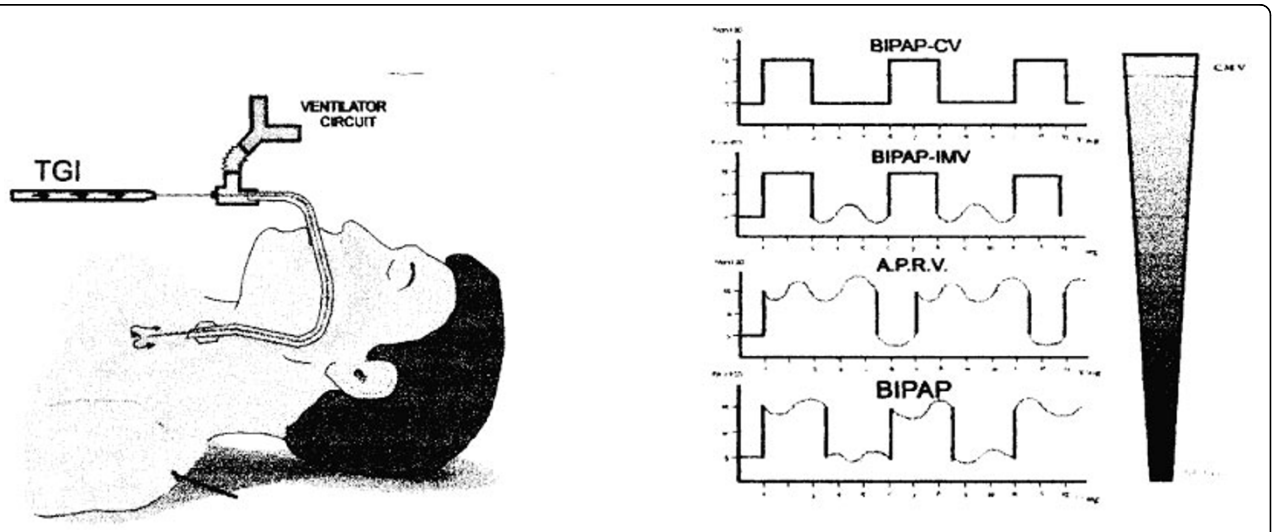

Figure 1 (abstract P084)

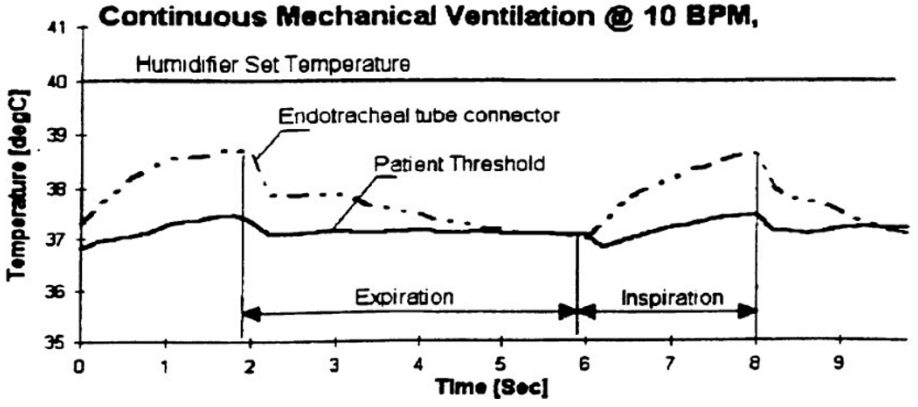

Figure 1 (abstract P085)

Table (abstract P085)

Temp loss Max (°C)	Temp loss Mean (°C) (SD)	Temp loss per cm (°C/cm) (SD)	Humidity loss Max (mg/l)	Humidity loss Mean (mg/l) (SD)	Humidity loss per cm (mg/l/cm) (SD)
3.7°C	1.43 (0.77)	0.13 (0.06)	8.8	3.83 (2.15)	0.35 (0.16)

Measurements given as time averages of ten breaths, averaged over the 5 patients

port attached directly to the Y-piece. A K type thermocouple (response time 0-90% = 0.1 s) mounted on a suction catheter was inserted through the port to measure temperature in the centre of the circuit at two sites: the middle of the suction port at the exit of the Y-piece, and in the ETT just prior to the teeth.
Results: Temperature and humidity loss were recorded over the portion of ETT protruding from the teeth during inspiration and expiration (see figure for a typical breath). The losses during inspiration were:
Conclusions: Gases undergo a significant temperature and humidity loss as they pass through even the short length of ETT outside the patient threshold. To compensate for this, the humidifier must be set at least 1.4°C above the desired gas temperature. These losses will be greater when flexible extensions are used (eg a 10 cm extension will incur a loss of 2.9°C and 6 mgH_2O/l).

P086

Influence of bronchodilatation on impedance of the respiratory system in mechanically ventilated COPD patients

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Critical Care 1998, **2(Suppl 1):**P086

Introduction: Several authors studied the effect of bronchodilatation on the inspiratory resistance and compliance in mechanically ventilated patients. In this study, the respiratory mechanics during expiration are measured following bronchodilatation in mechanically ventilated COPD patients.
Method: The total expiratory resistance (Rrs, exp) and reactance (Xrs, exp) were measured by means of the forced oscillation technique (FOT). A psuedorandom noise signal of 4 to 26 Hz was delivered through the expiratory outlet of the ventilator. Flow was measured at the entrance of the tube, and pressure was measured with a fine catheter beyond the outlet of the endotracheal tube. The inspiratory resistance (Rrs, insp) and compliance were obtained with the interruption technique. The results before and after bronchodi-latation were analysed with a paired t-test. 10 patients with obstructive pulmonary disease (COPD) were examined before and after bronchodilatation with 10 puffs fenoterol (1000 µg) given by a MDI (Metered-Dose Inhaler) in the inspiratory circuit.
Results: A significant decrease in Rrs, exp was recorded after fenoterol inhalation at nearly every frequency. At 10 Hz the Rrs, exp before inhalation was 15.91 (± 7.6) before and 12.905 (± 7.59) hPa/l/s after bronchodilatation (P = 0.005). At 20 Hz, Rrs, exp was respectively 10.25 (± 6.0) and 8.695 (± 5.4) hPa/l/s (P = 0.0005). There was a corresponding decrease in Rrs, insp from 17.09 (± 7.07) to 13.72 (± 5.20) hPa/l/s (P = 0.038)/ Xrs, exp after bronchodilatation was not significantly different at the lower frequencies (4–14Hz), but it was at the higher frequencies: at 20 Hz, Xrs,exp increased from -8.87 (± 4.75) to -6.88 (± 5.53) hPa/l/s after bronchodilatation (P = 0.030). There was no significant change in inspiratory static compliance before and after fenoterol: 57.8 versus 55.9 ml/hPa (P = 0.50). the intrinsic PEEP (PEEPi) decreased significantly: 4.75 (± 3.17) versus 3.5 (± 2.48) hPa after bronchodilatation (P = 0.032).
Conclusion: 1. The expiratory and inspiratory resistance and the intrinsic PEEP decrease significantly after fenoterol administration by MDI in ventilated COPD patients. 2. Although the compliance did not change, we observed an increase of expiratory reactance at frequencies >16 Hz.

P087

Automatic static pV curves measurement (RM software)

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Critical Care 1998, **2(Suppl 1):**P087

Objective: To develop software capable of managing the ventilator to perform standard pV curve measurement and to test it on a lung model.
Methods: Adult Star (Infrasonics, Inc) ventilator was used for our study. The RM software was created in Visual Basic for Win 95, using software orders from the manufacturer. It is based on occlusion method for pV curve measurements as described by Levy *et al*., Baseline ventilation is interrupted just for one test breath. Flow and pressures are measured from built in single screen Silverman pneumotachometer and proximal pressure transducer. Data are automatically collected in Microsoft Excel file. Our lung model was lung simulator SMS (Sandland manufacturing service Ltd., Harlow-Essex-England).
Protocol: We tested the RM software in four different settings: combination of two compliances (20 and 50 ml/cmH_2O) each with resistances 5 and 20 cmH_2O/l/s. Five pV curves were done for each setting. Ten tidal volumes were applied (100, 200, 300 ...1000 ml) to get one pV curve.
Results: Regression analysis was performed for each pV curve. Mechanical properties of our lung model implies the use of non-linear regression: Vt = A × p × sin (B × p+C) +D, where A, B, C, D are the

Table (abstract P087)

	A	B	r^2
compl. 50 ml/cmH_2O, rezist. 5 cmH_2O/l/s	36.7 ± 1.3	101.6 ± 21.5	0.975
compl. 50 ml/cmH_2O, rezist. 20 cmH_2O/l/s	35.5 ± 1.1	92.1 ± 19.2	0.97
compl. 20 ml/cmH_2O, rezist. 5 cmH_2O/l/s	21.6 ± 0.4	114.6 ± 17.0	0.98
compl. 20 ml/cmH_2O, rezist. 20 cmH_2O/l/s	20.8 ± 0.6	121.4 ± 24.6	0.98

regression parameters, however for mathematical simplicity we used linear regression Vt = A × p +B. The correlation coefficient and A, B parameters were pooled from each settings measurement and mean ± SD were calculated:
Our results showed little variability for each setting. Resistance didn't affect the measurement of compliance as was expected.
Conclusion: RM software for PC is reliable on repetitive measurements and precise enough to measure static pV curves in a lung model with tidal volumes exceeding 150 ml. Further validation with independent pneumotachometer and pressure transducer is necessary. Thereafter RM software probably can be used in clinical settings.

P088

Time required for PaO_2 equilibration during mechanical ventilation with changes in FiO_2

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Critical Care 1998, **2(Suppl 1):**P088

Introduction: Although it's a general practice to obtain blood gas sample after 30 min when FiO_2 was changed during mechanical ventilation, exact timing for blood gas analysis has not been very well documented. In this study we aimed to investigate the time required for PaO_2 equilibration during pressure controlled ventilation (PCV) with changes in FiO_2.
Patients and methods: 25 adult patients with stable blood gas values (5 female, 20 male) on PCV (Servo 900C Siemens, Elema, Sweden) with FiO_2:0.35, frequency: 12 breaths/min, tidal volume: 10 ml/kg and PEEP: 5 cmH_2O were studied.
Following a control blood gas measurement at FiO_2:0.35 and determination of PaO_2 ($PaO_2$35), FiO_2 was increased to 0.55 for 60 min and again returned to 0.35 without any change in ventilatory parameters. Blood samples were obtained and immediate blood gas measurements were performed on 3, 5, 7, 9, 11, 15, 20, 25, 30 min in both periods and at the 60th minute in FiO_2:0.55 period. The PaO_2 value measured at the 60th minute of FiO_2:0.55 ($PaO_2$55) was accepted as representative of equilibration.
The timing of PaO_2 values reaching either the $PaO_2$55 and $PaO_2$35 levels were recorded for each patient and average (Mean ± SD) of these values were calculated.
Results: The average (Mean ± SD) time period necessary to reach $PaO_2$55 and $PaO_2$35 were 9 ± 7.33 min and 7.08 ± 6.02 min respectively. The numbers and the percentages of the patients reaching their own $PaO_2$55 and $PaO_2$35 values for each sampling time were listed in Table 1.
Conclusion: We concluded that after FiO_2 changes during PCV, 10 min will be adequate for obtaining the blood gas sample representative for equilibration of PaO_2.

P089

Pre-hospital tracheal intubation assisted by fibroscopy in patients with suspicion of cervical spine lesion: a pilot study

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Critical Care 1998, **2(Suppl 1):**P089

Introduction: There is still some controversy about the best manner to manage, in the pre-hospital phase, the patients requesting tracheal intubation and suspected to suffer from a cervical spine lesion. The present observation reports the use of a new, entirely autonomous, equipment for in the field tracheal fibroscopy.
Methodology: An anaesthetist, trained to tracheal fibroscopy, has at his disposal a medical vehicle and the equipment for emergency pre-hospital tracheal intubation.
Results: Five patients were intubated with the 'in the field' tracheal fibroscope (9, 16, 21, 22 and 62 years of age). The intubation was carried out without any problem on 4 victims despite their spine was immobilised with a cervical collar and that blood was present in the pharynx. One intubation proved itself to be more difficult on a patient who had undergone several unsuccessful and traumatising attempts by the first physician on the scene.
Discussion: Some practical details seem to be at importance for correct management of a fibroscopic guided tracheal intubation in the pre-hospital environment. First, the quality of the images transmitted by the fiberoptic equipment; second, the oxygenation of the patient during the tracheal intubation process; third, the aseptic aspects of this manoeuvre; fourth, the 'ready to use' aspect of the associated material (gloves, suction); fifth, the training level of the physician in charge of the tracheal intubation process; sixth, the level of accompanying analgesia or anaesthesia.
Conclusion: As tracheal intubation through fibroscopy could be a 'gentle' technique, the use of 'in the field' fibroscopic equipment would be encouraged in a pre-hospital phase to reduce the risk of hypoxaemia associated with many difficult tracheal intubations and the severity of pharyngeal and laryngeal trauma produced by the 'classical' direct vision laryngoscope.

P091

Bedside percutaneous tracheostomy: experience with 40 critically ill patients

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Critical Care 1998, **2(Suppl 1):**P091

Text: In intensive care unit patients requiring prolonged mechanical ventilation, tracheostomy is necessary. As an alternative to the standard surgical method, percutaneous techniques are available.
Since November 1996, 40 patients (34M, 6F) have been electively selected for percutaneous tracheostomy (PCT) at a University Hospital with a 9-bed combined medical-surgical ICU. PCT was performed at bedside with the Portex Percutaneous Tracheostomy Kit (Portex Ltd, Kent, England). The procedure time and early complications were recorded.
Patients were between 18 and 86 years (46.4 ± 3.1). The procedure was successful in all patients and the average duration of placement was 9.05 ± 0.7 min (3–20 min). An 8 or 8.5 mm cannula was inserted in each case, introduced between the 1st and 2nd or 2nd and 3rd tracheal cartilages.

Table 1 (abstract P088) The numbers and the percentages of the patients reaching their own $PaO_2$55 and $PaO_2$35 values for each sampling time

Minute	3	5	7	9	11	15	20	25	30	
FiO_2:0.55 Period	8 (32%)	4 (16%)	2 (8%)	4 (16)	1 (4%)	3 (12%)	1 (4%)	1 (4%)	1 (4%)	n = 25
FiO_2:0.35 Period	8 (32%)	7 (28%)	5 (20%)	2 (8%)	-	1 (4%)	1 (4%)	-	1 (4%)	n = 25

The average duration of artificial ventilation before PCT was 9.8 ± 0.8 days (2-28 days), after PCT was 12.1 ± 1.2 days (1–32 days). Mean duration of PCT was 20.9 ± 3.6 days (1–140 days). There were no PCT-related deaths. The only procedure related complication was bleeding at the stoma site which resolved within applied pressure. 20 patients were decannulated. Early clinical examination revealed hoarseness in one patient. Stomas were closed within a few days, leaving an approximately 1 cm length scar.
Our study suggests that PCT is a simple and safe method and can be performed rapidly at the bedside in the ICU.

P092

Esophageal acid and bile reflux in mechanically ventilated patients

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Critical Care 1998, **2(Suppl 1):**P092

Introduction: Previous studies using scintigraphy have documented a high incidence (61%) of gastroesophageal reflux in mechanically ventilated (MV) patients. The aim of this study was to assess, over a prolonged period of time, the incidence and type (bile or acid) of reflux, the effect of body position on reflux, and the potential relationship between pathological reflux and esopahagitis in mechanically ventilated patients.
Methods: 24 critically ill, MV patients (mean APACHE II score: 21, mean age 64 ± 14 yrs, 15 men), hospitalized in a medical intensive care unit, were prospectively included for 24-h esophageal pH and duodeno-gastroesophageal reflux (DGER) studies (Digitrapper III pH-meter and fiber-optic sensor for the presence of bilirubin, Bilitec 2000, Synectics, Sweden) with single sensors placed 5 cm proximal to the lower esophageal sphincter (LES) and instrumented with a nasogastric tube. Exclusion criteria were: MV <3 or >8 days, previous initiation of enteral feeding, history of reflux esophagitis or gastric surgery, acute gastrointestinal bleeding or exophageal varices, or medication with prokinetic agents. All patients received stress ulcer prophylaxis with ranitidine 50 mg iv, tid. On the day before the study patients underwent esophageal endoscopy to determine the presence of esophagitis. Patients were placed in supine semi-recumbent position and turned on either left or right lateral sides at intervals as deemed appropriate by the attending nurse. The following variables were analyzed depending on body position (total time, time in supine, right, or left position): % time pH <4 (normal <3.4 %) or % time bilirubin absorption >0.14 (normal: <3 %), total duration of reflux, and number reflux episodes. Data are medians with interquartile ranges (IQR), significance was tested with the Mann-Whitney U test. Fisher's exact test was used to analyze relationships between the presence or absence of pathological reflux and esophagitis.
Results: After a median of 5 days of MV (IQR 3.8) 12 of 24 patients (50%) patients had pathological DGER (median % reflux time over the whole recording time independent of body position: 8%, IQR 0.62%). In contrast, only one patient had significant acid reflux (4.8% of the recording time) and the median pH in the lower esophagus for all 24 patients was 6.7 (IQR 6.7). The median duration where bile salts were present in the lower esophagus was 112 min (IQR 0.865 min), in 8 of 24 patients this time period exceeded 5 h. The median number of DGER episodes was 12 (IQR 0.37). The relative time of pathological reflux was significantly higher in left lateral and supine position as compared to right lateral position (7.1% IQR 0.64% and 8%, IQR 0.65% vs. 4.7% IQR 0.70%, P < 0.01. 12 of 24 patients (50%) had esophagitis. There was a significant positive relationship between the presence of pathological DGER and the presence of esophagitis (P = 0.04).
Conclusions: Under standard stress ulcer prophylaxis with ranitidine, critically ill patients with MV have a high incidence (50%) of DGER but not of acidic esophageal reflux. Reflux is highest in the left lateral and in the semirecumbent position. The presence of bile salts in the esophagus for prolonged periods of time suggest that: 1) the barrier function of the LES and the clearance function of the esophagus are deranged, 2) esophagitis in these patients may not only be a result of mechanical irritation due to the nasogastric tube, but may also be a chemical esophagitis, 3) intestinal fluids refluxing into the esophagus may be conducive to ventilator-associated pneumonia.

P093

Adrenocortical function and outcome in critically ill patients

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Critical Care 1998, **2(Suppl 1):**P093

Objective: To assess the value of measuring adrenocortical function parameters in predicting outcome and mortality in critically ill patients.
Methods: Prospective clinical investigation with no therapeutic interventions in which were involved 63 consecutive patients admitted to the medical intensive care unit. Adrenocortical function was assessed by plasma cortisol and dehydroepiandrosterone sulfate (DHEA-S) levels on days 1, 3 and 7 and by the short synthetic ACTH stimulation test performed within 24 h of admission to the ICU. Individual variables were compared with severity scores, biological data and outcome. Statistical analysis: Student test, Mann-Whitney U test P < 0.05 was considered significant.
Results: Mean age 57 ± 19, APACHE II score at admission 20 ± 7, there were 37 (54.4%) septic patients. In hospital mortality rate 43.1%. Busal cortisol concentrations were increased with a mean value of 32.22 ± 19.3. Of overall cortisol determinations 94% were above 15 µg/dl. No correlations were found between these levels and factors such as APACHE II score, MODS score, haemodynamic measurements, amount of vassopresor support neither mortality. Cortisol levels on day 3 correlated with the use of dopamine (p:.03) and noradrenaline (p:.02) and were able to discriminate between survivors and non-survivors (median 13.65 vs 30.3, P < 0.005). The response to ACTII test had a mean value of 45.4 ± 18 with a mean difference with basal cortisol levels of 13.85 ± 10. No one of these measurements did show any relationship with clinical variables of outcome. Global basal concentrations of DHEA-S were lower (median 65, range: 1–447) than normal values (r: 120–240) and showed a marked tendency to decrease over the time (median 30 on days 3 and 7). Levels of DHEA-S on day 1 showed a weak correlation with APACHE II score (r. 0.33; P = 0.039) DHE-S on day 3 was much higher in survivors than in non-survivors patients (median 41.1 vs 20.7; P = 0.002).
Two patterns of adrenocortical function were identified. In surviving patients plasma cortisol levels were normal or increased and gradually decreased whereas levels of DHEA-S showed an opposite pattern. In the other hand, in non-survivors cortisol levels persisted elevated and DHEA-S decreased. The ratio DHEA-S/cortisol on day 3 was a good indicator of final outcome with a median value of 1.92 in survivors and 0.79 in non-survivors (P = 0.009).
Conclusion: In critically ill patients the basal adrenocortical function is characterized by high plasma cortisol and low DHEA-S levels. The DHEA-S/cortisol plasma concentrations on day 3 might be used as a prognostic marker for identifying final outcome in this population.

P094

Treatment of postoperative lung injury in patients with SIRS by methylprednisolone

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Critical Care 1998, **2(Suppl 1):**P094

Introduction: Intraperitoneal hyperthermic perfusion (IPHP) is performed clinically as one treatment for cancer patients with advanced gastrointestinal cancer. All patients are fallen the systemic inflammatory response syndrome (SIRS) by IPHP. In our previous work, we clarified the elevated TNF-α in the serum of IPHP patients [1]. Glucocorticoids are well known inhibitors of TNF-α [2]. We examined serum TNF-α levels before and after administration of methylprednisolone (MPS) and compaired the lung injury score in postoperative days between the group of MPS and control.

Methods: Seventeen patients with gastrointestinal cancer were undergone surgery combined with IPHP. Group 1 (10 patients): MPS was not adminstrated. Group 2 (7 patients): MPS was administered before and during IPHP. We measured serum TNF-α levels and evaluate the metabolism, hematorogy, hemodynamics and the post-operative lung injury.
Results: In group 1, serum TNF-α levels was increased to 46.0 ± 25.7 pg/ml (mean ± SD) at the end of IPHP and patients were SIRS with the postoperative lung injury. In group 2, TNF-α was not detected but postoperative lung injury were improved.
Conclusion: MPS inhibited the production of TNF-α which was able to improve postoperative lung injury. Pre-emptive MPS might be one of strategy for treatment of lung injury during SIRS.

P095

A placebo-controlled study on the effects of corticosteroid inhalation therapy in ammonia induced lung injury in rabbits

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Critical Care 1998, **2(Suppl 1):**P095

Background: The use of inhalation corticosteroids in toxic pulmonary oedema caused by exposure to irritating gases is controversial. Their effects have not been demonstrated in controlled studies.
Study design: A randomised blind placebo-controlled study of the effects of budesonide inhalation in a rabbit model of toxic lung injury induced by ammonia inhalation.
Animals: Sixteen New Zealand White rabbits.
Intervention: Lung injury was induced by inhalation of a defined amount of aerosolised ammonia. Thirty and 150 min later the animals were randomised to receive either inhalation therapy with 0.5 mg budesonide or placebo.
Measurements and results: Airway pressures, haemodynamics and gas exchange were measured at baseline, 5 and 15 min after the ammonia administration, and every 30 min during a 6-h period after the first blind inhalation therapy with corticosteroids or placebo. The ammonia inhalation resulted in an acute severe lung injury detected after 15 min as a decrease in PaO2 from 23.3 (± 3.6) to 11.0 (±3.6) kPa ($P < 0.005$) and an increase in peak airway pressure from 13 (±2) to 17 (±2) cmH2O ($P < 0.005$). During the 6-h observation period, the blood gas parameters improved in all rabbits. In comparison to placebo, budesonide did not result in improved gas exchange or reduced airway pressure levels during the observation period.
Conclusion: In this animal model, corticosteroid inhalation therapy had no acute effects on ammonia induced lung injury.

P096

Late steroid therapy improves gas exchange and reduces organ dysfunction in acute lung injury caused by pneumococcal pneumonia

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Critical Care 1998, **2(Suppl 1):**P096

Introduction: Prophylactic or early glucocorticoid therapy have not proved to be useful in the treatment of acute lung injury (ALI). However, there is evidence of the beneficial effects of steroids in the fibroproliferative stage of ALI (late steroid therapy).
Materials and methods: We analyzed the clinical data of all patients who suffered from a severe pneumococcal pneumonia during 1993–97 and were treated in the ICU at our institution. Patients who required mechanical ventilation more than 10 days (n = 18) were selected for the study. Based on empirical data, late steroid therapy was started for 11 patients because of persistent impairment of gas exchange and/or inflammatory process of the lungs, and the remaining 7 patients served as controls. Methylprednisolone was intravenously administered with a daily dose of 80 mg and 40 mg. The dosage was gradually decreased. General treatment of the patient groups was similar including lung protective ventilatory strategies, prone positioning and invasive hemodynamic monitoring The steroid therapy was started within 9.3 days (range, 7–13 days) after hospitalization. Accordingly, the values of the control group were monitored on the day 10 after hospitalization. Mortality was assessed on the day 30.
Results: Age, sex, APACHE II-score and lung injury score, Multi-organ Dysfunction Score (MODS), CRP-level and PaO2/FiO2-ratio were comparable at the start of steroid therapy or day 10. The changes in CRP, MODS and PaO2/FiO2 between the day steroid treatment started (day 0) and 3 days thereafter differed significantly between the two groups.
Conclusions: Although the sample size of this retrospective study was small, our results support the increasing evidence of the advantages of late steroid therapy in acute lung injury.

P097

Corticoid treatment increases the risk of enterobacter aerogenes infection in intensive care unit

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Critical Care 1998, **2(Suppl 1):**P097

Text: The emergence of multiresistant Enterobacter aerogenes (E.a.) has serious implications in the management of intensive care patients because of increasing risk of nosocomial infection acquisition attributed not only to the severity of the underlying disease, but also to invasive procedures and contaminated life-support equipment. Acquisition of E.a. usually occurs either by colonization with an endogenous strain selected de novo from the patient's own flora (eg broad-spectrum antibiotic follow-up therapy) or by patient-to-patient transmission of strains by the health personnel. E.a. is a difficult-to-treat organism since it is intrinsically resistant to beta-lactam antibiotics and it readily develops multiple drug resistance following the clinical usage of broad-spectrum cephalosporins or carbapenems.
A prospective study comparing risk-factors for E.a. colonization/infection has been conducted in a 12-bed ICU patients (median age, length of stay, mortality rate, mechanical ventilation, antibiotherapy prior to ICU admission, urinary catheter, surgical drain and corticoid therapy). From February 25, 1995 up to May 12, 1995, prescription order of perineal swabs has been undertaken to all patients prior to admission, discharge and on a weekly basis, to rule out the unit specific incidence of E.a. acquisition. 146 patients were included in this study. Out of which, 14 (9.6%) had one or more perineal swabs positive for E.a. and 7 of them had a positive swab the day of the ICU admission.
The E.a. colonization/infection was not significantly associated with patient's median age, mortality rate, antiobiotherapy prior to ICU admission, mechanical ventilation, urinary catheter and surgical drain. A significant association had been noted with corticoid therapy and ICU length of stay (respectively 80 days for E.a. + and 3.0 days for E.a.-), also had been noted that the median SAPS 2 score for colonized/infected patients is superior to the median SAPS 2 score of the ICU patients (43 versus32). Nine patients with E.a. colonization/infection developped infection. Despite appropriate antimicrobial therapy, E.a. colonization was associated with a crude mortality rate of 43%.
These data suggest that corticoid therapy is a risk factor in E.a. colonization/infection in ICU patients and perhaps, indeed, increases the patients mortality rate. Further prospective study are needed to optimize these data and precise the other risk factors. The potential effects of risk factors emphasize the importance of specific measures for infection control in critically ill patients.

P098

Helicobacter pylori infection in intensive care: increased prevalence and a new nosocomial infection

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Critical Care 1998, **2(Suppl 1):**P098

Objective: The pathogenesis of acute gastric stress ulceration in the seriously ill is uncertain and any role of Helicobacter pylori infection is unknown. We aimed to assess the relationship between H. pylori

serological status and stress ulceration in seriously ill patients, as well as H. pylori serological status in Intensive Care nurses as a marker for nosocomial infection.
Design: Prospective epidemiological survey.
Setting: Adult Intensive Care Unit in a University teaching hospital.
Patients: 100 patients, 100 nurses and 500 blood donors as community controls.
Interventions: H. pylori serological status was measured in patients, staff and controls using a rapid whole blood test. Upper gastrointestinal bleeding and risk factors for acute stress ulceration were recorded.
Measurements and main results: In seriously ill patients, H. pylori seropositivity (67%) was significantly higher than in the control group (39%) ($P < 0.001$). In patients, seropositivity was not related to age, country of birth, diagnostic category, severity of illness or risk score for stress ulceration. There was a trend towards increased macroscopic gastric bleeding in seropositive patients. In Intensive Care nurses, H. pylori seropositivity (40%) was significantly higher than in age'matched controls (19%) ($P < 0.001$). Only duration of Intensive Care nursing was significantly associated with seropositivity ($P = 0.02$).
Conclusions: The unexpectedly high H. pylori seropositivity rate in this seriously ill cohort raises the possibility that under Intensive Care conditions H. pylori infection may modulate responses to illness and injury, with consequent clinical implications. Furthermore, the elevated seropositivity rate in Intensive Care nurses suggests that H. pylori can be nosocomially transmitted.

P099

Tetanus not forgotten

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Critical Care 1998, **2(Suppl 1):**P099

Introduction: Tetanus still lingers with us although we have fairly good immunization programme in the country. There are no cases of neonatal tetanus in our hospital for the past 10 years.
Materials and methods: Retrospective study was done on 12 cases of generalised adult tetanus diagnosed clinically and admitted to our hospital from Jan 1995 to Nov 1997.
Management: Three cases were treated conservatively in the medical ward. Nine cases were admitted directly to ICU from the A&E Dept. Of the cases admitted to ICU, three were on conservative treatment: isolation in semi dark room, invasive monitoring, anti-tetanus toxoid, human hyperimmune antite-tanus globulin, titrated diazepam infusion, i.v. crystalline penicilline and metronidazole, and wound desloughing. Six needed ventilatory support: two underwent tracheostomy, and only one needed labetalol infusion. Proper nutrition was taken care of in all the patients.
Observation: Conservative management in the medical ward was satisfactory and all patients were discharged well. Patients admitted to ICU: 88.88% are above the age of 50 years, males more than females, average incubation period was 10 days, all patients had outdoor injuries, average stay was 14 days, 55.55% had autonomic dysfunction, 66.66% had nasocomial infection, there were two deaths (22.22%): one due to severe uncontrolled autonomic dysfunction with bradycardia, another due to septicaemia.
Conclusion: Tetanus is still a problem in elderly age group in our humid climate. Autonomic dysfunction is among the major complications. Titrated diazepam infusion without ventilation had satisfactory results.

P100

Nosocomial infection surveillance in Belgian ICUs: aim and methodology of the feedback

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Introduction: The risk for nosocomial infecions (NI) in ICU's is five to ten times higher than in the other hospital care units, with increasing mortality, morbidity, length of stay and costs. Previous studies demonstrated a significant decrease in NI after the set up of effective surveillance programs. If the surveillance is performed in a multicentric setting with representative sample, the results can be dysplayed as a whole but also aggregated for each individual ICU (IICU). The production of meaningful feedback reports may help IICU to evaluate its own situation as compared to that of the whole studied group (WS).
Objectives: The aim of the study was to provide IICU with its own incidence of Nosocomial Pneumonia (NPN) and Blood Stream Infection (NBSI), and their mortality rate after controlling for the risk factors. The risk factors (RF) are the case mix at admission (severity of illness = SAPSII score and the pathologies), the exposition to devices at risk (mechanical ventilation and central venous catheters) and the length of ICU stay. These 3 last RF are counfounding variables depending on the intensisty of ICU resources' use.
Material and methods: At the end of 1995, all Belgian ICUs were invited to join a voluntary prospective NI surveillance network which was based on the criteria defined in the HELICS project. Participation was for one are two 3-months periods, starting in January 1996. During the first two trimesters of 1996, 64 different ICU's, from 28% of the Belgian acute care hospitals, have joined the study. A total of 8475 patients were observed. Data included: (i) patient characteristics at admission: administrative data, type of admission, SAPSII score, prior surgery or antibiotics, impaired immunity and infection at entry; (ii) during ICU stay, daily exposure to mechanical ventilation, central venous catheters and treatments; (iii) if a NPN and/or a NBSI occured during ICU stay, diagnostic criteria and microbiological data; (iv) discharge data: vital status and date.
Results: Two kinds of feedbacks were produced for IICU with results grouped by trimester: descriptive and analytical. The descriptive feedbacks reported firstly, the observed results of the WS and IICU concerning the case mix at admission, the intensity of devices use, length of ICU stay, mortality and NI rates and secondly, the distribution of those variables throughout the WS as well as the localisation of IICU, expressed in percentile, within each distribution. The analytical feedbacks produced specific standardised rates (SR) for the intensity of devices use and length of stay weighted for the case mix, and the SR for mortality and NI rates weighted for the ICU resources use and the case mix. Moreover, those SR may vary widely as a consequence of hazard, specially for small ICUs, so that confidence interval (CI) must be calculated for IICU specific SR.

P101

Epidemiological impact of the antimicrobial therapy on *Acinetobacter* spp. isolated from ITU patients

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Critical Care 1998, **2(Suppl 1):**P101

Background: *Acinetobacter* spp. are Gram-negative bacteria which may be isolated as comensals from human skin, throat and intestine, but are also responsible for hospital infection. Today *Acinetobacter* is considered to be a significant nosocomial pathogen in outbreaks of nosocomial infections predominantly in intensive therapy units (ITU).
Purpose: To analyse epidemiology and factors influencing *Acinetobacter* spp. outbreaks.
Setting: A six-bedded surgical ITU in a 700-bed teaching hospital. The research was conducted from January 1995 till June 1996.
Methods: Relationships between amount of isolated *Acinetobacter* spp. strains (in total 190) and antibiotics consumption, expressed in defined daily dose (DDD), were analysed using linear correlation. To find out

Table (abstract P101)

amikacin	aminoglycosides	cefotaxim
$P < 0.05$	$P < 0.05$	$P = 0.01$
y=-0.02x+15.99	y=-0.009x+16.0	y=-0.05x+13.08
r =-0.58	r =-0.54	r =-0.62

whether there is any relation between *Acinetobacter* out-breaks and overpopulation on ITU, all data were categorised for the frequency table. Paerson Chi-square test was used to identify relationship between the crosstabulated variables.
Results: Strong correlation between resistant *Acinetobacter* isolates and amikacin, aminoglycosides and cefotaxim consumption is shown in table. Crosstabulated variables analyses proved influence of overpopulation on ITU on the *Acinetobacter* outbreak's ($P < 0.05$).
Conclusion: This study illustrates the influence of antimicrobial therapy on outbreaks of resistant *Acinetobacter* strains.

P102

Control of nosocomial infections in ICU patients in the Pomeranian School of Medicine in Poland

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Critical Care 1998, **2(Suppl 1):**P102

Background: Antibiotics represent the most commonly prescribed medical therapies for hospitalised patients. The practice of 'spiralling empiricism' has increasingly led to the unnecessary administration of antibiotics, resulting in the emergence of infections with antibiotic-resistant bacteria.
Purpose: To define the influence of antibiotic use on the etiology of nosocomial infection.
Setting: A six-bedded surgical intensive therapy unit (ITU) in a 700-bed teaching hospital. The research was conducted from January 1995 till June 1996. In August 1995 we have changed antibiotic guidelines on our ITU (third generation cephalosporins, fluoroquinolones and vancomycin were used only as the last option and never in prevention)
Methods: We have compared three consecutive periods of 6 months (I'95, II'95, I'96). 1276 samples for microbiological culture, mainly from bronchial tree, wounds, blood and urine, were obtained in routine manner. From 60% positive cultures 1216 strains were isolated. Antibiotics consumption was expressed in defined daily dose (DDD).
Results: Over 18-months there was no statistically significant deference in mortality rate on our ITU. There were statistically lower monthly consumptions of ceftriaxone form 60 to 0 DDD ($P < 0.05$) and quinolones from 282 to 110 DDD ($P < 0.05$) in I'95 and II'95 respectively. Vancomycin use decreased from 133 DDD in I'95 to 34 DDD in I'96 ($P < 0.05$). There was no statistically significant increase in amount of isolated pathogen strains in analysed periods. We have observed improvement in activities of third generation cephalosporins and fluoroquinolones.
Conclusion: This study illustrates the influence of antimicrobal therapy on the species and the resistance of strains isolated in nosocomial infection. Restrictive antibiotics policy do not affect ITU outcome. Better strategies for antibiotic administration in the ITU setting may improve their efficacy and reduce costs. Therefore, antibiotic policy would be mandatory in each hospital and department.

P103

ICU acquired late pneumonia: epidemiological, clinical, bacteriological and histological aspects of a 3 years study

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Critical Care 1998, **2(Suppl 1):**P103

Objective: To evaluate the incidence and the characteristics of ICU acquired late pneumonia and to correlate the clinical diagnosis of pneumonia to histological findings; to identify and emphasize the risk factors of its onset.
Subject and methods: ICU acquired late pneumonia was defined by the presence of new and persistent infiltrates to the chest X-ray (appeared at least 72 h after admission) in addition to at least one of the following: a) purulent sputum; b) T° >38°C or <36°C; c) white blood cells count >12 000 or <4 000/mm^3. Tracheal aspirate, BAL or PSB were performed to obtain microbiological samples. We evaluated 573 patients, 380 males (66%) and 193 females (34%), consecutively admitted in a medical and surgical ICU from 1994 to 1996; the median age was 64 years. Patients ventilated at the admission were 395 (69%); 229 patients (40%) were admitted in ICU after a surgical procedure. The Apache II and the SAPS I scores at the admission were respectively >16 in 46% of patients and >9 in 76% of patients. The overall ICU mortality was 33%. We observed 112 episodes of pneumonia (crude incidence 19%): 52% of patients had undergone a previous surgical procedure; Apache II score was >16 in 63% of patients while Saps I score was >9 in 93%. Pneumonia lethality was 49%. All the dead patients were ventilated. In 47% postmortem examination was performed. Chi square test with Yates correction, T Student's test and Fisher's exact test were performed for statistical analysis.
Results: The incidence of pneumonia was higher in males than in females (22% vs 13%; $P < 0.05$); its frequency was higher in surgical than in medical patients (25% vs 15%; $P < 0.01$) and in ventilated patients than in not ventilated (26% vs 4%; $P < 0.000001$). Incidence in patients with Apache II >16 was 27% ($P < 0.0001$ vs Apache II <16); in patients with SAPS I >9 frequency was 24% ($P < 0.00001$ vs SAPS <9). The mean length of ICU stay (LOS) of patients with pneumonia was 36 days, while LOS of patients without pneumonia was 13 days ($P < 0.0000000001$). In 94 patients (84%) we obtained positive microbiological samples; gram positive germs were observed in 44% of isolates, gram negative in 38%, fungi in 17%. Post-mortem examination confirmed the diagnosis of pneumonia in 50% of cases; acute pulmonary oedema, ARDS and pulmonary infarction were the most common causes of misdiagnosis.
Conclusions: Pneumonia is one of the most common nosocomial infections, particularly in ventilated critically ill patients, and it is burdened by high lethality. Our data evidence that male sex, mechanical ventilation, high severity disease indexes scores, previous surgery and length of ICU stay are important risk factors for the onset of late pneumonia. Relationship between ARDS and pneumonia is strict, as ARDS may be both the result or the cause of pneumonia. How best to diagnose ICU acquired late pneumonia is still under debate, considering the frequent discrepancy between clinical and histological diagnosis.

P104

The contribution of viral presence to severe exacerbation of asthma

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Critical Care 1998, **2(Suppl 1):**P104

Purpose of the study was to evaluate the contribution of viral presence as a possible trigger of the severe asthma. Allergens, physical effort, cold-air, gastroesophageal reflux and other possible triggers were not taken into consideration in this study.
84 patients with severe asthma hospitalized at the Clinic of Pulmology during the winter period of 1996, were clinically assessed by random choice. We have examined blood samples for viral serology the first day of their hospitalization and after two weeks. The following results were obtained expressed in percentage. In 31 (36.9%) patients we found positive isolates for viral presence: Influenzae A in 12 patients (38.7%), Parainfluenzae in 6 patients (19.3%) RSV in 5 patients (16.1%), Mycoplasma pneumoniae in 3 (9.6%) and RV in 5 (16.1%). Positive viral presence after 2 weeks showed 6.4 % (2 patients).
Although this is a small group of patients to be taken for definitive conclusions about the viral infection as a major trigger for exacerbation of severe asthma, their presence especially in winter period plays an important role in worsening of the disease.

P105

Function of different ICU ventilators under hyperbaric conditions

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Critical Care 1998, **2(Suppl 1):**P105

Introduction: ICU-ventilators are designed for use at normobaric conditions. Under certain circumstances patients need mechanical

ventilation during hyperbaric oxygen therapy. The aim of the investigation was to analyse the function of four different ICU-ventilators [EVITA-4, Microvent, Oxylog 2000 HBO (Drägerwerk AG, Germany) and Servo ventilator 900 C (Siemens-Elema, Sweden] under 5 (normobaric, 1.3, 1.6, 1.9 and 2.8 ATA, EVITA-4 and Oxylog 2000 HBO) or 6 (additionally 6 ATA, Servo ventilator 900 C and Microvent) different atmospheric pressure conditions, regarding the difference of present and effectively applied volume and pressure from those set at the control panel.
Methods: We tested the following ventilator modes: volume (VCV) and pressure controlled ventilation (PCV, EVITA-4 and Servo ventilator 900 C only), the electromechanical lung simulator LS 1500 (Drägerwerk AG, Germany) consisting of a motor driven bellow.
During VCV tidal volume was set at (V_T) = 750 ml, respiratory rate (f) = 15/min, I:E ratio = 1:2, positive endexpiratory pressure (PEEP) = 0 cmH_2O. During PCV (f) = 10/min inspiratory pressure (P_{insp}) was set in order to achieve a V_t of 750 ml keeping all others ventilator parameters constant. The V_T applied by the ventilator was measured as the linear displacement of the bellows at each ambient pressure. (P_{aw}) was measured inside of the bellows.
Results: During VCV applied V_t of the ventilator decreases significantly with increasing ambient pressure while PCV with constant P_{insp} and PEEP V_t was stable at each depth.
Conclusions: Under hyperbaric conditions PCV should be preferred due to the stability of V_T applied. If PCV is not available, V_T needs to be adjusted during VCV depending on the actual ambient pressure.
Acknowledgement: We thank Drägerwerk AG, Germany for kindly providing us the lung simulator LS 1500.

P106

Work of breathing imposed by different ventilators under hyperbaric conditions

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Critical Care 1998, **2(Suppl 1):**P106

Introduction: The continuous increase in gas density caused by compression is likely to affect the work of spontaneous breathing (WOB) under hyperbaric conditions. In intubated patients breathing spontaneously through demand flow ventilator systems WOB is additionally influenced by the WOB component imposed by the ventilator (WOB_{imp}). Since the gas density dependent components of the ventilators available (eg inspiratory and expiratory valves) have been designed for use under normobaric conditions, WOB_{imp} may differ significantly with increasing ambient pressure. Our aim was to analyze WOB as well as WB_{imp} with four different ventilators under hyperbaric conditions in a lung model study.
Methods: spontaneous breathing was simulated by the electromechanical lung model LS 1500 (Drägerwerk AG, Germany) consisting of a motor driven bellows. Lung model settings were: spontaneous tidal volume (V_T) = 500 ml, respiratory rate (f) = 20/min, compliance of the respiratory system (CRS) = 50 ml/cm H_2O and resistance (R) = 5 cm H_2O×s/l. The ventilators EVITA-4, Microvent, Oxylog 2000 HBO (Drägerwerk AG, Germany) and Servo ventilator 900C (Siemens-Elema, Sweden) were tested in the modes CPAP (0 cm H_2O) and Pressure Support Ventilation (PSV, 5 and 10 cm H_2O over CPAP except of the Oxylog 2000 HBO that do not provide a PSV-mode) under 5 (1, 1.3, 1.6, 1.9 and 2.8 ATA, EVITA-4 and Oxylog 2000 HBO) or 6 (additionally 6 ATA, Servo ventilator 900 C and Microvent) different atmospheric pressure conditions respectively. The motor driving electrical signal modulated by the linear displacement of the bellows was used as pleural pressure (P_{pl}), the displacement of the bellows as flow (V) signal. Airway pressure (P_{aw}) was measured inside the bellows. WOB and WOB_{imp} were calculated by integration of the inspiratory P_{pl} and P_{aw} drop over V respectively.
Conclusion: WOB and WOB_{imp}, increased significantly with atmospheric pressure. Due to the marked differences between the ventilators the properties of each one needs to be known in order to assess the impact on WOB.
Acknowledgement: We thank Drägerwerk AG, Germany for kindly providing us the lung simulator LS 1500.

P107

Respiratory mechanics during nitrous oxide and xenon anesthesia with and without metacholine-induced bronchoconstriction

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Critical Care 1998, **2(Suppl 1):**P107

Introduction: The use of xenon (Xe) as inhalative anesthetic agent might impair respiratory mechanics because of the relatively high density of this gas (5.897 g/l) when compared to nitrogen (N_2, 1.250 g/l) or nitrous oxide (N_2O, 1.964 g/l). The aim of this study was to compare inspiratory airway resistance (R_{aw}) as well as mean and peak airway pressure (P_{aw})

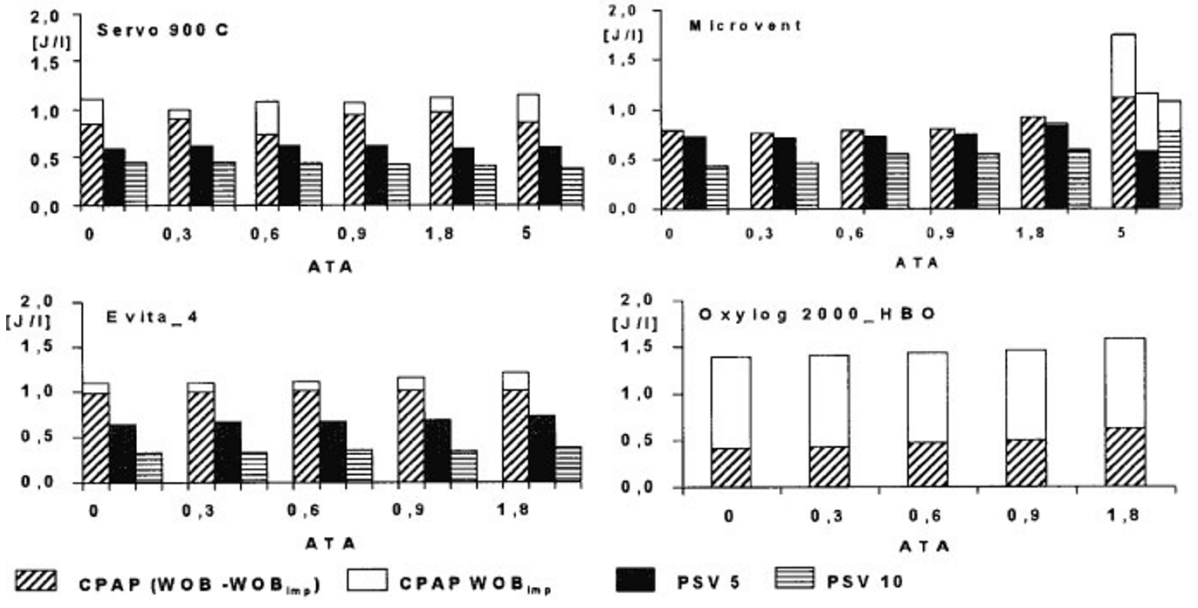

Figure (abstract P106) Results.

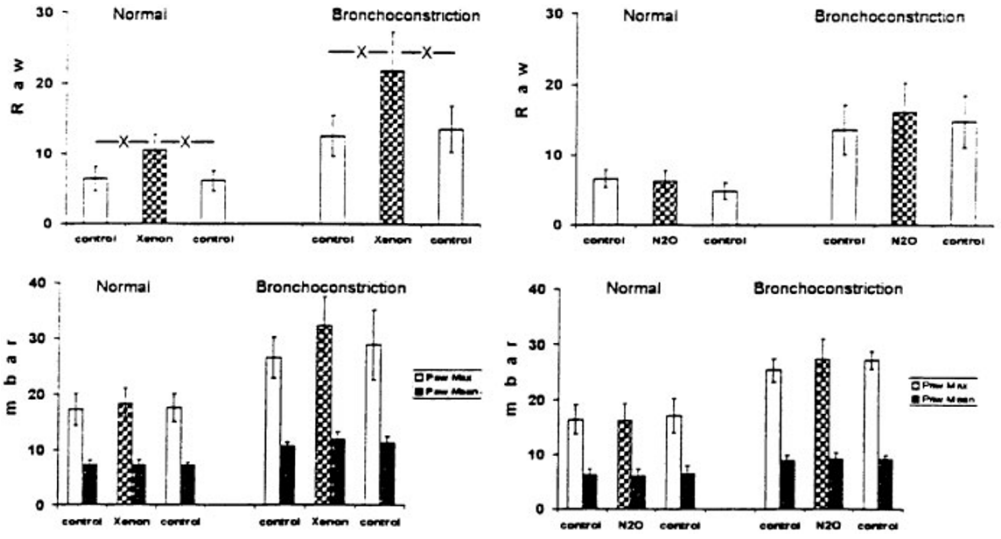

Figure (abstract P107) Results. X =$P < 0.05$. Friedman ranks signed ANOVA, followed, when significant, by the Student-Newman-Keuls method.

in pigs under normal conditions and with metacholine-induced bronchoconstriction during Xe versus N_2O anesthesia.

Methods: Two groups of anesthetized and paralysed pigs (N_2O $n = 5$, Xe $n = 6$) were ventilated with constant inspiratory flow provided by a semi-closed anesthesia circuit (CICERO, Drägerwerk AG, Germany) with a fresh gas supply correspondoing to half-minute ventilation. Ventilator settings were: tidal volume (VT) = 12 ml/kg, respirtory rate (f) = 12/min, duration of inspiration (TI) = 1.5 s, inspiratory breath hold (iBH) = 1 s and PEEP = 0 cmH_2O. P_{aw} was measured through a port proximal to the endotracheal tube with a differential pressure transducer (140PC, Honeywell Inc., Plymouth, MN) and airflow (V) by a heated pneumotachograph (Fleisch No. 2, Fleisch, Switzerland) connected with a differential pressure transducer. Animals were ventilated for three sequential periods of 45 min with a (control) mixture of 70% N_2 and 30% O_2 (period 1 and 3) and a testgas mixture of 70% Xe or N_2O and 30% O_2 (period 2). At the end of each period we performed three series of end-inspiratory airway occlusions in order to calculate R_{aw} and determined peak P_{aw} as well as mean P_{aw} (for a period of 2 min). For the second part of the study we induced a bronchoconstriction by a continuous metacholine infusion (16-32 µg/kg per min) during ventilation with the control gas mixture and repeated the same study protocol once again.

Results: X = $P < 0.05$. Friedman ranks signed ANOVA, followed, when significant, by the Student-Newman-Keuls method.

Conclusions: In contrast to the marked increase in R_{aw}, changes in P_{aw} during Xe anesthesia were less impressive but should be individually considered whenever using this gas as inhalative anesthetic agent.

Acknowledgement: We thank Drägerwerk AG for kindly providing the CICERO EM.

P108

Arterial oxygen partial pressures during nitrous oxide and xenon elimination

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Critical Care 1998, **2(Suppl 1):**P108

Introduction: A fall in arterial oxygen partial pressure (PaO_2) during nitrous oxide (N_2O) elimination is a well known phenomenon denominated as diffusive hypoxia that is caused by the relatively fast

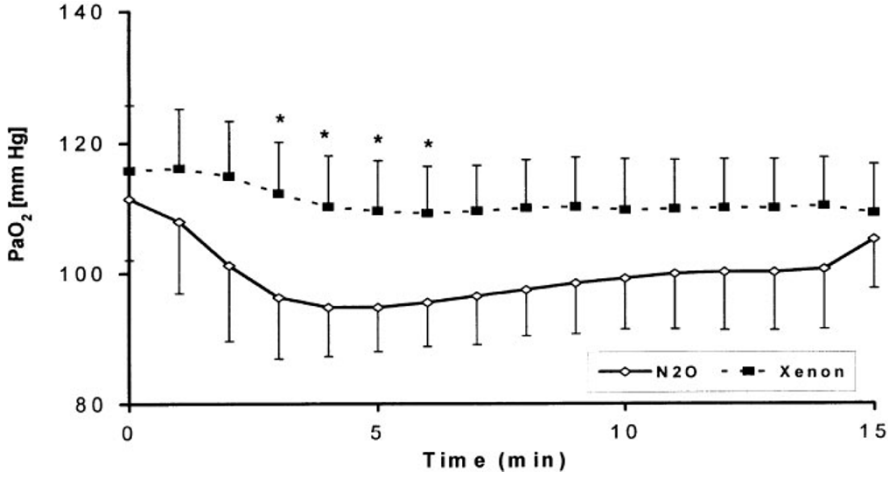

Figure (abstract P108) Results. Data are mean ± SD, $^*P < 0.05$ RS Mann Whitney.

N_2O-elimination compared with the slower simultaneous N_2-uptake. On the one hand, the occurence of diffusive hypoxia during Xenon (Xe) elimination could be supposed because of the rapid recovery from an inhalational (Xe)-anesthesia that can be explained by the low blood/gas partition coefficient (λ_{Xe} = 0.l4, λ_{N20} = 0.47). On the other hand, since diffusion of gas molecules is highly dependent on molecular weight (MW_{N2} = 28, MW_{N2O} = 44, MW_{Xe} = 133), the velocity of Xe-elimination should not exceed N_2-uptake very much. Therefore we compared PaO_2 during the course of Xe- and N_2O elimination.
Methods: After approval by the institutional animal ethics committee 11 pigs (Xe group=6, N_2O=5) were anestethized and paralyzed. The animals were ventilated using a standard semiclosed anesthesia circuit (Cicero EM, Drägerwerk AG, Germany) with a fresh gas flow (70% Xe + 30% O_2 or 70% N_2O + 30% O_2) corresponding to the minute ventilation. Ventilatory parameters were: tidal volume (V_t) = 12 ml/kg BW, respiratory time (f) = 12/min, inspiration rate (Ti) = 1.5 s, inspiratory breath hold = 1.0 s. After equilibration (45 min) fresh gas composition was switched from Xe or N_2O respectively to nitrogen (N_2) keeping FiO_2 as well as the ventilatory parameters constant. PaO_2 was measured continuously throughout the equilibration period and up to 15 min after switching to N_2 by the continuous blood gas monitoring device Paratrend 7 (Biomedical Sensors, New York, NY).
Results: Data are mean ± SD, $^*P < 0.05$ RS Mann Whitney.
Conclusions: Since PaO_2 decreased to a much lesser degree during Xe-elimination compared with N_2O. Diffusive hypoxia during recovery from Xe-anesthesia seems to be unlikely to occur.
Acknowledgement: We thank Drägerwerk AG, Germany for kindly providing us the Cicero-Xenon EM.

P109

The effect of positive end-expiratory pressure during partial liquid ventilation in acute respiratory failure

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Critical Care 1998, **2(Suppl 1):**P109

Objectives: To investigate the effects of PEEP application during partial liquid ventilation (PLV) on gas exchange and lung mechanics in an animal model of ARF.
Design: Prospective, randomized study
Setting: University research laboratory
Subjects: Six piglets weighing 7 to 12 kg
Interventions: After induction of anesthesia, tracheostomy and controlled mechanical ventilation animals were instrumented with two central venous catheters, a pulmonary artery and two arterial catheters, and an ultrasonic flow probe around the pulmonary artery. Acute respiratory failure was induced by the infusion of oleic acid (0.08 ml/kg) and repeated lung lavages with 0.9% Nacl (20 ml/kg), the protocol consisted of 4 different PEEP levels (PEEP 0, 5, 10 and 15 cmH_2O) randomly applied during PLV. The oxygenated and warmed PFC liquid (30 ml/kg) was instilled into the trachea over 5 min without changing the ventilator settings.
Measurements and results: Airway presures, tidal volumes, respiratory compliance, airway resistance and arterial blood gases were measured. Data were obtained at baseline and after lung injury and at each PEEP level during PLV. Data analysis: values are given as mean ± SEM. Comparisons were made by ANOVA for repeated measures. A P value of <0.05 was considered significant.
The infusion of oleic acid combined with 2–5 lung lavage induced a significant reduction of PaO_2/FiO_2 from 485 ± 28 torr to 68 ± 3.2 torr ($P < 0.01$) and of Cstat from 1.3 ± 0.06 to 0.67 ± 0.04 ml/cmH_2O/kg ($P < 0.01$).
Conclusions: Partial liquid ventilation is a useful technique to improve oxygenation in severe ARDS. The application of PEEP during PLV further improves oxygenation and lung mechanics.
Acknowledgement: The work was supported by grants of the Austrian Nationalbank Nr:6496

P110

A new management of humidification under superimposed high-frequency jet-ventilation in combination with a new prototype of a jet-ventilator

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Critical Care 1998, **2(Suppl 1):**P110

Background and goal of study: This study introduces a new prototype of an eletronic jet ventilator which is capable of simultaneously delivering two separate jet streams with different frequencies to the patient. This ventilation technique is called superimposed high-frequency jet-ventilation (SHFJV). We want to show, in a prospective, randomized, observational study, that the problems of humidification, under SHFJV can be prevented, using this new jet-ventilator (Alexander 1, Fa. Fesco, Vienna, Austria).
Material and methods: After institutional approval forty patients, 16 female, 24 male with a median age of 67 years (range 55 to 79 years) were randomly allocated to one of four groups (A, B, C, D) ten in each group, receiving either SHFJV by the Alexander 1 (group A and group B), or high frequency oscillation (HFO) by a VDR 4 (group C), or conventional mechanical ventilation (CMV) by an Evita (Group D). All patients were ventilated for more than 100 h because of respiratory insufficiency [1]. The relative humidity (RH) of the inspiration gas (FM-C1, E u E. Elektronic, Unterwiesen, Austria) and its temperature (temperature sensor line 21076 A, Hewlett Packard, Palo Alto, CA) were measured twice a day. Bronchoscopy (Olympus BF Type 20D, Olympus Optical Co., LTD, Shirikawa, Japan) was performed twice a day too. Humidification and warning of the ventilation gas was done using three different humidification systems. In group A, we used a combined form of a humidification and warming-system. Whereas the entrained gas (bias flow) was humidified by a hot water humidifier (Aquapor, Type 8406640 Fa. Dräger, Corp., Lübeck, Germany), humidification of the jet gas was achieved by a continuous infusion of 0.9% saline via a special jet adapter into the high pressure jet line. The instilled saline infusion was warmed by a fluid warmer (HL-90 INT, Level 1 Technologies Corp., Rockland, MA, USA) up to 37°C before it reached the jet gas. In group B, we used the same system without the fluid

Table (abstract P109). Blood gases and respiratory variables during PLV with different PEEP levels

	BL	ALI	PEEP-0	PEEP-5	PEEP-10	PEEP-15
PaO_2/FiO_2 (torr)	485 ± 28**	68 ± 3	269 ± 49**	274 ± 53**	320 ± 50**	401 ± 46**
Qs/Qt(%)	20.5 ± 5**	48 ± 3	33 ± 3**	33 ± 3**	30 ± 2**	24 ± 2**
pH	7.39 ± 0.01	7.28 ± 0.02	7.26 ± 0.03	7.26 ± 0.03	7.27 ± 0.04	7.29 ± 0.1
$PaCO_2$ (torr)	42 ± 2	44 ± 4	47 ± 5	48 ± 5	47 ± 6	45 ± 5
PIP (cmH_2O)	26.1 ± 1**	38.5 ± 2.4	52.6 ± 1.6*	43 ± 2.4*	35 ± 0.8	39.5 ± 0.9
Pplat(crnH_2O)	17.1 ± 1**	31.6 ± 2.3	25.6 ± 1.7*	25.6 ± 1.4*	27.3 ± 1.1*	32.6 ± 1.2
Paw (cmH_2O)	9.3 ± 0.2**	14.1 ± 0.47	12.8 ± 0.3	14 ± 0.2**	17 ± 0.2*	21.5 ± 0.2*
Cstat†	1.3 ± 0.1**	0.67 ± 0.04	0.71 ± 0.04	0.82 ± 0.1*	0.95 ± 0.1*	0.94 ± 0.1*
Rawm††	20 ± 3.9*	25.5 ± 4.4	30.6 ± 4.6*	26.5 ± 3.1	21.1 ± 3.4	21 ± 4.1

$^*P < 0.05$ vs ALI, $^{**}P < 0.01$ vs ALI, BL: baseline; ALI: Acute Lung Injury; †ml/cmH_2O/kg, ††cmH_2O/l/s

warmer. In group C and D, we used a hot water humidifier. In all four groups, several patients were exposed to intermittent prone position in case of extremely severe ARDS. Data were statistically analyzed using *t*-test and Fischer-test (rectification according to Yates).

Results and discussion: To evaluate the amount of tracheobronchial mucosal injury, a scoring system was used, taking into account the size of the area and the extent of macroscopic epithelial damage. Group A, C and D had a mucosal injury score of zero, no significant pathologic evidence could be seen. The temperature values (group A: 31.4°C; group C: 32.1°C; group D: 34.2°C:) were insignificantly different. In group B, the temperature was significantly lower (27°C) than in all other groups. Inflammation of the tracheal mucosa was found and the mucosal injury score was significantly higher.

Conclusion: Using the ALEXANDER 1 for SHFJV with high humidity, almost all the problems, which are associated to this ventilation technique, like tracheal epithelial inflammation, necrotizing tracheobronchits (NT), etc can be prevented.

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P111

A new method of quantification of atelectatic areas: a pilot study

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Critical Care 1998, **2(Suppl 1):**P111

Background and goal of study: This study reports of a new way to verify the recruitment of atelectatic areas with a mobile CT, in patients who are served superimposed high frequency jet ventilation (SHFJV) [1].

Material and methods: After institutional approval four patients, three male and one female with a mean age of 52 years (ranging 21 to 83 years) received SHFJV for four hours by a prototype of a new electronic jet ventilator named ALEXANDER 1. Blood gas analyses were taken every half hour during the whole study period. A thorax CT (mobile CT, Philips Tomoscan M, Netherlands), was taken of every patient before and after the period of ventilation with the possibility of 3D reconstruction. The ventilated areas of each thoracic CT-picture were digitally remastered and volumetricly measured by a serial scan of the lungs (matrix 512 to 512, zoom factor 1.4; slicethickness 1.0 cm, pitch 1.0 cm, trash hold of -400 to -1000 HE). A high resolution CT (HR-CT) was performed of every patient's lungs (slicethickness 0.2 cm, pitch 1.5 cm, same trash hold and same matrix as in the serial scan) before and after jet-ventilation, to detect any alteration of the parenchyma or changing of (he diameters of the bronchi. Data export was performed via DICOM III on a Philips Easy Vision 2,1.2. Sun Sparc Station 5.

Results and discussion: The situation of every lung improved. The average amount of the improvement of the ventilated areas were 329 cm, which represented an average increase of 11.7%. In analogy of these values, we saw that the PaO_2 measurements of the arterial blood gas analyses were improving too. The average increase of the PaO_2 value amounted to 40.4% within the period of SHFJV, meaning that the improvement of the ventilation (recruitment of the atelectatic areas) leads to a better oxygenation. Regarding the HR CT, we saw no dilatation of the bronchi, but a decrease of the atelctatic areas.

Conclusions: The improvement of the ventilation and oxygenation can be umpirely objectified with this new method. This possibility improves the critically regarded situation of the SHFJV.

Reference

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P112

Improved oxygenation with superimposed high frequency jet ventilation at resonant frequency

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Critical Care 1998, **2(Suppl 1):**P112

Introduction: Superimposed high-frequency jet-ventilation (SHFJV) is a new form of a combined high frequency (HF) jet ventilation technique in treatment of ARDS. Since the HF jet-stream improves oxygenation partially due to enhancement of the intra-pulmonary gas mixture [1] the question arises which frequency would be the most effective. Animal models and in vitro experiments demonstrate that the best results may be achieved with frequencies close to the resonant frequency (RF) of the lungs [1,2]. In this study we tried to find RF using SHFJV.

Materials and methods: SHFJV is a combination of a pressure controlled low-frequent and a pressure controlled HF jet-ventilation. The RF was studied in two patients groups with SHFJV. Group 1 included pulmonary healthy patients (n = 11) and group 2 included patients with ARDS (n = 13). The individual RF was determined in each patient analysing the ventilation-pressure waves which were recorded at 0.5 Hz intervals starting with 5 Hz up to 16.5 Hz. The amplitudes of the recorded pressure waves were analyzed and the average calculated at each examined frequency. The frequency with the maximum pressure amplitude represented the RF [3]. After RF was determined the patients were ventilated for 30 min using SHFJV at a frequency different than the RF followed by 30 min of SHFJV at RF. FiO_2 levels and airway pressure did not change in the study period. Blood gas analysis was performed in intervals of 5 min throughout the study.

Results: In contrast to non-resonant frequency in group 1 PaO_2increased from 113 mmHg to 122 mmHg with SHFJV at RF. In group 2 PaO_2 increased from 89 mmHg to 101 mmHg with SHFJV at RF.

Discussion: Our results demonstrate an improvement of PaO_2 when applying HF ventilation at the individual RF compared to non-resonant frequencies. Although the effects of SHFJV, as with other HF jet ventilation techniques, are not fully understood, studying RF with its improvement of oxygenation may be another step towards explaining the beneficial effects of HF ventilation techniques observed.

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P113

Nitric oxide application during superimposed high-frequency jet-ventilation in patients with ARDS

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Critical Care 1998, **2(Suppl 1):**P113

Introduction: Inhaled nitric oxide (NO) reduces pulmonary hypertension in severe ARDS and improves arterial oxygenation by redistributing blood flow to areas with a normal ventilation/perfusion ratio [1]. As high peak inspiratory pressure (PIP) may contribute to pulmonary damage ventilatory strategies like high-frequency (HF) ventilation search to minimize PIP. This study was designed to evaluate the combined benefits of superimposed high-frequency jet-ventilation (SHFJV), a new HF jet-ventilation technique, with addition of inhalational NO.

Methods: 10 patients with severe ARDS were evaluated. All patients where ventilated with a conventional respirator (Evita, Dräger, Germany). The indication for SHFJV was a Horrowitz Index below 100. An electronic prototype jet-ventilator (Alexander 1, Reiner, Austria) used for SHFJV provided simultaneous low-(14-20/min) and high-frequency (400-600/min) jet-streams, which were applied with a special jet-adapter. For application of NO we used the Pulmonox mini (Messer Griesheim, Austria) including a specially developed computer software for precise addition of NO (10 ppm) to the HF jet-stream during inspiration [2]. After 3 h of jet-ventilation we additionally applied NO.

Table 1 (abstract P113)

	CPPV	SHFJV	SHFJV and NO
Oxygenation	19.7	16.8	13.9
Horrowitz	96	118	149
PIP (cmH_2O)	34	30	30

Results: PaO_2/FiO_2 and Horowitz index increased during SHFJV and NO application, while PIP could be reduced maintaining the same levels of CO_2 (Table 1).
Conclusion: The beneficial effect of SHFJV on oxygenation can be combined with the selective effects of inhaled NO. Thereby, impaired pulmonary function can be further improved.
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P114

Nitric oxide improves pulmonary vascular resistance but not oxygenation in ARDS, heart transplant, and pulmonary hypertension

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Critical Care 1998, **2(Suppl 1):**P114

Introduction: We study the effects of inhaled NO on oxygenation (P/F ratio), and pulmonary vascular resistance (PVR) in 15 patients with ARDS, cardiac transplant and pulmonary hypertension for a minimum of 48 h.
Methods: Data were collected prior to NO therapy, 24 and 48 h after NO was initiated. For each subject PVR and P/F ratio for the three time periods were plotted against the corresponding dose of inhaled NO (ppm). Using these plots linear regression analysis was performed. The slopes of the regression lines (b) were averaged for each of the three groups and a student's t-test was performed on each group's data to identify significant correlation.
Results: The PVR was found to be decreased (b = -5.38), ($P < 0.01$) in all three groups. NO increased the P/F ratio (b = 1.69), but this was not statistically significant. When considering the groups individually, the ARDS group ($n = 3$) had on average a decrease in PVR (b = -7.02), and improvement of P/F ratio (b = 4.71). This group received an average concentration of NO of 22.7 ppm for an average of 10 days. The cardiac transplant group ($n = 6$) showed improvement in the PVR (b = 5.59) with almost no effect on the P/F ratio (b = 0.345). This group received an average of NO of 34.8 ppm for an average of 6 days. The pulmonary hypertension group (n = 6) revealed a significant reduction in the PVR (b = -3.81) with a $P < 0.025$, and there was increase in the P/F ratio (b = 1.528). This group received an average concentration of NO of 41.4 ppm for an average of 5.5 days.
Conclusion: Inhaled NO had a greater effect on PVR than on P/F ratio. In the cardiac transplant group, NO decreased the PVR but had little effect on oxygenation (P/F). In the pulmonary hypertension group, NO decreased the PVR but not improvement in P/F ratio. In this study, the only significant effect of NO was on the PVR in patients considered as a whole and in the pulmonary hypertension subgroup. Patients with ARDS had the least benefit of NO therapy. We attribute this lack of response in oxygenation to severe underlying pulmonary condition as well as other comorbid illnesses.

P115

Inhaled nitric oxide: how to deliver it?

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Critical Care 1998, **2(Suppl 1):**P115

Introduction: Clinical applications of inhaled nitric oxide (inhNO) therapy gave rise to the development of delivery systems applicable to routine clinical care. This study reviewed the various components necessary for an adequate clinical use of inhNO, covering the NO gas mixture cylinders, inhNO delivery techniques and specifications.
Methods: Computerized search (CURRENT CONTENTS, MEDLINE) of published original research and review articles (~260), conference abstracts and compendiums up to December 1997 (~60), personal files with clinical and experimental use, and contact with expert informants were selected in technical, experimental and clinical reports from the recent English, French, German, and Spanish literature if pertaining to the administration of inhNO.
Results: The production of NO gas mixture cylinders must be certified with respect to gas purity, stability, and concentration (limits between 100 and 1000 parts-per-million), guaranteed calibration, and specific color. In order to maintain a safe and constant concentration of NO in inspired gas, NO would need to be injected proportionally to the flow in the main circuit and followed by adequate mixing of NO and N_2/O_2. This would be expected to occur with: (1) mixing a constant proportion of N_2, O_2 and NO pre-ventilator (or with a gas mixing chamber): with this system, flow in the inspiratory limb could be continuous or phasic, constant or variable, and not be expected to effect NO concentration; but drawbacks are inability to precisely adjust preventilator mixing, increased time availability for creation of toxic NO_2 gas, and putative deterioration of the ventilator internal components by the oxidative gas; (2) NO is injected in the inspiratory limb with some limitations: at a continuous and constant rate of NO and gas flow for infant ventilators; sequentially (during inspiration only) of an adult phasic flow ventilator where main circuit flow is at a constant rate (volume ventilation, square wave flow, and patient heavily sedated or sedated/paralyzed); (3) with variable flow rate (decelerating, ramp, and sine) for volume-, pressure-controlled ventilation or variation in patient ventilatory effort, NO injection in the inspiratory limb is titrated using an ultrafast response system that consists of an inspiratory limb pneumotach (or thermoanemometer) generating an electrical signal to a mass flow meter that adjusts the NO injection on a millisecond basis as flow varies within or between breaths. The synchronized delivery allows a precise and constant administration of NO with a minimal production of NO_2 and oxidation danger.
Discussion: The great expectancies generated by inhNO action have led researchers to design personal inhNO delivery system but only with mitigated results. At present, biomedical companies are finding a financial interest in designing a delivery system which will suit the needs of clinicians considering the effect of the ventilatory mode, ventilatory settings, NO delivery device being used, and injection site.

P116

Evolution of thorax X-rays in ARDS patients with or without inhaled nitric oxide

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Critical Care 1998, **2(Suppl 1):**P116

Introduction: In a pilot randomized placebo-controlled clinical trial of acute respiratory distress syndrome (ARDS) patients treated with inhaled nitric oxide (inhNO), we have measured a chest X-ray score during 10 days post-randomization for control (15 patients receiving usual care) and experimental (15 patients with usual care plus inhNO) and compare its evolution in time and between groups with lung function and outcome.
Methods: This study was approved by the Human Research and Ethic Committee of Centre Hospitalier de l'Université de Montréal. All therapeutic interventions were standardized. Lung function was assessed by hypoxia score (HS = PaO_2/FiO_2), PEEP level, dead space ventilation, lung compliance, and venous admixture. The optimal dose of inhNO was determined daily between 0.5 and 40 parts-per-million. Nonresponders to inhNO were defined as patients presenting a 20% increase in HS after initial optimal dose of inhNO determination. Daily morning radiographs were obtained on portable chest X-ray equipment. After completing the study, 255 radiographs of the 30 ARDS patients were analyzed in blinded and serial fashion by three independent readers. Based on previous studies [1-3], radiographic criteria were selected in order to reflect the pattern of air-space consolidation (parenchymal opacification, atelectasia) associated with vascular pattern (indistinct vessels) and possible presence of interstitial pattern (septal lines, peribronchial cuffing, pleural effusion)

particularly considering the evolution with time (until day 10 after randomization). The reliability of the technique was determined by looking at intra- (45 radiographs blindly evaluated twice) and inter-observer variabilities.

Results and discussion: ARDS resulted mainly from sepsis (25/30). Observed baseline characteristics were similar between groups. During the first day, HS increased greatly in patients treated with inhNO: +70.4 mmHg (+59%) vs. +14.2 mmHg (+9.3%) for control group (P = 0.02), venous admixture decreased from 25.7 to 15.2% in the inhNO group, and only from 19.4 to 14.9 % in the control group (P = 0.05). The status of the lung correlated well with the chest X-ray score. Intra- and inter-observer variability were reasonable. Five out of 15 patients were nonresponders. After the first day of therapy, no further beneficial effect of inhNO could be detected, whereas studied parameters were never affected by usual care in the control group. Forty percent of patients treated with inhNO were alive and weaned from mechanical ventilation 30 days after randomization compared to 33.3% in the control group (P = 0.83). The 30-day mortality rate was similar in the two groups: 60% in patients treated with inhNO vs 53.3% without inhNO (P = 0.71); most deaths (11/17) were due to multiple organ dysfunction syndrome (MODS). On the 5 direct lung injury-induced ARDS, only 1/3 died in the control, 0/2 in the inhNO group. The 30-day mortality rate of nonresponders, and responders to inhNO was 80%, and 50%, respectively. No correlation was found between the evolution of the chest X-ray score and the outcome, the ARDS origin or the treatment.

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P117

Adenosine as pulmonary vasodilator in ARDS

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Critical Care 1998, **2(Suppl 1):**P117

Background: Pulmonary hypertension plays a major role in the physiopathology of ARDS. Because some studies report a predictive value of increased pulmonary vascular resistances on mortality in patients with ARDS, treatment of this pulmonary hypertension seems to be justified. However, traditional intravenous vasodilators agents have both pulmonary and sistemics effects. Adenosine, a new agent, has been shown to have potent selective pulmonary vasodilator actions in patients with primary pulmonary hypertension when is infused directly in pulmonary artery.

Objectives: To assess the vasodilator pulmonary effects of adenosine and its consecuences on cardiac performance and gas exchange, in patients with ARDS-induced pulmonary hypertension.

Methods: Patients with ARDS admitted to the ICU were included in this prospective study. All of them received mechanical ventilation (PCV-IRV). Haemodynamic monitoring was made by Swan-Ganz catheter. Arterial pressure was monitored in an invasive mode and mixed venous saturation was recorded too. Cardiac output was measured with thermodilution method. Haemodynamic stability in the last 12 h regardless the use of inotropic drugs, a $pO_2 \geq 100$ mmHg and a pH≥ 7.2, were goals to achieve before entering in the study. Variables not measured directly, were calculated with standar formulae. Transthoracic echocardiography was used to assess systolic and diastolic function of both ventricles, by calculating left ventricular ejection fraction (LVEF) and right ventricular shortening fraction (RVSF) in the assessment of systolic function and measuring maximal flow velocities of E and A waves in the case of diastolic function. Continuous intravenous infusion of adenosine was performed by a central venous line with increasing doses of 0.001, 0.01, 0.03 and 0.05 mg/kg per min. Haemodynamic and oxymetric parameters and echocardiographic measurements were recorded before the start of adenosine infusion and after each increase in the dose. Statistical analysis was made with ANOVA and Student's T tests, considering $P \leq 0.05$ as significance level.

Conclusions: Adenosine decreases pulmonary hypertension in ARDS only in high doses, but producing systemic effects too, decreasing cardiac output and mean arterial pressure. Gas exchange is impaired because inhibiton of hypoxic pulmonary vasoconstriction. Diastolic function is improved but systolic one is impaired in both ventricles after the use of adenosine.

P118

Use of prostacyclin in pulmonary hypertension

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Critical Care 1998, **2(Suppl 1):**P118

Introduction: The use of drugs such as epoprostenol which dilate the pulmonary vessels is indicated in patients with primary pulmonary hypertension in order to improve their clinical status before being transplanted.

We describe our experience in six patients with primary pulmonary hypertension who received prostacyclin and underwent lung transplantation sometime later.

Material and methods: Six patients aged between 19 and 50 years old (2 female, 4 male). Base diagnosis was primary pulmonary hypertension. In all of them a haemodynamic study with Swan-Ganz catheter was performed. Patients were treated initially with acenocumarol and diltiazem. If they presented auricular fibrilation or low right ventricular function, digoxin was associated. If the end telediastolic right ventricular pressure was increased, dicumarinic was associated. If the right ventricular function became worse, prostacyclin was added to the treatment.

Results: Dose of prostacyclin: 4–6 ng/kg per min
Time of waiting before lung transplantation: 25 days to 6 months
Clinical improvement of right ventricular function: 5 patients
Dysnea after moderate efforts: 3 patients
Improvement of pulmonary artery pressure: 6 patients

Conclusions: Prostacyclin is an usefull treatment of pulmonary hypertension to improve the clinical status and the haemodynamic parameters in these patients and it helps until lung transplantation can be performed.

Table (abstract P117)

	MAP	MpaP	cF	CI	Eyecc. Vol	LVSWI	RVSWI	SVRI	PVRI totale	PVRI arteriolar	Ratio PVRI/SRVI	PaO_2	Qs/Qt	Ratio speed Flow RV A/E
Basal	82	28	112	3.8	57	37	12	1496	581	354	0.39	109	29	0.33/0.5
First infusion	71*	25*	99*	3.1*	54*	30*	10*	1523*	634*	407*	0.42*	92*	37*	0.54/0.45*
Second infusion	70*	27*	97*	3.2*	56.7	32*	12*	1476*	664*	393*	0.45*	90*	36*	0.63/0.35*
Third infusion	63*	21*	95*	3.4*	61.6*	31*	10*	1228*	486*	231*	0.39	83*	42*	0.55/0.41*
Fourth infusion	60*	18*	90*	3.5*	62.1*	30*	9*	1170*	429*	167*	0.37*	80*	41*	0.4 7/0.43*

*Denote statisitical significance to respect basal values

P119

Use of a clinical protocol to assess the respective indications of prone position and nitric oxide in patients with ARDS

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Critical Care 1998, **2(Suppl 1):**P119

Inhalation of nitric oxide (NO) and prone position ventilation (PPV) have been showed to improve the PaO_2/FiO_2 ratio in patients with acute respiratory distress syndrome (ARDS). The aim of this study was to identify which of the following treatments (PPV, NO or PPV + NO) improved the PaO_2/FiO_2 ratio most in a patient. Ten consecutive patients presenting with severe acute respiratory failure (PaO_2/FiO_2 <150 mmHg) unrelated to congestive heart failure were studied.
The time course of the treatment was as follow: supine position (SPV) (H0 control value), PPV (H0 to H2), SPV (H2 to H3), PPV + NO (H3 to H5) and SPV + NO (H5 to H6). Oxymetric parameters were measured at the end of each cycle of treatment. During the protocol, ventilator settings were unchanged. A patient was considered as responder to a treatment when the PaO_2/FiO_2 ratio increased by a value of 20 mmHg compared to the control value. After the protocol time course, each patient received the treatment according to the best oxymetric results.
Two patients were no responders to PPV and 8 patients responded to PPV with an increase of PaO_2/FiO_2 of 122.8 ± 104.5 mmHg (mean ± sd). Five patients were responders to NO with an increase of PaO_2/FiO_2 of 51.8 ± 20.2 mmHg. Only one patient was not responsive to NO and to PPV, but responded to PPV + NO combination (+ 65 mmHg).
According to the results, the treatments selected were: 1) PPV + NO in 6 patients: increase of PaO_2/FiO_2 by a mean of 149.7 ± 89.6 mmHg; 2) PPV in 3 patients: increase of PaO_2/FiO_2 by a mean of 131.3 ± 124 mmHg; 3) NO alone in one patient: increase of PaO_2/FiO_2 by 75 mmHg.
Although the aim of the study was not to compare the 2 methods, it seems nevertheless that PPV was more effective than NO. An additive effect of PPV and NO was found in 6 out of 10 patients and especially in one patient not responding to PPV or NO alone.

P120

The role of positioning in the prevention and therapy of ALI and ARDS in polytrauma patients: results of a prospective study with 100 cases

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Critical Care 1998, **2(Suppl 1):**P120

Introduction: Since its introduction into intensive care medicine in the early 80s, the positive effects of kinetic therapy have been proven in different patient groups. However, polytrauma patients with severe chest injuries have not yet been studied in large numbers. According to the principles of evidence based medicine, only a small body of literature exists. With this in mind, we planned to create a greater data base in this subgroup of trauma patients to work out a baseline for an evidence based level I study.
Methods: From 1994 to 1997, in a consecutive series 100 patients were treated in an open prospective trial with a standardized protocol including therapy guidelines for the application of either kinetic therapy or prone positioning. There were 73 male and 27 female patients with a mean age of 35 years. In 80% of the cases, a traffic accident was the cause of injury. The severity of trauma and illness in this group was characterized by an ISS (injury severity score) of 35 (15–75) and an APACHE II of 11 (6–28) on the first day. Outcome predictors were ventilation time, stay on the ICU and in hospital, as well as total hospital mortality. A short-term outcome parameter was an increase of PaO_2/FiO_2 ratio in the first 72 h.
Results: 100 patients were treated with this concept in a kinetic bed with positioning. Whenever possible, extreme positioning of 60° was used, in 10 patients with severe atelectasis prone positioning was performed in addition for a mean time of 2 days. The mean treatment time in the kinetic bed was 5 days (2–21), the time on ventilator therapy was 12 (3–62), length of stay on the ICU 18 (5–67) days and in hospital 28.5 (8–220) days. Positive PaO_2/FiO_2 ratio changes in the first 72 h of the therapy were observed in 70% of patients. Mortality in the treatment group was 10%. Cause of death in all patients was the development of multiple organ failure.
Conclusions: Analysing our results, we found a much better outcome than predicted by the initial scoring in this severly injured patient group. The rate of secondary lung damage was very low. According to our findings, standardized kinetic therapy is one approach to improve the outcome in polytrauma patients by reducing severe pulmonary complications.

P121

Low cost prone positioning of critically ill ARDS patients with the MPS (modular prone positioning system)

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Critical Care 1998, **2(Suppl 1):**P121

Introduction: Despite the many benefits of prone positioning in critically ill patients with respiratory failure and acute respiratory distress syndrome (ARDS) on the intensive care unit its technical aspects are not yet sufficiently defined. Different approaches exist with special beds for prone positioning, but these are difficult to handle, often not available and involve high costs. With this in mind, we developed an easy handling prone positioning system (MPS) that requires no special beds and run at low cost.
Methods: From 01.01.1996 to 31.07.97, 10 patients with severe atelectasis and ARDS were treated in the authors' institution by the MPS. The cause for prone positioning was in all cases bad gas exchange (PO_2/FiO_2 <200 mmHg) and severe atelectasis of conventional X-ray and CT scan. The positioning was performed over consecutive cycles of 12 h supported by physiotherapeutical measures like percussion and bronchioalveolar lavage. During the prone positioning the positive end-expiratory pressure (PEEP) was raised to 10–12 mmHg in the initial phase.
Results: The intermittent prone positioning was performed for a mean of 3 days (1–4). In all cases the PO_2/FiO_2 ratio rose to values over 300 mmHg after 24 h. According to the treating nurses and intensivists the handling of the MPS is easy and it provides better monitoring of the patient than previously used methods. The rental costs of the system, $600 for the prototype, were significantly lower than the costs for special prone positioning beds.
Conclusion: The MPS is a cost effective device yielding many benefits for prone positioning in critically ill patients with severe atelectasis and ARDS.

P122

Pulmonary gas exchange in pigs improves in the prone position with abdominal distension

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Critical Care 1998, **2(Suppl 1):**P122

Partial pressure of oxygen (PaO_2) in arterial blood tend to be higher in the prone compared to supine position. Whether similar improvements in gas exchange occur in the presence of abdominal distension is not clear. We studied the effect of position on gas exchange in eight ketamine anesthetized, mechanically ventilated pigs with abdominal distension. A intraabdominal rubber balloon, was used to increase intraabdominal pressure. Gas exchange was measured in the supine and prone positions, with and without abdominal distension, in random order using the multiple inert gas elimination technique. In presence of normal abdomen, only PaO_2 increased ($P < 0.05$). In contrast, in the

prone position with abdominal distension, the PaO_2 ($P < 0.01$) increased and $AaPO_2$ ($P < 0.05$) and $\tilde{A}_A$/ heterogeneity, indicated by log SD ($P < 0.01$) and [(a-A)D] area ($P < 0.05$) were decreased in the prone compared to the supine position. We conclude that the prone position increases PaO_2 by improving gas exchange in pigs with abdominal distension.

P123

Does Tendelenburg position and sheet covering of the face affect respiratory function in cardiac patient?

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The Tendelenburg position (TP) and the sterile sheet covering of the face (SCF) are two manoeuvres routinely employed to cannulate a central vein and position the Swan-Ganz catheter. The two manoeuvres however can interfere with the respiratory function, decreasing the functional residual capacity, redistributing the pulmonary blood flow and favouring the rebreathing of the expired gases [1]. In this study we evaluated the impact of the two manoeuvres on the respiratory gas exchange in the cardiac patient.

Method: We studied 50 cardiosurgical premedicated patients without respiratory disease and we divided them into 5 groups: Group A_1 = 10 elective coronary patients (CP) with left ventricular ejection fraction (LVEF) >45% supplied with O_2 40% by a ventimask; Group A_2 = 10 CP with LVEF >45% breathing room-air; Group B_1 = 10 CP with LVEF <45% supplied with O_2 40%; Group B_2 = 10 CP with LV EF <45% breathing room-air; Group C = 10 end stage heart disease patients with LVEF <30% undergoing heart trasplantation, supplied with O_2 40%. Before induction of anaesthesia all patients were placed in TP (30°) and had their face completely covered by sterile sheets, to cannulate the internal jugular vein and position the Swan-Ganz catheter. The arterial blood samples to measure oxygen (PaO_2) and carbon dioxide ($PaCO_2$) tension were drawn: before TP and SCF (Time 1), before removing TP (with SCF) (Time 2), before removing SCF (without TP) (Time 3), 5 min after SCF removal (Time 4). Statistical analysis was performed by ANOVA test, significant for $P < 0.05$.

Results: The main results are reported in Table 1. There are no significant differences among the five groups in the times applied for TP and SCF.

Discussion: The analysis of our data shows that: a) the association of TP and SCF (time 1 versus time 2) caused a significant increase in PaO_2 in all patients receiving O_2 and a small and not significant decrease in patients breathing room-air; b) The removal of TP (time 2 versus time 3) caused a small increase in PaO_2 in all groups but group C who showed a significant increase in PaO_2; c) the SCF (time 1 versus time 3) induced a significant increase in PaO_2 in all patients receiving supplemental O_2 and a small and not significant increase in patients breathing room-air. We did not observe any significant change in $PaCO_2$ values in all groups.

We conclude that the TP and the SCF, frequently employed in anaesthesia, ICU and emergency medicine, ensure a good respiratory gas exchange in cardiac patient, even when supplemental O_2 is not supplied or LVEF is markedly reduced.

Table 1 (abstract P123). PaO_2 and $PaCO_2$ values recorded at the four times

Times		1	2	3	4
PaO_2	A_1	111.9± 28	147.2 ± 41*	157± 42	116 ± 25*
	A_2	78.6 ± 8	78.1 ± 8	82.7 ± 9	78.7 ± 14
	B_1	97.8 ± 17	146.5 ± 33*	156.6 ± 40	102.5 ± 13*
	B_2	87.9 ± 19	82 ± 12	88.2 ± 10	86.7 ± 10
	C	144.8 ± 27	208.7 ± 35*	233.7 ± 37*	152.2 ± 31*
$PaCO_2$	A_1	40.1 ± 4	40.3 ± 4	41.2 ± 4	40 ± 5
	A_2	40.9 ± 3	41.3 ± 4	41.1 ± 5	41.1 ± 5
	B_1	40.1 ± 5	41.6 ± 5	43.6 ± 6	43.8 ± 7
	B_2	38.9 ± 4	40.8 ± 4	40.6 ± 5	38.5 ± 3
	C	36.3 ± 6	37 ± 5	36.3 ± 4	35.6 ± 5

*$P < 0.05$ versus the previous value within each group

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P124

Effect of PEEP levels on ventilation in prone position in patients suffering from acute lung injury

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Critical Care 1998, **2(Suppl 1):**P124

Objectives: Prone position (PP) improves oxygenation and respiratory mechanics in patients suffering from acute lung injury (ALI). Aim of our study was to better understand lung recruitment due to ventilation in PP.

Methods: 4 sedated and paralysed suffering from ALI (3M/1F;mean age 59.8 ± 15.4; LIS: 2.30-3.15). Mechanical ventilation was done in volume-controlled mode with a computer controlled Servo Ventilator 900 C (Vt: 8-10 ml/kg; RR: 12-18 b/min; Ti: 33%; Tpaus: 5%; FiO_2 0.4-0.6). Lung mechanics was studied during a computer controlled low sinusoidal flow oscillations inflation. Pressure and flow were read by the computer. Volume was calculated by integration of flow. The distending pressure (Pdist) was calculated by subtraction of resistive pressure drop in connecting tubes and airways. Compliance (Crs) was evaluated by plotting volume against Pdist. Each study breath was preceded by a 6 s long expiration during which PEEP was allowed to fall to zero and volume retained by PEEP (V_{ret}PEEP) evaluated. Alveolar dead space (Yd_{alv}) was obtained by a single breath test for CO_2. Patients were studied in stable condition in supine position (SP) with a PEEP level of 5 cmH_2O. PEEP was then set at 10 cmH_2O and after 15 min the study repeated. The same procedure was followed after the patients were turned prone. The following parameters were analysed: EKG, blood pressure, blood gases, Crs, Vt, V_{ret}PEEP.

Results: In the table the mean values are expressed. Patients were stable during the study, and no side effects were observed. One patients resulted non responder.

Conclusion: From our preliminary results, the improvement in oxygenation in PP seems to be due to a better lung recruitment and a reduction in Vd_{alv}.

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Table (abstract P124)

	PEEP 5 cmH_2O		PEEP 10 cmH_2O	
	SP	PP	SP	PP
Crs, ml/cmH_2O	52 ± 15	65 ± 6	54 ± 9	67 ± 12
PaO_2/FO_2	154 ± 33	277 ± 45*	171 ± 21	290 ± 18*
V_{ret}PEEP, ml	383 ± 34	399 ± 45	671 ± 56	694 ± 26
Vd_{alv}*ml	267 ± 19	194 ± 32*	311 ± 13	201 ± 23*

*$P < 0.01$

P125

Cytokine removal from plasma of patients with SIRS by the Biologic-DTPF™

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Critical Care 1998, **2(Suppl 1):**P125

The BioLogic-DTPF System™ uses a single lumen 10F venous catheter and combines a hemodiabsorption system using 2 l of sorbent suspension, flowing through the dialysate side of a parallel plate cellulosic dialyzer with whole blood perfusion on the blood side (the BioLogic-DT™ System), in series with a push-pull pheresis system (BioLogic-PF System™). Bidirectional plasma flow (80–100 ml/min) across the 0.5 micron PF membranes provide direct contact between plasma protein and powdered sorbent suspension of either charcoal or charcoal and silica. *In vitro* tests using whole blood have demonstrated that the BioLogic-DTPF clears cytokines (TNF-α, IL-lβ, and IL-6) at a rate of 15–25 ml/min, without evidence of saturation of sorbent during 90 min run times. Systemic Inflammatory Response Syndrome (SIRS) is the most common manifestation of cyrokine mediated disease in ICU patients. A Food and Drug Administration-approved Investiganonal Device Exemption permits a phase I preliminary safety and efficacy study of a single 6 h BioLogic-DTPF treatment of 8 patients with SIRS and organ failure due to sepsis.

Results: In treatment of 4 patients with charcoal, no adverse events occurred, hemodynamics were stabilized and less pressor agent was required. Cytokine levels decreased during treatment and remained significantly lower the next day.

The broad and nonspecific cytokine binding by the BioLogic-DTPF may quench both the proinflammatory and anti-inflammatory responses of SIRS and prove beneficial in treatment of patients.

P126

Immunological effects of CWHD in critically ill patients

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Critical Care 1998, **2(Suppl 1):**P126

Acute renal failure as part of the multi-organ dysfunction syndrome (MODS) is a severe complication in critically ill patients. Hemodynamic instability is common in these patients and exacerbated by hemodialysis (HD). Therefore, continuous veno-venous hemodiafiltration (CVVHD) is used as an alternative to conventional HD. The aim of the study was to test the hypothesis that initiation of CVVHD elicits an acute activation of the immune system followed by immunosuppression.

Patient and methods: Fifteen consecutive, septic patients with acute renal failure were treated with CVVHD in the ICU. The study was approved by the Regional Ethical Committee on Human Research and informed consent was obtained from the patients or a close relative. The cellular response was measured as the distribution of the $CD3^+$, $CD4^+$ and $CD8^+$ lymphocytes (flow cytometry), and the leukocyte adhesion molecules CD1la, CD11b, CD16, CD18, CD44 and CD42 (flow cytometry). The humoral response was estimated as plasma cortisol (RIA), the proinflammatory cytokines TNFα and IL-8 and the anti-inflammatory cytokine IL-10 (ELISA), and the complement split products C3d and C4d (RIE).

Results: Ten men and five women were included. Eleven patients developed MODS after abdominal surgery, 4 patients suffered from medical diseases. Mean age was 59 years (range 25–75 years). Mean APACHE II score before CVVHD was 19 (range 8–27). Nine patients (60%) died in septic shock. Mean duration of CVVHD treatment was 9 days (1–21 days). TNFα and IL-8 were detectable in all patients, while IL-10 was detectable only in a few patients. Low cytokine concentrations were measured in the ultra-filtrate. Big intra- and interindividual variations were demonstrated for all the immunological parameters. In summary, no

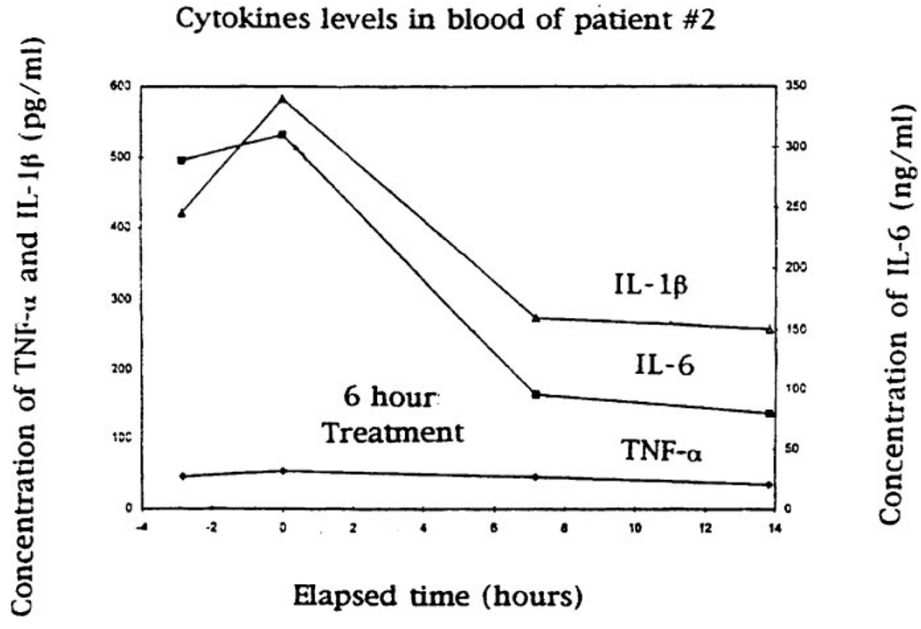

Figure (abstract P125) Results.

significant changes were demonstrated in any of the immunological variables.
Conclusions: The hypothesis that CVVHD induces an acute activation of the immune system followed by immunosupression was not confirmed in the present study. The heterogenic patient material with different underlying diseases and various duration of illness before start of CVVHD may contribute to the large variation in the measured immunological markers.

P127

Reversal of intractable circulatory failure complicating septic shock with short time high volume haemofiltration (ST-HV-CVVH) after failure of conventional therapy: a prospective evaluation

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Critical Care 1998, **2(Suppl 1):**P127

Objectives: According to our previous retrospective study, shorttime high volume haemofiltration may have beneficial effects on the haemodynamic course and outcome of patients with refractory septic shock. Therefore, a prospective study was performed to confirm (or not) these preliminary results.
Design: Prospective open study over 20 consecutive patients.
Setting: Fifteen bedded adult polyvalent intensive care unit in a general hospital with more than 45% of the admissions coming through the emergency department.
Methods: Twenty patients with septic shock were included according to entry criteria including haemodynamic status, acid-base balance, septic status, respiratory support and renal status.
Technique: It consisted in an exchange of 35 l in a 4 h period of time, achieving a neutral balance. A Gambro device was used with polyacrylonitrile membranes and bicarbonate was used as buffer. After, the patient was put on low volume haemofiltration exchanging 24 l a day.
Results: 1) Influence on the haemodynamic course: data were analysed using non parametric statistical methods. A responder was defined using 4 criterias as shown by the following table (criteria: C). 2) Influence on the outcome : 9 patients out of 11 responders survived at day 28. Both groups (survivors N = 9 and non survivors - N = 11) were similar on admission in terms of APACHE II score (31.1 vs 32.3 $P > 0.05$), SAPS II score (69 vs 68.5 $P > 0.05$) but were significantly different regarding the time of intervention (6.1 h vs 14.2 h $P < 0.01$). The global expected mortality was 79.1% and the observed mortality was 55%. Using the angular transformation as statistical test, the difference was significant with a P value below 0.05.
Conclusions: Our prospective open study is confirming our preliminary results by suggesting that ST-HV-CVVH is able to reverse intractable circulatory failure complicating septic shock and to improve survival. Early intervention is related with a better outcome. Outcome is well predicted by the early haemodynamic response and not by conventional scoring systems. In our institution, at the present time, this therapy is restricted to cases unresponsive to conventional therapy.

P128

Successful treatment of refractory toxic streptococcal syndrome associated with severe lactic acidosis using a combined haemofiltration technique with a bicarbonate based replacement fluid: report of 4 consecutive cases

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Critical Care 1998, **2(Suppl 1):**P128

Objectives: Devastating toxic strep syndrome has still high mortality race (about 30%) despite all (he therapeutical interventions that have been

Table 1 (abstract P127). Inclusion criteria

1) Haemodynamic status	Mean arterial pressure :	<55 mmHg
	Inotropic support: after failure of maximal dosages of dopamine (1 st step) (15 µg/kg/min), dobutamine-epinephrine (2d step) (15 µ/kg/min and 1 µg/kg/min respectively).	as last step, epinephrine was used up to 0.5 µg/kg/min for more than 2 h without results.
	Cardiac index	<2 l/min/m^2
	Wedge pressure	>14<18 mmHg
2) Acid-base balance	Arterial pH	<7.15
	Serum lactate	>5 mmol/l
3) Septic status	SIRS criteria	3 out of 4
	Objective source of sepsis	Always present
4) Respiratory support	Mechanical ventilation	All the patients
	paO_2/FiO_2 ratio	<100
5) Renal status		No incidence on the inclusion criteria

Table 2 (abstract P127)

Time after onset of the procedure	Parameters	Responder group $n = 11$	Non responder group $n = 9$	P value
T 0: Time 0	pH	7.14	7.12	>0.05
	Mean arterial pressure	50.9	46.1	>0.05
	Cardiac index	1.77	1.89	>0.05
	Inotropic support	E = 38.2 µg/min	E = 35.9 µg/min	>0.05
T2 = 2 hours	Cardiac index (1stC)	Increase >50%	no S. increase	<0.01
after the start	SvO_2 (2nd C)	Increase >25%	no S. increase	<0.01
T4 = 4 hours	pH (3rd C)	>7.3	<7.15	<0.01
after the start	Inotropic support (4th C)	50% reduction in E/NE	no s. reduction	<0.01

E, epinephrine; NE, norepinephrine; S, significant.

developped in the last decade. The mortality of the refractory cases lies above 80%. Several descriptions of favorable outcome have been presented using plasmapheresis and intravenous immunoglobin therapy. Amongst the available tools, short lime high volume haemofiltration (ST-HV-SVVH) could be used as therapeutic rescue. We report here a retrospective study of 4 consecutive cases of refractory toxic strep syndrome in terms of haemodynamic course and outcome.
Design: Retrospective study.
Setting: Fifteen bedded, adult polyvalent intensive care unit in a general hospital.
Methods: The four cases were in agreement with the consensus definition of toxic strep syndrome. They were treated with conventional therapy first including high doses of penicillin, surgical debridment when needed and adequate critical care therapy.
Short time high volume haemofiltration was only used after failure of conventional therapy.
Technique: The technique consisted in the use at first of ST-HV-CVVH exchanging 35 l in a 4 h period of time with achieving a neutral balance. A GAMBRO device was used with polyacrylonitrile membrane (1.6 m^2 of active surface). Bicarbonate was used as buffer. The vascular access was obtained using a 14 french double lumen coaxial catheter allowing blood flow of 450 ml/min. After, the patient was put on low volume haemofiltration (24 l a day).
Results: 1) Influence on the haemodynamic and metabolic course
Despite the dramatic improvement, no 'P' value was calculated in view of the small number of cases.
2) Influence on the outcome: Global expected mortality according to the severity scoring (APACHE II and SAPS II) was on admission about 82.5%. Observed mortality at day 28: 25% (no *P* value was calculated). One responder died at day 18 from nosocomial pneumonia.
Conclusions: Short time high volume haemofiltration using bicarbonate based replacement fluid seems to be a valuable non conventional tool in toxic strep syndrom with severe lactic acidosis after failure of classical treatment. Response to the therapy is associated with higher likelihood of improvement. We need more cases to become statistically significant. We can speculate that the M-Protein and exotoxin A wich play a crucial role in the severity of the disease can be eliminated by the technique regarding their molecular weight.

P129

Continuous renal replacement therapy in critically ill neonates

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Critical Care 1998, **2(Suppl 1):**P129

Objective: To describe our experience with continuous renal replacement therapy (CRRT) in critically ill neonates.
Design: Prospective case report series.
Setting: A 12 bed multidisciplinary pediatric ICU and a 14 bed neonatal ICU in a University hospital.
Patients: From June 1985 to June 1997 36 critically ill oliguric or anuric neonates underwent continuous arterio-venous (n = 17) or veno-venous (n = 15) renal support. Four neonates were treated with continuous ultrafiltration (CUF) during extracorporeal membrane oxygenation (ECMO). Their mean age was 9.8 ± 1.5 days, their mean body weight 3.01 ± 0.1 kg. All patients were mechanically ventilated and 88% needed vasopressor support. Indications for CRRT were: low cardiac output (n = 10), multiple organ system failure (n = 18), severe diuretic resistant hypervolemia (n = 3), and severe metabolic crisis (n = 5).
Methods: The membrane surface area of the hemofilters ranged from 0.015 to 0.2 m^2 and the priming volume from 3.7 to 15 ml. For pump-driven hemofiltration a roller pump with pressure alarms, an air trap, an air bubble detector, and small blood lines was used. Fluid balance was controlled by a microprocessor controlled unit. The ultrafiltrate substitution fluid was based on bicarbonate and was partially or totally replaced according to the clinical situation.
Results: Mean duration of renal support was 97 ± 20 h, ranging from 14 to 720 h Operational data and survival rates during arteriovenous and veno-venous hemofiltration and continuous ultrafiltration during ECMO are given in Table 1.
Conclusion: Continuous hemofiltration either driven in the arteriovenous or veno-venous mode is a very effective method of renal support for critically ill neonates to control fluid balance and metabolic derangement.

Table (abstract P128). Status on admission

Haemodynamic status	Mean arterial pressure:	<52 mmHg
	Wedge pressure	between 16 and 18 mmHg
	Cardiac index	1.95 l/min/m^2
	Inotropic support	
	Maximal dosages of dopamine and dobutamine	
	{norepinephrine (mean)	1.1 µg/kg/min
	{epinephrine (mean)	0.61 µg/kg/min
Metabolic	Arterial pH (mean)	7.03
	Serum lactate (mean)	12.3 mmol/l.
Expected mortality	APACHE II: 34.1 (mean)	84%
	SAPS II: 71.5 (mean)	81.5%

Table (abstract P128)

Time after onset of the procedure	TO	T2 (2 hours)	T4 (4 hours)
Mean pH	7.03	7.17	7.39
Serum lactate	12.3 mmol/l	11.4 mmol/l	7.1 mmol/l
Cardiac index	1.95 l/min/m^2	3.82 l/min/m^2	4.34 l/min/m^2
Inotropic support	A = 0.61 µg/kg/min	A = 0.35 µg/kg/min	A = 0.19 µg/kg/min
	NA = 1.1 µg/kg/min	NA = 0.79 µg/kg/min	NA = 0.45 µg/kg/min

Table 1 (abstract P129)

	CAVH (n = 15)	CVVH (n = 17)	ECMO+CUF (n = 4)
Qb (ml/min)	7.0 ± 1.2	23.1 ± 2.4*	45.1 ± 2.8*†
Qf (ml/min/m^2)	3.3 ± 0.4	9.5 ± 1.9*	2.3 ± 0.4†
Duration (h)	103 ± 39	103 ± 20	49 ± 13*†
HF-exchange (h)	26.8 ± 6.0	54.4 ± 11.1*	48.4 ± 13.5*
Survival rate(%)	65	67	75

Qb, blood flow rate; Qf, ultrafiltration rates; EF, hemofilter; CAVH, continuous artenovenous hemofiltration; CVVH, venovenous hemofiltration; CUF, continuous ultrafiltration; ECMO, extracorporeal membrane oxygenation; *P < 0.01 CAVH vs CWK, CUF; †P < 0.01 CVVH vs CUF.

CUF can be easily performed during ECMO and should be started early in the presence of severe hypervolemia.

P130

Pharmacokinetics of meropenem in intensive care patients receiving continuous renal replacement therapy

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Critical Care 1998, **2(Suppl 1):**P130

Introduction: This study was conducted to determine the appropriate dose of meropenem in critically ill patients with acute renal failure treated by continuous veno-venous haemofiltration (CVVH) or haemodiafiltration (CVVHDF) who require this antibiotic therapy.
Methods: Ten critically ill patients (7m, 3f, mean age 65 years (range: 51–77 years), mean weight 80 kg (range: 51–119 kg), mean APACHE II 27.7 (range: 21-37) were included. All patients were receiving CVVH (n = 5) (haemofiltration rate 1–2 l/h) or CVVHDF (n = 5) (haemofiltration rate 1–1.5 l/h: dialysis rate 1–1.5 l/h) using a polyacrylonitrile (AN69) hollow fibre 0.9 m^2 filter (Multiflow 100, Hospal). All patients received a meropenem dose of 1 g 12 hourly, intravenously over 5 min. Venous serum samples were taken pre-dose and 5, 15, 30, 60, 90, 120, 240, 360, 480 min post-dose on day 3 to approximate steady state conditions. Haemofiltrate was collected for determination of a sieving coefficient. Samples were analysed by high performance liquid chromatography.
Results: Sieving coefficient for meropenem with the AN69 filter was 0.93 ± 0.06 (n = 9) indicating free flow across the membrane. Mean (± SD) serum concentrations at pre-dose, 5, 15, 30, 60, 90, 120, 240, 360, 480 mins post-dose were: 7.6 (5.1), 90.9 (23.9), 66.0 (13.0), 53.9 (15.7), 40.0 (10.3), 39.0 (9.2), 31.0 (10.4), 21.1 (6.9), 17.2 (6.2), 13.8 (6.4) mg/l respectively. Actual pre-dose (C_{trough}), 5 min (C_{peak}) and 480 min levels are given below. Serum concentrations remained above the MIC_{90} for *Ps. aeruginosa* (4 mg/l) in all patients for two-thirds of the dosage interval which is the target recommended for β-lactam antibiotics. A lower dose may not have been sufficient for all the patients.
Conclusion: A meropenem dose of 1 g 12 hourly is adequate in patients treated with CVVH or CVVHDF using an AN69 HF 0.9 m^2 filter.

P131

Measuring dobutamine (Db) clearance during continuous hemofiltration (CHF)

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Critical Care 1998, **2(Suppl 1):**P131

Extrarenal purification modifies the pharmacocinetics of many molecules, including the cardiotonics, which are frequently administered in conjunction with these techniques. The objective of this study was to measure Db clearance during CHF in ICU patients.
Patients and methods: 15 measurements were taken in 5 consecutive ICU patients (age: 75.4 ± 7 years, SAPS: 17.6 ± 6.6) under Db (posology (D): 16.5 ± 5 (µg/kg/min) and CHF (pump: Gambro AK10, hemofilter AN69S Hospal). Samples were taken from plasma afferent to the filter (Ca), the efferent plasma (Ce) and the ultrafiltrate (Cuf). Db clearance was assessed using HPLC with electrochemical detection in 18% acetonitrile. Clearances were calculated: instantaneous Cl (iCl = mass of Db extract/Ca) and total body Cl (tbCl = D/Ca) as well as the transmittance coefficient-spectrum (TCS = Cuf/Ca).
Results: 1) There was no correlation between the Db concentrations and the administered dose. 2) Average Db purification was 30% for CHF. 3) The iCl was 78 ± 52 ml, non correlated to the Cuf. 4) Average tbCl was 150 ± 160 ml/min, and 93.3% of the tbCl were over 40 ml/min. There was a negative polynomial correlation between tbCl and Ca (P < 0.01). 5) The TCS was 0.45 ± 0.28, irrespective of the posology, not influenced by coprescription of dopamine.
Conclusion: During CHF, Db purification is significant and transmembrane filtration is not the only involved mechanism. A non-linear elimination of the Db, implicating various factors, remains to be proved.

P132

Beneficial use of predilution in reducing the amount of anticoagulation and the occurrence of bleeding during CRRT in critically ill patients: a prospective randomized study

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Critical Care 1998, **2(Suppl 1):**P132

Objectives: Anticoagulation during CRRT is one of the major issues. We have to take into account three parameters: bleeding occurrence, filter life and filter efficiency. The purpose of the study was to assess prospectively the efficacy of the predilution technique in reducing the amount of anticoagulation during CRRT allowing to use it in critically ill patients at risk for bleeding.
Design: Prospective randomized study.
Setting: Fifteen bedded, adult polyvalent intensive care unit in a general hospital.
Methods: Twenty consecutive critically ill patients were randomized to have either a predilution set or a post-dilution one during CRRT using the prisma Hospal pump.
Full circuit standard heparinisation was used to achieve an APTT twice baseline. The vascath site was restricted to the right internal jugular vein. The pump speed was kept at 100 ml/min. Filter efficiency was assessed by the haemopermeability index (HPI). The HPI represents the ultrafiltrate flow divided by the transmembrane pressure. The filter efficiency is lost when the HPI has dropped by 70%. Filter life was measured in hours until the circuit clotted off. Data were analysed using non parametric statistical methods.

Table (abstract P130)

Patient	1	2	3	4	5	6	7	8	9	10
Replacement	CVVH					CVVHDF				
Rates (1/h)	1	1.5	2	2	2	1:1	1:1	1:1	1.5:1.5	1.5:1.5
C_{trough} (mg/1)	13.3	4.2	3.4	7.2	14.6	13.3	2.5	6.3	0.5	10.8
C_{peak}(mg/l)	90.1	127.7	85.2	73.2	81.7	116.3	101.2	115.0	63.1	55.3
$C_{480mins}$ (mg/l)	19.4	10.5	14.3	11.6	23.3	20.5	6.2	18.7	5.7	7.5

Table (abstract P132)

	Predilution group n = 10	Postdilution group n = 10	*P* value
Median filter life in hours	38.5	39.3	>0.05
Median filter efficiency in hours	32.3	33.9	>0.05
Symptomatic bleeding (during the study period)	1	4	<0.01
Median amount of heparin	451 U/h	742 U/h	<0.01

Table (abstract P132)

	Predilution group n = 10	Postdilution group n = 10	*P* value
Median haematocrit	25.1%	28.5%	<0.05
Median platelet count	116 × 10^9/1	131 × 10^9/l	<0.05
Median oncotic pressure	31.3 mmHg	37.2 mmHg	<0.01
Total calcium	3.8 mEq/l	3.88 mEq/l	>0.05

Entry criteria included normal prothrombine time (PT) and normal activated partial thromboplastin time (APTT). The platelet count had to be over 100×10^9/1. The study was restricted to the first filter of each patient.
Results: The two groups were well matched prior to the therapy for platelet count, haematocrit, oncotic pressure and total calcium measured in the serum.
As shown by the table, the predilution allows a reduction in heparin without imparing the filter life.
To try to understand the mechanism involved, we have also measured the haematocrit, the platelet count, the oncotic pressure and the total calcium in the circuit prior to the filter but after the dilution as shown by the following table.
Conclusions: The predilution technique is a good tool for clinicians in the setting of CRRT in critically ill patients at risk for bleeding. It allows the physician to reduce drastically the amount of heparin used without impairing the filter life and the filter efficiency. The mechanism involved seems to be the reduction of the oncotic pressure rather than other systems involving the calcium.

P133

Variations of veno-arterial and mucosal-arterial CO_2 gap during continuous veno-venous hemodiafiltration

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Critical Care 1998, **2(Suppl 1):**P133

Introduction: Veno-arterial CO_2 gap (P(v-a) CO_2) and mucosal-arterial CO_2) gap (P(g-a) CO_2 may help to detect tissular dysoxia. Continuous veno-venous hemodiafiltration (CVVHD) technics are well tolerated in septics patients.
Objectives: Change of P(v-a) CO_2 and of P(g-a) CO_2 during CVVHD.
Methods: Prospective study. Intubated and ventilated patients. Hemodynamics and systemic oxygen derived parameters were collected before and during CVVHD (H0-H6). CVVHD setting parameters (PRISMA®, HOSPAL) were standardised. Gastric mucosal PCO_2 continously monitored (NGS (TONOMETRICS) and TONOCAP® (DATEX). P(v-a) CO_2 and P(g-a) CO_2 calculated. Continuous measure of end tidal CO_2 ($PetCO_2$). Statistics: ANOVA, Scheffe *t* test for paired and unpaired values
Results: 7 patients (71.7 ± 5 years, SAPS II = 59.5 ± 3.7) included. $PetCO_2$ and P(v-a)CO_2 did not change from H0 to H6. P (g-a)CO_2 increased significantly at H1 (*P < 0.05) then progressively decrease but did not reach the initial value.
Conclusion: The marked increase of P(g-a)CO_2 during CVVHD could be explained by acid-base status in the mucosa independent of hemodynamics changes.

P134

Gastric tonometry in patients recovering from paracetamol overdose

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Critical Care 1998, **2(Suppl 1):**P134

Objectives: To investigate the relationship between gastric intra-mucosal pH and recovery from paracetamol overdose.
Design: Patients admitted to the liver intensive care unit, not fulfilling transplantation criteria, were prospectively enrolled. A gastrointestinal tonometer was placed into the stomach and the intramucosal pH was calculated every day until 10 days post overdose, by an intermittent saline bolus technique.

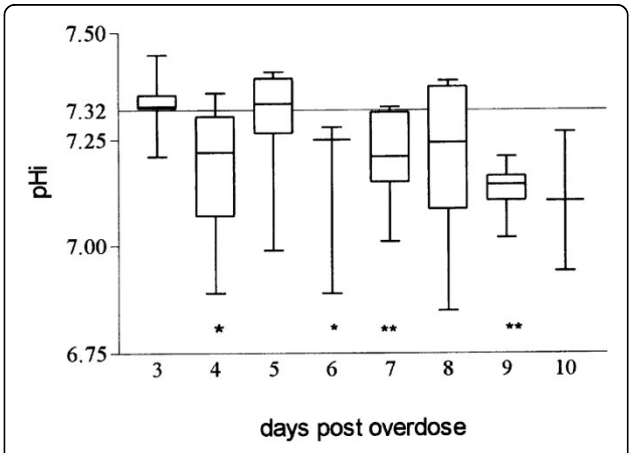

Figure (abstract P134) Results.

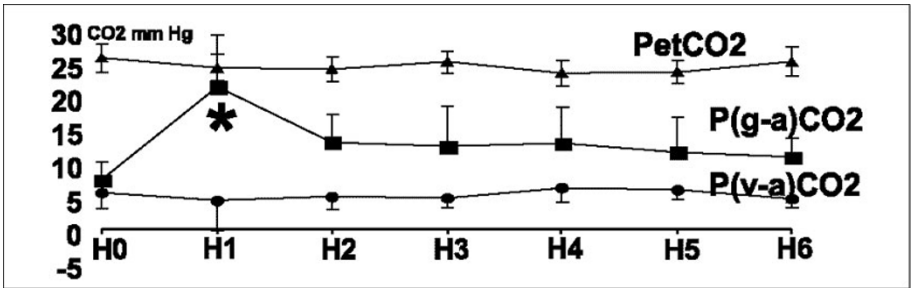

Figure (abstract P133) Results.

Results: 14 patients were studied, of which 2 subsequently died. Data are presented as a box and whisker chart, with the box representing medians, 25th and 75th quartiles and the whiskers the range. (*P value of 0.01 to 0.05 and **P value of 0.001 to 0.01 when compared to day 3).
Conclusions: Gastric intramucosal pH significantly falls in the recovery phase of paracetamol overdose and this is not related to outcome. This may represent diversion of blood away from the portal system to the regenerating liver.

P135

Regional variation in gastric intramucosal pCO_2 may confound tonometric measurement: an evaluation using two tonometers and continuously recirculating gas tonometry

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Critical Care 1998, **2(Suppl 1):**P135

Background: Gastric tonometry is used to assess splanchnic perfusion in critically ill patients, and relies on measurement of the pCO_2 in the tonometer balloon. Saline is most frequently used as the CO_2 vehicle, but phosphate-buffered saline and continuously recirculating gas tonometry (CRGT) have been used in an attempt to improve the accuracy of the tonometric pCO_2 measurements. Comparisons between these methods using two tonometers placed together have been made in vitro and in vivo (animal and human), but the assumption that two closely situated tonometer balloons containing the same vehicle produce the same pCO_2 reading has not been tested, which questions the validity of these comparisons. Using a single technique (CRGT) we investigated the reproducibility of paired tonometric measurements and their precision both in the laboratory and in patients.
Method: The study comprised *in vitro* and *in vivo* components. An equilibration chamber containing 0.9% saline was kept at 37°C and a constant pCO_2 of either 4.5% or 9.5%, monitored using a Paratrend 7 probe (Biomedical Sensors, High Wycombe, UK). Two Tonocap monitors (Datex, Helsinki, Finland) were calibrated and connected to two tonometers (Tonometric Division, Instrumentarium Division Helsinki, Finland) within the chamber and, after a 30 min equilibration period, 24 paired pCO_2 measurements were recorded at 10 min intervals at each CO_2 concentration. 10 intubated, ventilated and sedated critically ill patients were then studied, using two tonometers positioned in the stomach and connected to the two tonocap monitors. After a 30 min equilibration period 12 paired pCO_2 measurements were recorded per individual at 10 min intervals.
Results: During the *in vitro* study the pCO_2 of the saline was maintained at two steady means of 4.52 (4.48–4.54) and 9.47 (9.37–9.5) kPa. There was excellent agreement between tonometers, with a mean bias of 0.16 kPa (95% confidence interval -0.09 to 0.058), and limits of agreement -0.51 to 0.47 kPa. Agreement between each tonometer and Paratrend pCO_2 measurements was also good with biases of 0.110 and 0.103 kPa (95% confidence intervals -0.210 to -0.028 and -0.194 to -0.012 kPa) and limits of agreement -0.54 to 0.23 and -0.52 to 0.32 kPa. Agreement between tonometers *in vivo* was poor. Although the mean bias was 0.132 kPa (95% confidence interval 0.286 to 0.418 kPa), the limits of agreement were -2.83 to 3.09 kPa.
Conclusion: The limits of agreement between two tonometers in the stomachs of critically ill patients using CRGT were unacceptably wide. This may be due to inherent flaws in the technique *in vivo,* or to regional differences in intraluminal pCO_2.

P136

Impact of enteral feeding on gastric tonometry in ICU patients

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Critical Care 1998, **2(Suppl 1):**P136

Objective: This study investigates the impact of jejunal and gastric feeding on gastric mucosal pCO_2 ($PiCO_2$) in ICU patients.
Patients and methods: Seven stable mechanically ventilated ICU patients receiving ranitidine were studied. Nasojejunal and pHi nasogastric tubes were inserted and $piCO_2$ measured with air tonometry. Jejunal (J) and gastric feeding (G) was performed in 1 h intervals as

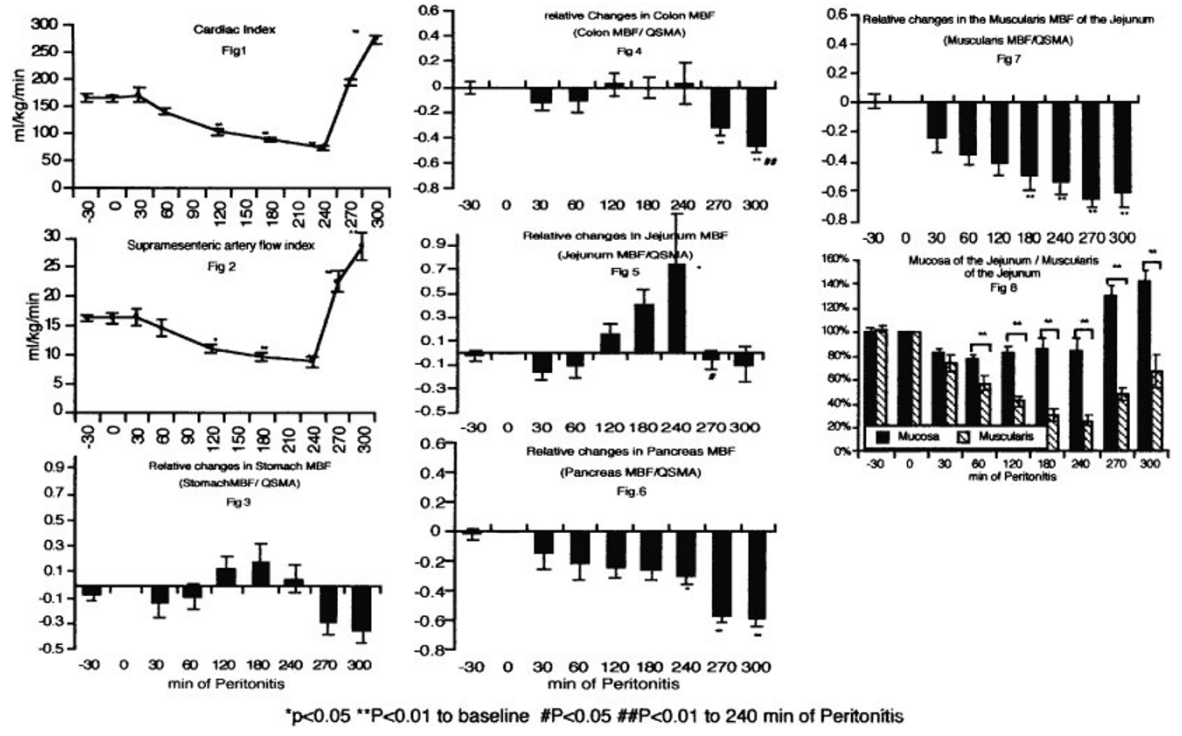

Figure (abstract P136) Results.

follows (period 1–9): 1 = baseline; 2 = J 40 ml/h; 3 = J 100 ml/h; 4 = no feeding; 5 = G 40 ml/h; 6 = G 100 ml/h; 7 = G bolus 200 ml; 8 = gastric emptying; 9 = no feeding.
Values are provided as means ± SD. ANOVA for repeated measures and Wilcoxon test were used for statistical analysis; $P < 0.05$ was considered significant.
Results: Patients remained stable during the study. Baseline pCO_2 gap ($piCO_2$-$paCO_2$) was 1.91 ± 0.66 kPa and did not change during the study (ANOVA $P = 0.44$; Fig. 1)
Marked interindividual variability was observed during gastric feeding mainly.
Conclusion: In ICU patients jejunal feeding does not influence $piCO_2$. The effect of gastric feeding is much less predictable and needs to be tested in each patient.

P137

Microcirculatory blood flow in the gastrointestinal tract during early septic shock

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Critical Care 1998, **2(Suppl 1):**P137

The autoregulation of microcirculatory blood flow (MBF) in the gut is impaired during sepsis. However, there is little data available on the distribution of blood flow in the different parts of the gastrointestinal tract and on the relationship between mucosal perfusion and supramesenteric artery flow (QSMA) during sepsis. The aim of this study was to elucidate the relationship between regional blood flow (QSMA) and the local flow in different tissues and parts of the gut and in the pancreas during early septic shock.
Materials and methods: Nine pigs (20–24 kg) were anesthetised endotracheally intubated and ventilated. Cardiac index (CI) was measured with thermodilution technique and mesenteric artery blood flow (QSMA) with an ultrasound flowprobe. Microcirculatory blood flow (MBF) was continuously monitored in multiple organs (pancreas, gastric-, jejunal-, colonic mucosa and muscularis of the jejenum) with a multichannel laser Doppler system. After baseline measurements a generalised faecal peritonitis was induced by instillation of 20 g of faeces in the abdominal cavity. After 240 min, i.v. fluids were administered which altered the hypodynamic shock to hyperdynamic septic shock.
Results and discussion: During the first 240 min (hypodynamic shock) CI and QSMA decreased by 50% ($P < 0.01$; Figs 1 and 2). Microcirculatory blood flow in the mucosa of the stomach and colon decreased similarly (Figs 3 and 4) while the mucosa of the jejunum was maintained close to baseline (Fig. 5). On the other hand, MBF in the pancreas and the jejunal muscularis decreased significantly more than the QSMA (Figs 6 and 7). Administration of i.v. fluids at 240 min was followed by a significant increase in CI and QSMA (Figs 1 and 2). Although this was followed by some increase in MBF in the mucosa of the stomach and colon as well as in the pancreas and jejunal muscularis, the relative amount of flow in these organs significantly decreased as compared with QSMA (Figs 3,4,5). MBF in the mucosa of the jejunum increased essentially parallel with the QSMA (Fig. 6).
Conclusion: a) In septic shock jejenunal mucosal blood flow is maintained despite decreased mesenteric flow (QSMA), probably through redistribution of flow from muscularis to the mucosa (Fig. 8).
b) Microcirculatory flow in the mucosa of the stomach and colon decreases parallell with QSMA during hypodynamic septic shock, while during hyperdynamic sepsis it decreases significantly compared with QSMA (Figs 3 and 4).
c) Microcirculatory flow in the pancreas decreases significantly more than QSMA both during hypodynamic and hyperdynamic septic shock (Fig. 6).

P138

The effects of dopexamine on renal function in surgical renal artery reconstruction: a pilot study

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Critical Care 1998, **2(Suppl 1):**P138

Aims: To evaluate the effects of dopexamine on haemodynamics and renal function in patients undergoing surgical renal artery reconstruction (RARS).

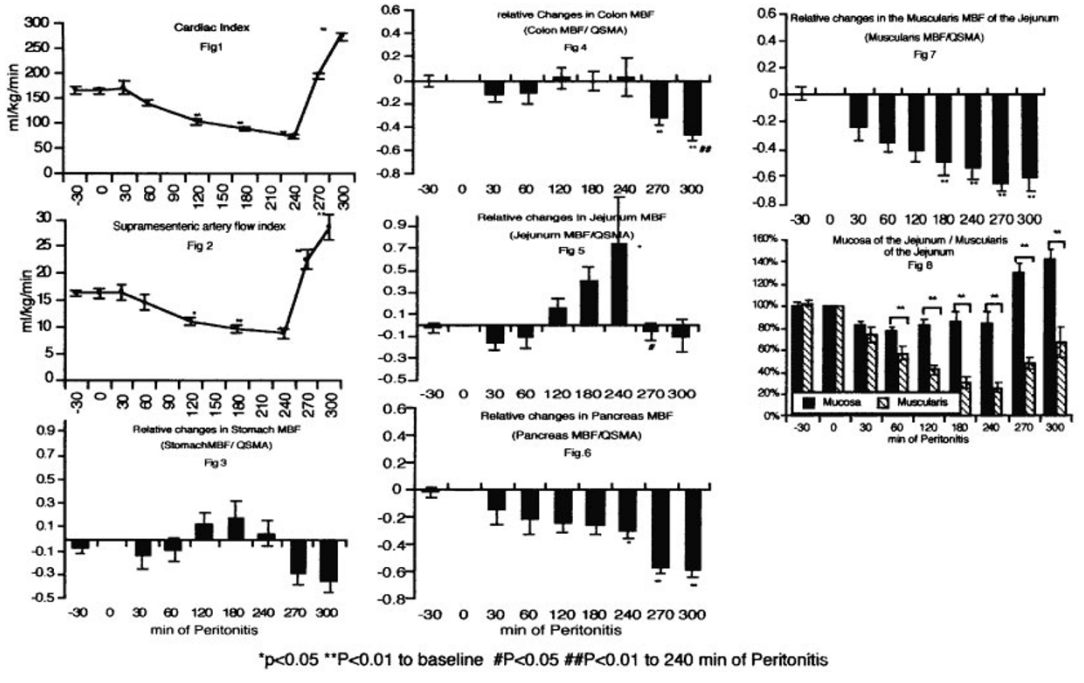

Figure 1-8 (abstract P137) Onset of Peritonitis at 0 min and Pentastrach administration at 240 min. Data presented as mean ± SEM. Paired ANOVA for repeated measurements was used for comparison. $P < 0.05$ was considered statistically siginficant

Table (abstract P138)

	Pre Drug	Post Ind'n	DPX End Surg.	24 h post	2–4 months	re Drug	post Ind'n	PLA End Surg.	4 h post	2–4 month
Iox	74.3± 31.23			62 ± 51.84		86 ± 29.94			53.6 ± 21.25	
CreaCl				56.7 ± 38.3					51.3 ± 21.6	
Creat	138 ± 63.5			184.2 ± 92.7	109.3 ± 23*	109.4 ± 25.7			174 ± 50.7	132.7 ± 9.8
% ΔCreat				30.3 ± 31.4					66.6 ± 61.5	
UrVol(24)				2.1 ± 1.03					3.2 ± 1.05	
pHi		7.39 ± 0.05	7.35 ± 0.09	7.28 ± 0.14			7.39 ± 0.1	7.37 ± 0.04	7.29 ± 0.06	
DO21	458 ± 87	520 ± 93*	699 ± 163*	643 ± 224		512 ± 78	412 ± 57	516 ± 81	552 ± 70	
VO21	112 ± 11	85 ± 40	101 ± 40	162 ± 71		130 ± 23	87 ± 7	83 ± 21	151 ± 26	
O2ER	24 ± 3	16 ± 6	14 ± 5	26 ± 7		26 ± 7	21 ± 3	16 ± 6	27 ± 5	

Methods: Ten patients (aged 54 to 75; 7 males), scheduled for RARS were randomised, following cardiovascular optimisation, to receive either dopexamine (1 µg/kg/min), introduced 2 h before surgery and continued for 24 h after surgery (DPX, $n = 5$), or placebo (PLA, $n = 5$). Anaesthesia was similar in both groups. Pre-operatively, all patients were assessed by renal angiography. Renal function was assessed by plasma creatinine, creatinine clearance and iohexol clearance [1]. Haemodynamics and splanchnic perfusion were assessed by invasive cardiovascular monitoring and gastric tonometry respectively. Data are expressed as mean ± SD. Statistics: Student's *t* test was used.
Results: The 2 groups were comparable with reference to demographic data and surgical procedures (POSSUM predicted risks:DPX mortality 21%, morbidity 72%; PLA mortality 22%, morbidity 75%). There was 1 death in each group in the first 8 weeks after surgery. Data was incomplete for iohexol clearance due to technical difficulties (numbers in subscript).There was no significant difference between the groups in iohexol or creatinine clearance (Iox, CreaCl, ml/min), plasma creatinine (Great, µmol/l), urinary volumes (UrVol, l), pHi, oxygen delivery (DO_2I) and consumption (VO_2I, ml/min/m^2) and oxygen extraction ratio (%). Results are shown in the table overleaf (*$P < 0.1$, significance = $P < 0.05$):
Conclusion: In this small group, dopexamine at this dose did not appear to offer a significant benefit to patients undergoing RARS.
Reference

1. Brown SC, O'Reilly PH: **Iohexol clearance for the determination of glomerular filtration rate in clinical practice: evidence for a new gold standard.** *J Urol* 1991, **146**:675-679.

P139

Comparing the effects of dopexamine and dobutamine on splanchnic parameters in patients with severe sepsis

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Critical Care 1998, **2(Suppl 1):**P139

Introduction: This prospective randomized study was designed to assess the effect of low dose dopexamine Hcl (dp) and dobutamine Hcl (db) on splanchnic blood flow as measured by gastric intramucosal pH (pHi), hepatic metabolism of lidocain to monoethylglicinexylidide (MEGX), and plasma disappearance rate of indocyanine green (PDR/ICG).
Methods: 16 critically ill patients, meeting the criteria for the diagnosis of severe sepsis, were assigned either to receive dopexamine (1 µg/kg/min) or dobutamine (5 µg/kg/min). Baseline measurements of pHi, MEGX, PDR/ICG as well as hemodynamic, respiratory parameters, oxygen derived variables and arterial lactate were measured. At the end of a 2 h infusion of an appropriate drug, a repeated set of the measurements were taken.
Results: Both drugs produced significant increases in cardiac index, apparently due to a significant increase in heart rate. SVI (stroke volume index) remained unchanged with dopexamine, however some increase was observed with dobutamine. DO_2I (oxygen supply) increased similarly in both groups (16% dp, 19% db) with VO_2I (oxygen consumption) increasing more with db compared to dp. Lactate values after each drug administration appeared to be significantly lower than baseline values (dp 2.08 ± 0.53, db 2.50 ± 1.99 ± 0.99).
No significant improvement in the splanchnic parameters was observed with dopexamine. PHi increased significantly with db (7.26 ± 0.04 to 7.33 ± 0.07 $P < 0.05$). PDR/IICG and MEGX values showed significant increases with db (PDR/ICG from 15.5 ± 9.1 to 21.3 ± 10.3%; MEGX from 19.8 ± 11.2 to 28.8 ± 18.4 $P < 0.05$), and stayed constant with dp, however both parameters measured atbaseline were higher in dp group than in db group.
Conclusion: This study demonstrated the expected effects of each drug as mentioned in the previous studies. Our data showed that in severely septic patients, dobutamine leads to greater effectiveness in improving these accepted splanchnic parameters than dopexamine. However, how well and accurate these parameters reflect the abnormalities of splanchnic organ blood supply and their metabolism needs to be investigated by further studies.

P140

Hepatic O_2 transport and energy balance in hyperdynamic porcine endotoxin shock: N^G-monornethyl-L-arginine (L-NMMA) versus noradrenaline

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Critical Care 1998, **2(Suppl 1):**P140

Introduction: Nitric oxide synthase (NOS) inhibition is currently investigated as a treatment of arterial hypotension associated with septic shock, but controversial data are available with respect to hepatic O_2 balance. Therefore we studied the effect of NOS inhibition with L-NMMA on liver O_2 transport as well as energy balance, in comparison to a standard treatment with noradrenaline (NOR) in a hyperdynamic endotoxin (ETX) shock model.
Methods: Thirty anesthetized pigs were randomly assigned to 3 groups 12 h after induction of endotoxic shock with continuous LPS infusion: ETX group: no drug therapy ($n = 8$); NOR group ($n = 11$) and L-NMMA group ($n = 11$): vasopressor therapy with NOR and L-NMMA was titrated to maintain MAP at preshock levels. Hepatic blood flow (Transonic® Doppler ultrasound), O_2 kinetics as well as mean and frequency distribution of intracapillary HbO_2 saturation (remission spectrophotometry, EMPHO) were measured.
Results: Data are median and interquartile range. *$P < 0.05$ vs preshock (RM ANOVA on ranks). **$P < 0.05$ between groups (ANOVA).
Conclusions: Although, in contrast to NOR, L-NMMA did notfurther increase macrocirculatory liver O_2 availability, there was no difference between the two treatments with regard to microcircula-tory O_2 supply and O_2 uptake. Hence, neither of the two treatments improved liver energy balance.
Acknowledgement: L-NMMA (546C88) was kindly provided by GlaxoWellcome, UK.

Table (abstract P140)

		Preshock	12 h	18 h	24 h
Liver DO_2	ETX	2.3 [1.9;2.8]	2.2 [1.7;2.7]	2.7 [2.0;3.0]	2.0 [1.4;2.6]
ml/min/kg	NOR*	2.3 [1.8;2.8]	2.0 [1.5;2.4]	3.1 [2.8;3.6]**	2.6 [1.9;4.1]
	L-NMMA	2.5 [2.2;2.9]	2.5 [2.1;2.61	2.3 [1.7;2.8]	2.0 [1.1;2.6]
Hepatic	ETX	54 ± 5	51 ± 7	51 ± 7	47 ± 10
intracap. HbO_2	NOR	59 ± 6	54 ± 8	61 ± 7	58 ± 12
Mean ± SD	L-NMMA	59 ± 8	56 ± 10	55 ± 10	58 ± 7
Liver VO_2	ETX	0.7 [0.5;1.1]	0.6 [0.4;0.8]	0.6 [0.4;0.8]	0.6 [0.3;0.7]
ml/min/kg	NOR	0.7 [0.5;1.1]	0.6 [0.4;0.8]	0.6 [0.4;0.8]	0.6 [0.3;0.7]
	L-NMMA	0.8 [0.5;0.8]	0.8 [0.5;1.0]	0.6 [0.4;0.8]	0.5 [0.3;0.8]
Hepatic	ETX*	7.48 [17.46;7.50]	7.38 [7.34;7.42]	7.36 [7.34;7.381	7.30 [7.25;7.34]
venous pH	NOR*	7.49 [7.46;7.51]	7.33 [7.25;7.34]	7.32 [7.2817.371	7.22 [7.17;7.37]
	L-NMMA*	7.48 [7.44,7.49]	7.32 [7.31 ;7.341	7.29 [7.26;7.321	7.24 [7.16;7.30]
Hepatic	ETX*	24 [15;32]	26 [18;30]	34 [28;51]	61 [31;123]
venous Lac/Pyr	NOR*	31 [21;37]	38 [25;66]	95 [49;1 01]	104 [41;204]
ratio	L-NMMA*	21 [18;29]	28 [28;50]	60 [40;95]	148 [67;187]

P141

Intestinal O_2 transport and energy balance during hyperdynamic endotoxic shock in the pig: comparison of noradrenaline and N^G-monomethyl-L-arginine (L-NMMA)

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Critical Care 1998, **2(Suppl 1):**P141

Introduction: Vasopressor therapy is current practice for treatment of arterial hypotension associated with septic shock, but may result in gut dysfunction due to intestinal vasoconstriction. Therefore we compared the effects of vasopressor treatment with the nitric oxide synthase inhibitor L-NMMA with those of noradrenaline (NOR) on intestinal O_2 transport as well as energy balance in a porcine hyperdynamic endotoxic shock model.
Methods: Thirty anesthetized pigs were studied; 12 h after induction of endotoxic shock with continuous LPS infusion animals were randomly assigned to receive either no drug therapy (ETX, n = 8), or vasopressor support with noradrenaline (NOR, n = 11) or L-NMMA (L-NMMA, n = 11), respectively, in order to maintain MAP at preshock levels. Portal venous blood flow (Transonic flow probes), arterial-portal venous O_2 extraction, ileal mucosal intracapillary HbO_2 saturation (remission spectrophotometry EMPHO) and arterial-ileal mucosal PCO_2 gaps were measured.
Results: Data are median and interquartile range. *P < 0.05 vs preshock (RM ANOVA on ranks). (See table overleaf.)
Conclusions: Despite well-preserved O_2 availability neither of the two treatments could reverse the endotoxin induced derangement of intestinal energy balance.
Acknowledgement: L-NMMA (546C88) was kindly provided by GlaxoWellcome, UK.

P142

Endogenous glucose release in hyperdynamic porcine endotoxin shock: N^G-monomethyl-L-arginine (L-NMMA) versus noradrenaline

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Critical Care 1998, **2(Suppl 1):**P142

Introduction: Inhibition of nitric oxide (NO) synthesis is currently investigated for the treatment of hypotension associated with septic shock. Since both endotoxin (ETX) and NO have been reported to influence

Table (abstract P141)

		Preshock	12 h	18 h	24 h
Portal venous	ETX	23 (19;28)	25 (29;28)	24 (20;29)	28 (19;31)
blood flow	NOR*	23 (20;26)	25 (18;28)	36 (26;37)	38 (28;42)
(ml/min/kg)	L-NMMA	24 (22;28)	32 (24;40)	26 (23;36)	30 (19;34)
O_2 extraction	ETX	34 (27;35)	29 (20;33)	26 (23;32)	26 (25;35)
(%)	NOR*	32 (26;35)	31 (27;41)	20 (18;24)	22 (17;32)
	L-NMMA	31 (29;34)	31 (27;35)	31 (27;31)	31 (24;54)
ileal mucosal	ETX	43 ± 13	39 ± 21	37 ± 10	30 ± 10
intracap. HbO_2	NOR	46 ± 15	44 ± 12	44 ± 8	45 ± 14
Mean ± SD	L-NMMA	48 ± 12	43 ± 11	42 ± 11	42 ± 12
Portal venous	ETX*	25.1 [22.0;29.1]	25.3 [22.5;28.5]	31.8 [22.8;34.7]	42.7 [40.0;54.5]
Lac/Pyr ratio	NOR*	28.1 [26.1;31.3]	31.3 [24.8;37.6]	46.4 [39.0;53.3]	44.7 [36.6;65.9]
	L-NMMA*	20.8 [18.6;29.5]	26.5 [25.3;40.4]	39.9 [28.4;50.5]	48.0 [44.3;53.2]
ileal mucosal-	ETX*	12 (9;13)	13 (11;20)	17 (14;25)	20 (19;28)
arterial PCO_2 gap	NOR*	13 (4;15)	19 (16;29)	19 (13;26)	15 (11;53)
(mmHg)	L-NMMA*	13 (11;16)	23 (17;29)	37 (13;53)	44 (28;45)

Table (abstract P142)

		Preshock	12 h	18 h	24 h
Liver lactate	ETX*	13 [11;17]	5 [-1;8]	2 [-3;5]	-6 [-16;5]
uptake	NOR*	9 [6;16]	-2 [-7;4]	-4 [-11;3]	-5 [-10;6]
(µmol/min/kg)	L-NMMA*	9 [7;14]	3 [0;4]	-8 [-10;-4]	-17 [-24;9]
Endogenous glucose	ETX*	25 [20;28]	32 [29;38]	32 [22;39]	36 [29;65]
production	NOR*	23 [20;24]	34 [31 ;37]	43 [36;50]**	35 [28;49]
(µmol/min/kg)	L-NMMA*	23 [18;26]	30 [27;35]	26 [25;43]	29 [23;33]

gluconeogenesis we compared the effects of standard vasopressor therapy with noradrenaline (NOR) to L-NMMA on endogenous glucose release during long-term ETX induced shock.
Methods: Pigs were studied in a normotensive, hyperdynamic shock model with volume resuscitation (HES 6%) to keep intrathoracic blood volume constant. Animals were randomly assigned to three groups 12 h after start of ETX infusion. ETX group: no drug treatment (n = 8); NOR group: treatment with NOR (n = 11); L-NMMA group: treatment with L-NMMA (n = 11), both titrated to maintain MAP at preshock levels. Hepatic uptake of glucose precursors as well as endogenous glucose formation (stable isotope approach) were measured.
Results: Data are median and interquartile range. *P < 0.05 vs preshock (RM ANOVA on ranks).**P < 0.05 between groups (ANOVA).
Conclusion: Despite their similar effects on liver hemodynamics and O_2 kinetics neither NOR nor L-NMMA influenced the ETX-induced dissociation between liver uptake rates of glucose precursors and total *de novo* glucose formation rate.
Acknowledgement: L-NMMA (546C88) was kindly provided by GlaxoWellcome, UK.

P143

Factors influencing serum lactate concentration in ICU newborns

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Critical Care 1998, **2(Suppl 1):**P143

Serum lactate concentration provides clinically important information on metabolic status of critically ill neonates.
Aim: The purpose of the study was to assess some factors influencing lactate levels during first 48 h of intensive treatment.
Setting: A university hospital pediatric intensive care unit (PICU).
Methods: 173 neonates (gestational age 35 hbd /median/, mean birth weight 2045 ± 808 g, SNAP score -9 /median/) subsequently admitted to PICU in first two days of life were studied. Blood lactate levels, blood gases, electrolytes and glucose levels were determined at the admission and after 24 and 48 h of PICU treatment. SNAP score and data concerning oxygen transport into the tissues were collected simultaneously.
Results: Blood lactate levels increased with low mean arterial pressure (P < 0.001), low Apgar score (at 5 min), P < 0.01 at admission, P < 0.05 in 24 h, ns in 48 h, low temperature at admission, P < 0.001, low hematocrite P < 0.05 and high SNAP value, P < 0.001. No significant correlations between lactates and other demographic and clinical data were observed.
Conclusions: Based on our results we conclude that hypoperfusion and bad clinical condition (SNAP score) has the strongest impact on blood lactates. Of interest we found persistent effect of asphyxia evaluated as Apgar score and hypothermia at the admission on high lactate incidence.

P144

Abdominal sepsis in the surgical intensive care unit: a description and search for prognostic factors

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Critical Care 1998, **2(Suppl 1):**P144

Introduction: Patients with AS treated in the surgical ICU suffer substantial morbidity and mortality, despite efforts of modern intensive care and economical means being invested. The present study was performed in order to describe this cathegory of patients and if possible to identify factors of potential prognostic importance.
Methods: All consecutive patients treated due to AS in the surgical ICU at Lund University Hospital during the period January 1983 to December 1995 were analysed retrospectively. Information on demography, scoring according to APACHE II, SSS and MODS scores, complications and mortality was assessed.
Results: Totally 210 patients, 75 females and 135 males, with a mean age of 65 years were included in the study. Median time of hospitalization was 26 days including 6 days at the ICU accounting for a median cost of 48.112 USD/ hospital stay. The main cause of AS was visceral perforation (42%). Abdominal bacterial cultures were dominated by enteric bacteria (80%), while blood cultures showed equal frequences of enteric and skin bacteria (21%). Most patients were subjected to surgical intervention (88%).
Complications were frequent, dominated by organ failure, seen in 83%. Pulmonary, cardiac and renal failure were most frequent. Multiple organ failure, defined as failure of >2 organ systems, developed in 52%. The total mortality rate was 28%, the most common cause of death being MODS (69%). APACHE II and SSS scores did not significantly differ between patients with or without concommitant MODS nor between survivors and non-survivors. A trend towards correlation between high scores and poorer outcome could be seen. A MODS score of >4 predicted development of multiple organ failure (P < 0.001), but did not predict mortality.
The presence of previous deseases did not significantly influence on morbidity and mortality, nor did age, sex, underlying diagnosis nor bacterial culture findings. The occurrence of organ failure correlated with poor prognosis and fatal outcome, the more organ systems that failed, the stronger the correlation. Pulmonary (P < 0.05), cardiac (P < 0.001) and renal (P < 0.001) failure all increased the risk of lethal outcome, as did multiple organ failure (P < 0.001).
Conclusions: Abdominal sepsis causes substantial morbidity and mortality, mainly due to the frequent development of multiple organ dysfunction syndrome. The condition consumes substantial economical resources and health care facilities. Factors of prognostic importance are all associated with the development of multiple organ failure syndrome and not to individual factors like age, sex, previous diseases or diagnosis.

P145

O'Gilvie's Syndrome (colonic pseudo-obstruction) in the intensive care unit

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Critical Care 1998, **2(Suppl 1):**P145

Background: O'Gilvie's syndrome (colonic pseudo-obstruction) is a gastrointestinal motility disorder affecting the whole bowel but involving mainly the colon. It produces an acute massive dilation of the large bowel without organic obstruction. The cause of the disease is not known but it seems to involve some autonomic neurologic disorder affecting the myenteric plexus. For unknown reasons it affects selectively elderly, COPD patients with critical diseases (sepsis, polytrauma, vascular disease, etc.). The mainstay of the differential diagnosis is to exclude any cause of mechanical ileus. The treatment of the syndrome is mainly supportive including administration of fluids and electrolytes, total parenteral nutrition, and cisapride. If after these measures

Table (abstract P145)

Age	Sex	Diagnostic	Treatment	Outcome
77	Male	COPD/Pneumonia	Cecostomy	Alive
76	Male	COPD/Pyelonephritis	Colonic NG Tube	Alive
72	Male	COPD	Cecostomy	Alive
68	Male	COPD/Pneumonia	Colonic NG Tube	Alive
67	Male	COPD	Colonic NG tube+lavage	Alive
65	Male	COPD	Colonic NG tube+lavage	Alive

pseudo-obstruction still persists, colonoscopic decompression is required. An endoscopic placement of a transanal large bore nasogastric tube in the transversus colon is suggested. Continuous lavage of the colon through the tube could be useful. If after these measures the colon is still dilated, surgery with cecostomy is indicated.
Results: In the next table we report our experience in six cases of O'Gilvie syndrome patients during the years 1996–1997.
Conclusion: In our experience O'Gilvie's syndrome is much more common than reported. Medical treatment including cisapride is valuable but in severe cases colonoscopic decompression with transanally NG tube placement with continous lavage is required. In some cases a surgical decompressive cecostomy may be necessary.

P146

Gastric emptying as assessed by paracetamol absorption is normal 32 h after elective abdominal aortic aneurysm surgery (AAA)

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Major potential complications following AAA include 1) MODS, possibly related to GI barrier dysfunction [1-] and 2) stress ulcers, seen on gastroscopic examination in as many as 80% of patients []. Enteral nutrition may prevent both these complications, especially if given early. However patients are often denied this form of treatment because of concerns of delayed gastric emptying. Instead they are subjected to nasogastric (N/G) decompression, shown to be unnecessary and even harmful [3]. We used the paracetamol absorption test to document the presence of intact or abnormal gastric emptying in the immediate postoperative period.
Methods: We studied 13 consecutive patients admitted to the ICU for routine postoperative care following elective AAA. Gastric emptying using the paracetamol absorption test was assessed 6, 18 and 32 h following surgery. The test was considered normal if the area under the concentration curve from 0–60 min (AUC60) after giving 1 mg of paracetamol through the N/G tube was >600 mg/min/1. Other factors noted included i) demographic data;and ii) time to extubation, removal N/G tube and start of enteral feeding.
Results: Patients mean age was 69 ± 12 years; M:F ratio 12:1
1) Results gastric emptying (mean ± SD):

Table (abstract P146)

	6 h	18 h	32 h
AUC60	200.6 ± 168.7	681.2 ± 283.2	642.75 ± 397
No. patients			
>600 mg/min/l	1	9	12

Table (abstract P146)

Extubation (h)	AUC60>600 (days)	Removal N/G (days)	Enteral feeding (days)
4.1	1.3	3.2	3.9

2) Mean time to end-points:
Conclusions: This study showed that 69% of patients hava normal gastric emptying at 18 h and 92% at 32 h following elective AAA. We suggest that unnecessary N/G tubes may be removed and enteral nutrition started to the benefit of the patient 32 h post AAA.
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P147

Glycaemia influences glucose metabolism in sepsis during hyperinsulinemic clamp

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Objectives: The optimal glycaemia in critically ill is not known. We investigated glucose metabolism in septic patients during hyperglycaemic clamp.
Patients and methods: In 10 non-diabetic stable septic patients on mechanical ventilation with baseline glycaemia >6mmol/1 and continuous insulin infusion, two hyperinsulinaemic clamps (target insulinaemia 250 U/l) were performed after 8 h of no caloric intake. Target glycaemia was 5 mmol/1 (step 1) and 10 mmol/1 (step 2) respectively. Glucose uptake was calculated as the amount of glucose per time needed to maintain target glycaemia. Glucose oxidation was calculated from indirect calorimetry and urinary nitrogen losses. Values are provided as means ± SD, paired T test was used for statistical analysis and $P < 0.05$ was considered significant.
Results: Glucose uptake was at step 1 significantly lower than at step 2 (3.9 ± 2.5 mg/kg/min and 6.9 ± 1.93 mg/kg/min, respectively; $P < 0.001$). Glucose oxidation was also significantly lower at step 1 (2.4 ± 1.38 mg/kg/min and 4.46 ± 1.65 mg/kg/min, respectively; $P < 0.01$). Energy expenditure did not change (2280 ± 418 kcal/ 24 h and 2235 ± 216 kcal/ 24 h, respectively).
Conclusion: During hyperinsulinaemic clamp in sepsis glucose uptake and oxidation depend on glycaemia. Higher glycaemia may be beneficial in terms of higher glucose uptake and oxidation which is not accompanied by higher energy expenditure suggesting the suppression of catabolism.

P148

Role of a short parenteral nutrition coupled with early enteral nutrition in the critically ill: a double-blind randomized study versus placebo

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Critical Care 1998, **2(Suppl 1):**P148

The critically ill, stressed, sometimes undernourished may develop an intestinal dysfunction which leads to multiple organ failure. Early enteral nutrition (EN) is usually recommended but may fail to provide an adequate amount of substrate. Parenteral nutrition (PN) is used in case of failure or contraindications of EN. However, the role of early EN coupled with PN has not been evaluated. We conducted a double-blind, randomized, placebo-controlled study to assess the influence of adjuvant PN (Vitrimix KV, Pharmacia Upjohn) and early EN on the improvement of nutritional parameters, morbidity and mortality in the critically ill, excepted after elective surgery. Statistical analysis, in intention to treat, used parametric tests (chi-2, ANOVA). Two groups of 60 patients (EN + placebo versus EN + PN) have been enrolled: 82 males, 38 females, admitted for medical (51%) or 33 non elective surgical emergencies (49%), SAPS2 (42 ± 14), who were either normonourished (59%), moderate (32%) or severe undernourished (9%). On follow-up from D0 to D4, we observed a significant improvement in nutritional proteins (transthyretine, RBP, transferrine) in the treated group, but not from D0 to D7. Mortality on D90 was identical in both groups (17 vs 18) as were the number of days of ventilatory support (11 vs 10), the cumulative number of nosocomial infections (29 vs 30), the length of stay in intensive care (16.9 vs 17.3), the OSF score measured on D0, D4,

D7, D14 and D21 and the OMEGA score (263 vs 244). In contrast, we observed a significant reduction in the number of days of inotropic support (3.8 vs 4.4, $P = 0.0001$) and the length of hospital stay (31.2 vs 33.7, $P = 0.0022$). These results suggest that a short PN coupled with early EN is safe, synergistic and cost-effective. By immediately achieving a minimum energetic uptake, it may provide the time necessary for EN to restore intestinal function.

P149

Nutritional protocols improve energy supply and reduce nitrogen loss in critical illness

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Critical Care 1998, **2(Suppl 1):**P149

Efficient artificial nutrition (AN) in critically ill patients may be associated with reduced catabolism as well as reduced mortality from sepsis. To evaluate the present practice of AN at our medical ICU we documented nutritional indicators during time interval A (January–April 1997). At that time we introduced nutritional protocols during ward rounds to improve the efficiency of AN during B (May–July 1997) and C (August–October 1997). In 103 patients who required AN for at least 4 days we analysed estimated energy requirement (Ere), prescribed energy supply (Ep), real energy supply (Er), percent of real enteral energy supply (Eer), the prevalence of hyperglycemia (HG) as well as nitrogen loss/24 h (NL) and ICU mortality rate (MR).

Results: (not including period B):

We observed that (a) total and percentage of enteral calory intake could be improved, while (b) N_2-loss was reduced as was (c) prevalence of hyperglycemia. (d) Real energy supply remains lower than doctors' prescriptions.

Conclusions: Nutritonal protocols (I) improve total and enteral energy supply and thereby (II) reduce catabolism in critically ill patients. (III) The 'gap' between prescriptions and performance proves to be consistent and remains a challenge for continuous quality improvement. A potential effect on ICU survival needs to be verified by further optimization of AN in larger patient groups.

P150

Acute liver failure (ALF) in a specialist intensive care unit: a 7 year experience

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Critical Care 1998, **2(Suppl 1):**P150

Objective: To define the workload of a liver intensive care unit with respect to aetiology and outcome, including transplantation in patients with ALF.

Table (abstract P149)

Day #4	no protocol A ($n = 33$)	with protocol C ($n = 25$)	Day #4	no protocol A ($n = 33$)	with protocol C ($n = 25$)
Ere (kcal/day)	2072 ± 463	1852 ± 307	HG (%)	24	16*
Ep (kcal/day)	1480 ± 663	1759 ± 246*	APACHE III	73 ± 29	76 ± 27
Er (kcal/day)	1146 ± 671†	1334 ± 504†*	NL	9.4 ± 6.2	6.6 ± 3.5*
Eer (%)	46	71*	MR (%)	30	24

$^{*}P < 0.05$ vs period A, $^{\dagger}P < 0.02$ Ep vs Er, means ± SD (Wilcoxon test)

Table (abstract P150)

	1991	1992	1993	1994	1995	1996	1997
Paracetamol overdose	66	86	101	102	140	106	99
Viral	4	9	10	3	16	0	8
NANB hepatitis	4	12	8	7	17	14	12
Drug	4	2	5	15	11	6	4
Other	8	12	20	17	25	20	26
Total	86	121	144	144	199	146	149

Design: A retrospective analysis of 989 patients admitted consecutively with severe hepatic dysfunction, over a 7 year period.

Results: Aetiology of acute liver failure presented as patient episodes.

The spectrum of disease presenting as ALF has remained largely unchanged except for the recent identification of patients with haemophagocytic lymphohistiocytosis (11 cases since 1993). Overall survival has improved from 50/86 (58%) in 1991 to 101/149 (68%) in 1997. Over this time period the number of patients undergoing liver transplantation has increased from 11 in 1991 to 18 in 1997 (to November) and ITU survival in this group has remained stable at 82% and 78% respectively.

Conclusion: Improvements in the medical management of ALF and the identification of suitable candidates for liver transplantation have resulted in an increased survival. The prompt recognition and referral of patients with severe hepatic necrosis to centres offering transplantation may result in further improvements in survival.

P151

Conservative therapy for blunt abdominal and thoracic traumas

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Critical Care 1998, **2(Suppl 1):**P151

Blunt thoracic and abdominal traumas in adult, are responsible for a remarkable number of admissions in our Clinic. The aim of this study is to establish the criteria for the nonsurgical treatment in such traumas. During the period January 1993–September 1997, 7000 patients with blunt abdominal or thoracic traumas were delivered to the emergency department of our Hospital. 1200 of them were hospitalized. This number of admissions represent the 15% of all admissions in our Hospital during the same period. The mean age was 36 ± 5 years (range: 22–64 years) whereas the mean hospitalization period was 7 ± 2 days (range: 4–10 days). The most common causes were the car and motor vehicle accidents, the falls and the fights. 75 patients (6.25%) underwent surgical treatment. In 198 cases (16.6%) the traumas concerned the spleen, in 167 (13.9%) the liver, in 172 (14.3%) the injury had to do with the spleen and the liver, in 183 cases (15.25%) the trauma concerned the genitourinary system and in 215 cases (17.9%) the chest was injured. The rest 265 cases were minor trauma of the abdomen or the chest. All patients had a very closed clinical observation with careful physical examination, adequate radiographic studies (X-ray of the chest, ultrasonography, computed tomography) and blood analysis for baseline chemistries, complete blood count, PT, APTT and amylase. Peritoneal lavage was performed in all cases of abdominal tenderness. Splenectomy was performed in 31 cases, haemostasis of the liver in 35 cases, nephrectomy in 14 cases and placement of a ureteral double-J stent in 18 cases. Only 7% (84 cases) of the thoracic blunt traumas required surgical treatment.

It seems that the conservative therapy of the blunt abdominal and thoracic traumas by the careful clinical surveillance, the use of ultrasonography and computed tomography, is a safe alternative method of approaching and treating such type of injuries.

P152

Score systems and cardiovascular function in a series of consecutive patients with acute severe acute pancreatitis

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Critical Care 1998, **2(Suppl 1):**P152

Introduction: The score systems in Severe Acute Pancreatitis (SAP) are based on the clinical and/or analytical variables and are useful in the Emergency Area Triage (EAT).
Objective: To compare general prediction model, disease-specific score systems and cardiovascular function situation through the pressure-adjusted heart rate (PAR) with mortality.
Method: Prospective study of clinical and laboratory testing in 93 SAP patients treated in the Intensive Care Unit over five years, from 1991–95. On apply APACHE II and Ranson Score at 24 and 48 h. Cardiovascular function at 24, 48 h and first week through PAR, calculated as the product of the heart rate (HR) multiplied by the ratio of the right atrial (central venous) pressure (RAP) to the mean arterial pressure (MAP); PAR=HR×RAP/mean BP [1].
Results: Average age of the 93 cases was 63.9± 13.9 years (26–88), 45.2% being women. Etiology was biliary in 53.5%, alcoholic in 12.8%, pharmacological in 2.8% and idiopathic in 31.4%.
Conclusions: In our SAP patients series 24 h APACHE II score has more prognostic value than Ranson score in mortality. Cardiovascular function at 48 h, pressure-adjusted heart rate (PAR), predict clinical outcomes; it is important to prevent the ocurrence of potentially-life threatening events if there is hemodynamically unstable with a PAR >8. Patients died when a PAR was >14.8 during first week.

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P153

Difficulties in substance abuse rehabilitation in a rural trauma center

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Critical Care 1998, **2(Suppl 1):**P153

Objective: Drug and alcohol abuse is prevalent among trauma patients. The trauma incident however may provide an opportunity to confront the patient with a potential abuse problem and facilitate rehabilitation. We sought to evaluate the effectiveness of a program designed to assist trauma patients with their substance abuse problems in our rural Level I trauma center.
Methods: Starting in April, 1994, our Trauma service identified and referred all trauma patients judged to have a potential substance abuse problem to our Drug, Alcoholism and Addictions Program (DAAP). These patients received pertinent in-hospital counselling and education and were informed of available follow-up. Telephone interviews were conducted to determine the long-term effectiveness of the program in regards to a substance-free lifestyle and a potential for further morbidity.
Results: From 4/8/94 to 6/26/96, a total of 3397 trauma patients were entered into the Trauma Registry. Of these, 762 (22.4%) tested positive for alcohol and 473 (13.9%) tested positive for other substances. Of these, 100 patients or 10.3% of the net 966 patients who tested positive for one or more substances were identified and confronted regarding their substance abuse problem(s). Reasons cited for other patients not being included in the program were abbreviated hospital stays, physician apathy, and a failure of the subspecialty services to seek this consultation. Only 16 patients could be contacted for follow-up. All but 2 of the 16 patients who were contacted had stopped or curtailed their alcohol or drug use. Notably, one of the non-rehabilitated patients did subsequently have a traffic citation driving under the influence of an intoxicating sustance.
Conclusions: Despite a programmatic approach, only a fraction of substance-abusing trauma patients are successfully approached into altering their lifestyles. In patients where counselling is provided, lifestyle changes are potentially attainable. The poor long-term follow-up of these patients may underscore the difficulty of rehabilitation of the trauma population.

Table (abstract P152)

	Mortality						
	No			Yes			
Variable	n	Media	SD	n	Media	SD	P^*
24 h APACHE	66	8.9	3.9	26	13.1	6.8	0.000
48 h APACHE	60	9.2	4.8	20	14.9	8.4	0.000
24 h RANSON	66	2.7	1	26	2.8	1.1	ns
48 h Ranson	66	1.8	1.2	23	2.7	1.4	0.004
24 h PAR	53	5.6	3.3	11	6.1	4.9	ns
48 h PAR	52	7.6	4.8	17	20.7	10.5	0.005
1 week PAR	8	7.3	3.5	6	14.8	7.5	ns

*t Test.

P154

The encephalopathy of acetaminophen induced acute liver failure is associated with cerebral endothelial activation

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Critical Care 1998, **2(Suppl 1):**P154

Background: The development of acute hepatic encephalopathy in acute liver failure (ALF) is poorly understood but may be precipitated by sepsis and is associated with sustained elevations of tumor necrosis factor alpha [1]. We have investigated whether the cerebral endothelium of patients with severe encephalopathy has evidence of cytokine induced activation.
Methods: Using immunohistochemistry we have examined the expression of the markers of endothelial activation ICAM-1, VCAM-1 and E-selectin in cerebral vasculature of the brains of 4 acetaminophen induced ALF patients who died of severe encephalopathy and 2 control patients who died sudden cardiac deaths. CD31 was used as a positive control.
Results: CD31 was detected in vessels of all sections studied. No E-selectin expression was detected. Significant ICAM-1 expression and lesser levels of VCAM-1 were detected in the cerebral endothelium ofencephalopathic patients but not in controls.
Conclusions: Acute hepatic encephalopathy is associated with cerebral endothelial activation. The effects of such activation may include changes in blood brain-barrier permeability [2] to the numerous neurologically active substances circulating in ALF and have a direct role in pathogenesis.

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P155

Acute pulmonary edema and transient leukopenia in haloperidol-induced neuroleptic malignant syndrome

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Critical Care 1998, **2(Suppl 1):**P155

Haloperidol is a very commonly prescribed neuroleptic. To our knowledge, only one case of haloperidol-induced acute pulmonary

edema has been reported. We reported a 33-year-old male adult with schizophrenia who ingested haloperidol around 40 mg, flunitrazepam (Rohypnol®) around 100 mg, and trihexyphenidyl (Artane®) around 30 mg. Acute pulmonary edema soon developed and was diagnosed with chest radiograms and arterial blood gas. It resolved 4 days later after treatment with endotracheal ventilation and diuretics. The neuroleptic malignant syndrome and transient leukopenia was also found in this case. Although the etiology of acute pulmonary edema remained unknown, we thought it was related to neurogenic origin secondary to neuroleptic malignant syndrome resulting from over-dosage of haloperidol. The neuroleptic malignant syndrome was self-improved 3 weeks later. However, the transient shift from leukopenia to leukocytosis has never been described in the English literature of neuroleptic malignant syndrome.

P156

A ten-year-analysis of cardiopulmonary resuscitations in Celje emergency medical service

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Aims: This study was performed to determine the survival rate among out-of-hospital cardiac arrests in Celje EMS and to identify predictors of survival.
Methods: Prehospital cardiopulmonary resuscitations between 1 January 1987 and 31 December 1996 in Celje EMS were retrospectively analyzed.
Results: 380 cardiac arrests were reported by the ambulance service in the same period. The patients' average age was 60.8 ± 17.4 years. 271 were males and 109 females. 86 (22.6%) resuscitations were successful. 40 (10.5%) patients were then discharged from hospital. The heart disease was the main cause for resuscitation in 73.4% of the patients. The average response time was 7.8 ± 5.6 min.
Survival was significantly greater with bystander-initiated CPR, initial rhythm of ventricular fibrillation or ventricular tachycardia and shorter response times. There were no differences in age and etiology (cardiac versus non-cardiac) of cardiac arrest between successfully and unsuccessfully resuscitated patients.
Conclusions: The overall survival rate from out-of-hospital cardiac arrest in our EMS is comparable with data published in other studies. Our data relieved improved survival rates when bystanders CPR was initiated and in an EMS system with short response time.

P157

HBO in replantation of extremity segments and autotransplantation of tissue complexes

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Critical Care 1998, **2(Suppl 1):**P157

The main existing indications for hyperbaric oxygenation (HBO) therapy are well known. But there are some works where the effect of HBO was studied in such illnesses which are not considered as indications for this method. So, the problem of the usage of the HBO under the threat of rejection of cutaneous flaps or grafts is under the study now (Wattel F *et al,* 1990).
Proceeding from the peculiarities of the therapeutic effect of HBO (Tabrah FL *et al,* 1994), with the help of HBO we have optimised the treatment of patients (after the replantation of extremity segments and autotransplantation of tissue complexes) who where operated using microsurgical equipment.
24 patients with the given pathology were treated in HBO unit during 1994–97 years. HBO sessions began in a day after the operation and where administrated once a day. The highest pressure of isopression was 1.7–2.0 ATA; the duration, 40 min. The average number of sessions for each patients was 8–10. The complete accommodation of replanted segments and transplants was noted in all the patients. Nevertheless the major accommodation factor of amputated extremity segments is a careful fulfilment of vascular anastomosis. It guarantees the reconstruction of blood flow in arteries and veins.
So we consider it justified use HBO in patients with critical ischemia term of abjuncted extremity segments and prolonged ischemia of complex flaps with their autotransplantation.

Table (abstract P156)

	Successful CPR	Unsuccessful CPR	*P*
Number (n)	86	294	
Age (years)	61.4 ± 19.4	60.6 ± 16.8	NS
Response time (min)	6.1 ± 3.9	8.3 ± 6.0	0.002
Bystander CPR (%)	30.2	12.6	<0.001
Initial rhythm (%)	VF/VT=77.9	VF/VT=25.2	
	PEA =16.3	PEA =19.0	<0.001
	asystole = 5.8	asystole = 55.8	
Etiology (%)	cardiac = 74.4	cardiac = 73.1	NS
	non-cardiac = 25.6	non-cardiac = 26.9	

P158

Management of cardiopulmonary emergencies in hyperbaric medicine

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Critical Care 1998, **2(Suppl 1):**P158

Introduction: Published data concerning cardiopulmonary emergencies during hyperbaric oxygen therapy (HBOT) are available, however, incidence is unknown [1]. Due to a tremendous increase in the number of HBO treatments throughout Germany since the recent installation of over 60 new hyperbaric institutions (mainly not attached to hospitals) a higher dimension of incidents is presumed. In multiplace hyperbaric chambers up to 12 patients are under video supervision from outside by chamber operators. Some problems arising from emergencies during HBOT are not evident in all situations.
Methods: Video recordings of megacode training sessions with an AMBU® resuscitation mannequin in a multiplace/multilock hyperbaric chamber (HAUX Starmed® 2200/5,5) were analyzed. Thereby the particularity of emergency management under hyperbaric conditions was evaluated.
Results: Without attending personnel in the hyperbaric chamber emergency situations will not always be recognized instantly. A further delay of 30-120 s in attending the emergency originates from the need of pressure equalization in the personnel lock. During this maneuver guidance of the patients inside the chamber from outside by the chamber operator is impossible due to increasing noise. Simultaneous surfacing of all chamber occupants is not advisable, but cannot be avoided in some cases to achieve conditions for efficient therapy because of limited space within the chamber. Evacuation of the emergency patient under pressurised conditions into the personnel lock can be facilitated by the use of a dividable stretcher which is stored under the opposite rows of seats in the main compartment.
Conclusion: Algorithms for the management of emergencies under hyperbaric conditions are essential as well as appropriate chamber architecture. Advanced treatment is accomplished after transfer of the emergency patient into the personnel lock, because panic reactions of other patients within the main chamber have to be anticipated. Routine monitoring of ECG, NIBP and $tcPO_2$ in all patients is mandatory if no personnel is attending inside the chamber during HBOT.

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P159

Comparison of multiorgan dysfunction (MOD) scores in prediction of 1 -year mortality of ICU patients

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Critical Care 1998, **2(Suppl 1):**P159

Introduction: MOD and secondary infections are main causes of death in intensive care unit. The developed scores and models for prediction of mortality, as APACHE II, III and MPM II predict outcome quite accurately in a large population but are rather inaccurate and should be applied with caution for a single ICU patient. Although the basic idea in development of MOD scores like MODS, LOD and SOFA was not to predict mortality, but to describe the number, severity and progression of organ failures, these scores seem to correlate with mortality. The objective of this study was to compare these new scores in prediction of 1-year mortality of ICU patients.
Methods: In year 1995 our mixed 10-bed ICU had 592 admissions. 333 patients were randomly chosen for this study. Data of all admissions was collected partly prospectively, but the MOD scores were calculated retrospectively because of availability only since 1996. All deaths were verified from the Finnish National Registry at June 1997. 1-year mortality rate for various values of APACHE III, MODS, LOD and SOFA scores were evaluated and compared by calculating area under receiver operating curves (AUCs).
Results: Areas under ROC (AUC) were 0.7817 for APACHE III, 0.7570 for LOD (day 1), 0.7226 for MODS (day 1) and 0.7215 for SOFA (day 1) in prediction of 1-year mortality.
Discussion: There is no clear consensus of method to be used in evaluation of MOD. Several scoring systems, as MODS, LOD and SOFA, have been presented, but they have not been properly compared in different patient populations. All of the scores clearly correlated with 1-year mortality in this study. The LOD score (at ICU day 1) had the highest predictive power with the AUC nearly equal to that of APACHE III.
Conclusions: In addition to usefulness of MODS, LOD and SOFA scores in assessment of multiorgan dysfunction, these scores may be used in prediction of mortality. Further studies are needed to evaluate the differences of these scores in this respect, as well as the possible advantage of combining a multiorgan dysfunction score at different timepoints (for example ICU days 3, 5 and 7), or its change, with baseline APACHE III score in prediction of mortality.

P160

Comparison of three severity of illness scoring systems for intensive care unit (ICU) patients

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Critical Care 1998, **2(Suppl 1):**P160

Background: Scoring systems have been proposed to assist in assessing prognosis, to compare ICU performance and to stratify patients for clinical trials. Three different models of severity of illness scoring systems (APACHE II, SAPS II and MPM 24) have been widely used to evaluate critically ill patients but which one is better to measure severity of illness and to predict hospital outcome?
Study objective: To compare the performance of these three scoring systems in the same cohort of patients.
Methods: Data was prospectivelly collected for each ICU admission. In order to strictly follow the models rules, patients who stayed less than 24 h at the ICU or were younger than 18 years or were burn, coronary care or cardiac surgery patients were excluded. The outcome measure was vital status at hospital discharge. The discrimination was evaluated using ROC curve area and for the calibration was used the Hosmer-Lemeshow goodness-of-fit test
Results: Out of 283 consecutives ICU admissions, there were 172 patients who were eligible by the criteria and had full sets of data. There were 69.2% male and 30.8% female patients; age was 45 ± 18.5 (61% had less than 50 years old) and postoperative care took up 99 (57.6%) cases, of which 84 (85%) were emergency surgery. Trauma was the admission cause for 65 (37.8%) patients. APACHE II was 17.6 ± 8.3 and SAPS II was 33.2 ± 16.1. ICU mortality rate was 34.3% and hospital mortality rate was 43.6%.

Table (abstract P160)

	APACHE II risk	SAPS II risk	MPM 24 risk	*P*
mean ± standard deviation	26.6 ± 23.9	22.1 ± 22.4	21.8 ± 21.3	-
sensitivity (%)	37.33	34.47	29.33	NS
specificity (%)	94.85	97.94	97.94	NS
predictive value positive (%)	84.86	92.86	91.67	NS
predictive value negative (%)	66.19	65.97	64.19	NS
area under ROC curve	0.8267	0.8573	0.8362	NS
goodness-of-fit test (C)*	38.5398	78.4671	72.060	-

NS, non significant; *df=8 $P < 0.00001$

Conclusions: The truest assessment of adequacy of a predictive model is through goodness-of-fit test that compares expected with observed frequencies. It is possible for a method to have a high ROC curve but to not fit an observed set of data well. At this study, all three models showed good discrimination power, that is, they were able to distinguish patients who lived from patients who died. Nevertheless, the calibration was very poor, that is, the predictions did not correlate with the actual outcome across the entire range of risk. This finding may be due to meaningful differences between this study casemix and the original development populations (too many emergency surgery and trauma patients in this study). Furthermore, resource utilization, type of treatment and quality of care should be reviewed and considered when evaluating hospital mortality.

P161

Effectiveness of the PRISM III score for predicting mortality in pediatric intensive care neurologic patients

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Critical Care 1998, **2(Suppl 1):**P161

Purpose: The Pediatric Risk of Mortality (PRISM) III score was developed from the Physiologic Stability Index (PSI) to assess pediatric ICU mortality and provide an objective data as a severity index. Although the PRISM score has been applied to many comparisions and analyses in previous studies, there are few reports applied to pediatric intensive care patients in Korea. To evaluate the effectiveness of the PRISM III score as a severity index for expecting mortality and find important variables influencing mortality, we applied this scoring scale to pediatric neurologic patients admitted to the ICU and analyzed the data statistically.
Methods: Data collection was done by careful review of medical records and scored each clinical variable. The outcome at discharge was determined as non-survival, survival, and hopeless discharge. Determination of mortality in the hopeless discharge group was done within 48 h after discharge by telephone interview. The study populations were classified into four groups : CNS infection (26 patients), acute encephalopathy (31 patients), status epilepticus (35 patients) and cerebrovascular disorder (4 patients). The difference of the PRISM III score between the survival group and non-survival group was compared by using the nonparametric Mann-Whitney test in the entire study population and for each diagnostic group. To confirm the degree of fitness between the actual mortality and predicted mortality, the Hosmer-Lerneshow goodness-of-fit test, a multiple logistic regression model was used. All clinical variables used for scoring were compared for survivals and non-survivals by the Chi-square test. *P* values <0.05 were considered significant.
Results: The PRISM III score was significantly higher in the non-survival group than in the survival group. Predicted mortality from the PRISM III score has fitted to actual mortality. According to the results of analyses in each diagnostic groups, the PRISM III score was higher in non-survivals of the acute encephalopathy and CNS infection groups, but statistically insignificant in the cerebrovascular disorders and status epilepticus groups.

The important variables of the PRISM III score associated with mortality were mental state, pupil reflex, systolic blood pressure, acidosis, blood sodium level, blood creatinine level, blood glucose level, and PT/PTT.
Conclusions: The PRISM III score is helpful in predicting mortality in pediatric intensive care neurologic patients, especially those in the acute encephalopathy or the CNS infection groups. However, this score was not useful in the status epilepticus group, and insignificant in cerebrovascular group. Due to the smallness of the study group, more massive and comprehensive studies are needed as a follow up to this study.

P162

Predictive value of APACHE II score is improved by combination with bioelectrical impedance analysis in multiple trauma patients

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Critical Care 1998, **2(Suppl 1):**P162

Background: Indication to extensive critical care could be ameliorated by combining APACHE II (AP II) scores [1] with the Phase-Angle (PA, ϕ), a global parameter of nutritional status derived from Bioelectrical Impedance Analysis (BIA) [2].
Methods: 40 (30 male/10 female) multiple trauma patents (age: 16-81 years) with a stay of >5 days on the Intensive Care Unit (ICU) were studied retrospectively. Routinely obtained daily measurements of nutritional status (BIA 101 Impedance Analyser, RJL-Systems) included calculations of PA.
Results: 10/40 patients (25%) died during ICU stay (Table). In all patients with AP II scores ≥20 (APACHE II-Class ≥5) determination of outcome would have been correct by Phase-Angle: all deceased patients had a PA <3, while surviving patients had a PA >4 ($P < 0.05$). Discriminance analysis of this data reveals a probability of 100% for prediction of survival and 94% for lethal outcome respectively.
Conclusion: Even in this small sample of multiple trauma patients there is a clear cutoff level of PA >4 for prediction of survival. We suggest the routine use of BIA for observation of ICU patents, but further studies are needed to establish the prognostic relevance of this method.

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P163

Evaluation of an integrated intensive care service in a department of geriatrics

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Critical Care 1998, **2(Suppl 1):**P163

Objective: Transferral of multimorbid elderly patients from a geriatric ward to an intensive care unit for deterioration for vital function may be associated with some serious problems: (1) environmental changes may lead to acute disorientation in geriatric patients, (2) the invasiveness of an extended ICU therapy may be felt to be inappropriate by the patient and his relatives in relation to multimorbidity and prognosis. However, abstaining from transferral to an ICU and witholding extended therapy may be inappropriate as well. Therefore, extended therapy including ICU service which is adjusted to the individual prognosis and needs of the elderly patients is required in a geriatric clinic. For economic reasons, this implemented extended therapy cannot include the more invasive and costly services of an ICU (eg respirator treatment, continuous hemofiltration). We report our experience with the implementation of extended therapy in a department of geriatrics.
Patients and methods: The nurses of the Department of Geriatrics (University Teaching Hospital) received special training in intensive care. Forty geriatric patients with multimorbidity and acute deterioration of their health state (eg impairment of renal function, severe pneumonia, pulmonary embolism, sepsis, cardiac arrhythmia with circulatory instability, unstable angina pectoris and contraindication for interventions) were included in the study. Therapy extension included continuous monitoring of ECG, RR, O_2-saturation and fluid balance, mask CPAP ventilation, intensified bronchial suctioning, continuous drugs (eg dopamine, norepi-nephrine, epinephrine, furosemide, theophylline, insulin, heparin). Evaluation included outcome, necessity of transferral to an external ICU, geriatric assessment (Barthel index, up-and-go test, Tinetti test as well as APACHE III score on admission and discharge) and acceptance of intensive care treatment implemented in the geriatric clinic by the patient and/or his relatives.
Results: In all 40 cases, the suggestion of extended therapy within the Department of Geriatrics was accepted by the patients themselves or their relatives. Eight patients had to be transferred to an ICU for extended ICU treatment (intubation and ventilation, continuous hemofiltration, surgical interventions). Eighteen patients did not survive. This treatment approach was highly appreciated by the patients and their relatives.
Conclusion: Extended therapy including services normally provided by an ICU which are implemented in a geriatric clinic may be an appropriate alternative or adjunct to transferral to an external ICU in multimorbid geriatric patients with a limited prognosis of survival. However, all decision-making in a deteriorating geriatric patient has primarily to depend on the decision of the patient himself and his relatives. Transferral of geriatric patients to an external ICU may be prevented by an implemented extended therapy in a substantial number of patients.

Table (abstract P162)

AP II class	AP II score	*n*	Died	ϕ Survivors*	Non-survivors*
1	0–4	0	-	-	-
2	5–9	4	0	5.7	-
3	10–14	8	0	4.3	-
4	15–19	11	0	4.1	-
5	20–24	9	3	4.4	2.9*
6	25–29	2	1	4.9	2.1*
7	0–34	6	6	-	2.2
8	>34	0	-	-	-

*ϕ survivors vs non-survivors, $P < 0.05$.

P164

Comparative study of intensive care unit (ICU) perfomance

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Critical Care 1998, **2(Suppl 1):**P164

Background and objective: It is possible to evaluate ICU performance using of severity of illness score, but is this methodology objective enough to draw comparison between different units?
Methods: Data were prospectivelly collected at two hospitals during 42 months. To provide homogeneity, all data were collected following the same protocol, verified by one author and calculated with the same software, developed at Health Informatics Center-Universidade Federal de São Paulo-UNIFESP.
At hospital B patients were younger (55.8% were 50 years old or less) than those of hospital A, 27.8% were admitted due to acute trauma. At hospital A, 59.4% of patients were 60 years old or older, only 6.7% were admitted due to trauma, 37.2 % were admitted after elective surgery. The area under ROC curve showed good degree of calibration but discrimination was not adequate for both hospitals: hospital B had higher number of observed than expected deaths at all ranges of risk and hospital A had less observed than expected deaths only at low-risk admissions.
Discussion and conclusion: The comparisons between institutions must be corrected for several factors: variations in casemix, patients co-morbidites, status of previous disease, delays in referral, social factors and access to

Table (abstract P164). Results

ICU	A	B	*P*
ICU beds (adults)	23	10	-
Occupancy rate (%)	69.4	92.4	<0.0001
ICU length of stay (days)	3.4 ± 6.1	9.4 ± 12.1	<0.0001
Total admissions	3928	1194	-
Age (years)	59.5 ± 19	46.3 ± 18.8	<0.0001
% elect.surg-emerg.surg-medical	35.5-17.5-47	5.0-34.5-60.5	<0.0001
APACHE II	14.3 ± 8.3	17.6 ± 9.2	<0.0001
% admissions with APACHE 11 < 20	22.2	39.4	<0.0001
Hospital mortality rate (%)	16.2	43.8	<0.0001
Standard mortality rate (S.M.R.)	0.81	1.61	<0.0001
% admissions with risk death <10	49.5	33.7	<0.0001
area under ROC curve	0.8820	0.8594	NS
goodness of fit test (10 df)	75.1 ($P < 0.001$)	241.2 ($P < 0.001$)	

Plus-minus values indicate standard deviation; NS, non-significant

current technologies. Furthermore it is questionable the appropriateness of an American index to Brazilian hospitals. Therefore we suggest that hospitals should build up their own databases and adjust theses scores accordingly, so that they can make more relevant comparisons.

P165

The recovery room as an intensive care unit

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Critical Care 1998, **2(Suppl 1):**P165

Introduction: Beds in intensive care units (ICU) are expensive and their number is limited. Unstable mechanically ventilated and postsurgical, patients, sometimes have to be treated outside an ICU, due to lack of an available open bed. In our hospital these patients are treated at the recovery room (RR) until a bed is available in the ICU. We prospectively studied the admission of acute care patients to the RR.
Methods: Patients who where admitted to the RR between March and June 1997 were studied. Patients were included if they were assigned to an ICU either before or during surgery, but could not be admitted due to lack of space. Primary medical and nursing care was provided by the anesthesiologists and the RR nursing personnel.
Results: Forty-three patients were included in the study. Mean (± SD) age was 51 ± 25 years. Thirty-seven patients (86%) were emergency room admissions, 6 of whom did not require surgery.
Duration of stay in the RR was 18 ± 17.6 h (median 12, range 2.5–97). All patients were intubated and mechanically ventilated, and had a central venous and an arterial lines on admission to the RR. Thrity-nine patients (90.7%) were still intubated on transport to the ICU. Three (7.0%) patients were children, ages 6, 7, 15. One patient died in the RR. Eight patients (18.7%) were assigned the medical/surgical ICU, 25 (58.1%) to the neurosurgical ICU, three (7.0%) to the pediatric ICU and seven (16.2%) to other locations.
Discussion: The RR with its monitoring equipment, nursing and anesthesia personnel is an attractive location to treat these patients. The following limitations were noted: 1. No additional nursing staff was provided. Therefore less attention could be paid to the 'routine' postoperative patients. 2. The space in our RR is limited and at times immediate postoperative patients had to be delayed in the operating room (OR). This way the yield of OR use was decreased. 3. The primary surgical services tended to lessen postoperative rounds at their RR patients, and communication with them was less than optimal.
Conclusion: While acute care patients can safely be admitted to RR, the duration of their stay should be as short as possible.

P166

Quality of life of long term ICU patients at 6 months after hospital discharge

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Objectives: to assess the quality of life (QOL) of hospital survivors who stayed at the medical ICU >3 days at 6 months after hospital discharge.
Patients and methods: Questionnaire of American Association for Respiratory Care (QAARC: 7 items, scale: min 1, max 7 points) was mailed to patients admitted to the ICU in 1995 who fulfilled the inclusion criteria. QAARC of the patients was compared to QAARC of local population. Statistics: means ± SD, Student's *t*-test; $P < 0.05$ considered significant.
Results: Out of 386 ICU admissions in 1995, 91 patients fulfilled the inclusion criteria. Response rate to QAARC was 70% (64 questionnaires). Fifty-one patients (mean APACHE II on admission 20.4 ± 4.8, age 51 ± 14 years, 35 males and 16 females) were alive at 6 months after hospital discharge and were further analyzed. Patients had acceptable but significantly lower physical fitness than controls (4.3 ± 1.8 and 5.3 ± 1.4 points, respectively $P < 0.01$) but had better emotivity within the last 2 weeks (5.6 ± 1.4 and 5.0 ± 1.3 points, respectively, $P < 0.05$). QOL was independent on admission APACHEII score and diagnosis group.

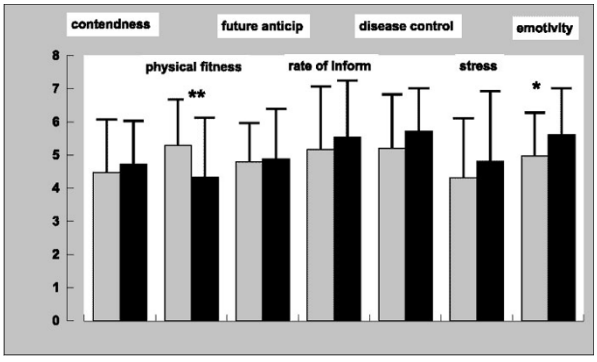

Figure (abstract P166) Results.

Conclusion: At least 56% of hospital survivors of long term medical ICU care survive and have acceptable quality of life at 6 months after hospital discharge.

P167

Core software for on-line data acquisition and post-hoc analysis: report of clinical testing and evaluation

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The continuing progress of standard medical care results in an overload of patient's data, which are difficult to handle by traditional techniques. A software package is perspectively an appealing choice to deal with such a challenge. Aim of this study was the development and testing of an automated real-time data acquisition and analysis system for intensive care survey. The system included two PCs, the first for data acquisition (PC1: 166 MHz Pentium CPU, 32 MB RAM, 2 GB HDD, A/DC National Instruments AT-MIO 16E-10), and the second for data analysis (PC2: 200 MHz Pentium CPU, 32 MB RAM, 2 GB HDD). PCs were both networked, with shared HDDs, keyboard, mouse, video output, and printout subsystem. Complete hemodynamic, respiratory and neurological parameters were monitored by HP Component Monitoring System 66S/68S, which included a VueLink interface to coupled ventilators and Licox GMS, Serial Output (RS-232, 38400 baud per s) and up to 8 waveform analog outputs. Original software for data acquisition, storage and analysis was developed by object-oriented LabVIEW 4.0. Data acquisition was performed by PC1. At start, the user is allowed to select up to 51 numerical parameters (serial input RS 232, 4 data strings per min) and up to 16 waveforms (analog input, sampling rate: 128–256–512 points per s). Flag points (free-text or codified) could be added. As an example, it was possible to display the waveforms, up to 5 trend graphs or 6 histograms of selected digital parameters. Up to 3 graphic trends from selected digital parameters were automatically printed on demand (every 6–8–12–24 h). The complete sets of numerical parameters were stored as following: a) read-only spreadsheet files, whose length was limited to 2 h each one because of technical reasons; b) daily spreadsheet files (1st data string of minute); c) binary files (waveform storage) with circular buffering in 48 h cycles (max. length). Post-hoc analysis was performed by PC2, regardless of eventual simultaneous data acquisition by PC1. When system starts, the user chooses the optional on-line or off-line work (from already stored data). The task can involve up to 8 digital parameters (trends) and up to 4 waveforms. Different software tools like cursors and pointers were available to retrieve significant events, to select time intervals and to zoom the graphs, allowing to perform different procedures. Analysis capabilities on numerical parameters (trends) included: frequency tables of selected parameters, numerical regressions, vector calculus. Input data from daily spreadsheet files could be edited. Waveform analysis included basic statistics, integral and derivative calculus. Different reports, graphs and tables were printed at request. The assessment of our system included a preliminary laboratory test and clinical tests. The system proved an easy interface to different equipment. The user interface and response times were favorably accepted. Data storage and display were reliable and flexible. The equipment can be located at patient bedside as conveniently as at a ward desk. The use of 2 CPUs linked in a local network allowed effective simultaneous data acquirement and analysis. Other features included highly configurable data acquisition, to suit the case at hand, easy and fast retrieval of information, automatic generation of complete and accurate reports to illustrate trends or to correlate different parameters. More extensive field tests should be carried out to assess the impact of the system to ICU and operating rooms and its effectiveness.

P168

The screen log: a tool for monitoring critical care clinical research activity

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Critical Care 1998, **2(Suppl 1):**P168

Introduction: Clinical research relevant to the care of critically ill patients has been ongoing for decades. Sponsors of research projects monitor site performance by providing a screen log (SL) which contains a record of enrolled patients (multicentre, uni-project in scope). The present study was undertaken to evaluate the utility of a unicentre, multi-project SL.
Design: Prospective evaluation of an SL for monitoring critical care clinical research activities in a Canadian tertiary care academic medical centre.
Methods: Consecutive patients admitted over a 2 year period to the Medical Surgical ICU were screened for eligibility into 3 protocols. Patients were defined as follows: 1. Eligible: met all inclusion criteria; 2. Excluded: study specific exclusion criteria; or prognosis was considered hopeless; or were enrolled in another study; or no consent; or missed; 3. Truly eligible: [eligible]-[met no exclusions + hopeless prognosis + enrolled in other protocol]; 4. Enrolled: consent obtained and patient randomized; 5. Recruitment efficiency: number of patients enrolled / number truly eligible.
Results: 54 patients/month were screened for a total of 1292 admissions. Table 1 presents screening and recruitment summary for 3 protocols in progress over varying lengths of time within the 2 year period of SL evaluation.
Conclusion: 100% screening with data entry into a SL database provides a quantitative description of enrolled patients into multiple clinical trials, the number not randomized and the reasons for non-randomization. The SL provides a method of accountability of research activity and identifies potential problems such as poor consent rates and missed patients. The SL provides the ability to evaluate recruitment strategies and recruitment efficiency over time. Short-term feasibility screening for projects may also occur.

Table 1 (abstract P168)

	Study A	Study B	Study C
Total eligible (% of total screened)	331 (48)	463 (36)	64 (13)
Total excluded (% of eligible)	274 (83)	405 (87)	52 (81)
study specific exclusion	131	202	32
hopeless prognosis	59	58	18
other study	36	52	0
Truly eligible	105	151	14
Total enrolled	58	53	12
Recruitment efficiency	55%	35%	86%