Poster Sessions
Clinical and experimental studies to assess cellular integrity in sepsis 036-049

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USING FLOW-CYTOMETRY ANALYSIS TO IDENTIFY SEPSIS IN ICU PATIENTS

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INTRODUCTION. Despite considerable research, treatment of sepsis frequently remains inadequate as a result of delayed diagnosis or excessive use of antibiotics. We aimed to identify a marker(s) of the immune system that could help to determine sepsis in intensive care unit (ICU) patients.

METHODS. The study included 105 patients who were expected to stay in the ICU for 4 days or more (Dec 2003 - March 2004 and Sept - Nov 2004). Blood was collected every day to perform flow cytometry analysis of the circulating leukocyes in a lysis, no wash direct staining technique with quantification of fluorescence using the Quantibrite kits for CD64 and HLA-DR antibody binding site enumeration on the surface of polymorphonuclear leukocytes and monocytes, respectively

RESULTS. The patients were allocated into 3 groups: Group 1 - patients with sepsis on admission (n=36); Group 2 - patients without sepsis throughout their ICU stay (n=44); Group 3 - patients who developed nosocomial ICU sepsis (NICUS) (n=25). On admission: CD64 expression was higher in septic (group 1) than non-septic patients (groups 2 and 3) (3595±2873 vs 2268±2327, p=0.001). The ROC curve for CD64 on admission showed a specificity of 74%, a sensitivity of 85%, with an area under the curve (AUC) of 0.82, positive predictive value of 57% and negative predictive value of 92% at the level of 1727 molecules/cell. HLA-DR expression was somewhat lower in septic (group 1) than non-septic patients (groups 2 and 3) (9738±5471 vs 11271±5747, p=0.3). In the NICUS group, a significant increase in CD64 was noticed with the clinical identification of sepsis (from 1240±784 to 2320±3298, p=0.03). The ROC curve for CD64 predicting sepsis showed a sensitivity of 81%, a specificity of 73%, an AUC of 0.76, a positive predictive value of 81% and a negative predictive value of 73% at the level of 1602 molecules/cell. HLA-DR expression showed a non-significant decrease in the 4 days preceding the clinical identification of sepsis (from 13556±6032 to 8787±2876, p=0.3).

CONCLUSION. Quantibrite CD64 is a useful marker for differentiation between septic and non-septic patients on ICU admission. It also can help to identify the development of sepsis in ICU patients.

Grant acknowledgement. we thank Pickton Dickinson Europe for supplying the FACScan flowcytometry throughout the whole study duration

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MONOCYTE FUNCTION (CD14+HLADR+) DURING FIRST ICU DAYS IN LONG TERM ICU PATIENTS

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INTRODUCTION. Expression of HLADr+ on monocytes was reported to be a parameter with significant predictive power in ICU patients (1). In our ICU a study on immunomonitoring of ICU patients was designed.

METHODS. Study was approved by local EC and waiver to informed consent was obtained. Patients who at D1 (D0 = admission) were estimated to stay in the ICU > 3 days were eligible. In this abstract preliminary analysis of early development (D1 and D4) of CD14+HLADr+ expression in 41 patients hospitalized from October 2004 to February 2005 is reported. Data are presented as median (Q25,Q75), correlation (Spearman R), Mann-Whitney U test and Wilcoxon test were used when appropriate, p< 0.05 considered significant.

RESULTS. Out of 41 patients (M/F 30/11; age 63 (58;71) years) 33 survived ICU stay (S) and 8 died (NS). APACHE II on admission was 26 (17;35). On D1, 6 patients (1 NS) had immunoparalysis CD14+HLADr+ < 40%, 19 patients (4 NS) had CD14+HLADr+ in range of 40-70% („gray zone") and 16 patients (3 NS) had no sign of monocyte dysfunction (>70%).
On D1, CD14+HLADr+ in S did not differ from NS (63% (45;73) and 64% (49;89), respectively). Secondary (n=28) and primary (n=13) ICU admissions also did not differ (62% (47;73) and 72% (47;83), respectively), though APACHE II was significantly different - 21(17;29) and 28(25;35), respectively (p=0.015). No difference in CD14+HLADr+ was also found in patients subgroups (medical patients (n=17) 71% (55;80)); surgical (n=18) 52% (39;67) and CPR patients (n=6) 73% (43;81). Out of 8 NS only 4 survived until D4 control. In 2 NS CD14+HLADr+ decreased by > 40% (absolute) which was not found in any S. APACHE II on admission did not correlate with CD14+HLADr+ on D1 and no correlation was also found in patients subgroups.

CONCLUSION. Preliminary data suggest that on admission CD14+HLADr+ does not correlate with APACHE II. Decrease in CD14+HLADr+ by > 40% within first 4 days of ICU stay can predict poor outcome.

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038

EFFECTS OF ACUTE HYPERGLYCEMIA / HYPERINSULINEMIA ON MONOCYTE HLA-DR EXPRESSION

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INTRODUCTION. Acute hyperglycemia is a known independent risk factor in critical illness. However, there is a lack of understanding of the cellular and molecular mechanisms behind this phenomenon. We hypothesized that the monocyte's ability to present antigen, indirectly assessed by its capability to express HLA-DR, is impaired in short-term hyperglycemia, providing one possible mechanism to explain the increased infection rate in acutely hyperglycemic patients.

METHODS. Venous whole blood was collected from 21 healthy volunteers, diluted 1:10 with RPMI and cultured for 24 hours under normal (100mg/dl) and hyperglycemic (400mg/dl) conditions. All samples were incubated at normal or high insulin levels (+100munits/l), and with or without 2h of LPS-stimulation (1ng/ml) at the end of the incubation period. Monocyte HLA-DR expression was measured with flow cytometry as mean channel fluorescence (MCF), using dual staining with anti-CD14 and anti-HLA-DR. Results are stated as mean ± SEM, and differences were tested using repeated measures ANOVA and the paired t-test.

RESULTS. 20 of 21 samples showed a decrease in MCF when glucose levels were raised to 400mg/dl. Hyperinsulinemia further decreased MCF in 17 of 21 samples. Although absolute levels of HLA-DR expression varied considerably among individuals, the described effects were highly reproducible and significant: There was a mean decrease in MCF from 2171 ± 205 (100mg/dl glucose) to 1941 ± 142 upon exposure to 400mg/dl glucose ($p<0.001$). When incubated with high insulin at 400mg/dl glucose, a further decrease to 1826 ± 144 MCF was observed ($p<0.01$ vs. 400mg/dl glucose alone). In samples without LPS, the differences were smaller, but still significant ($p=0.001$). In contrast, hyperinsulinemia alone did not affect HLA-DR expression in a normoglycemic environment ($p=0.1$).

CONCLUSION. Short-term hyperglycemia significantly decreases monocyte HLA-DR expression in vitro. Reduced HLA-DR correlates with impaired antigen-presenting capacity of monocytes and served as a predictor of adverse outcome in critically ill surgical patients. Paradoxically, hyperinsulinemia lowered mean HLA-DR expression in monocytes even further in this in-vitro hyperglycemic model. This effect of hyperglycemia to decrease monocyte HLA-DR expression may provide one mechanism with which to explain the higher morbidity and mortality in patients undergoing hyperglycemia of critical illness.

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PLASMA OBTAINED DURING HUMAN ENDOTOXEMIA INCREASES ENDOTHELIAL PERMEABILITY IN VITRO

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INTRODUCTION. In contrast to in vitro experiments and the clinical observation in septic patients, in vivo measurements of microvascular permeability do not demonstrate an increase during human endotoxemia. We investigated the effect of plasma obtained during human endotoxemia experiments on the permeability of endothelial monolayers and to correlate the effects with various mediators of vascular permeability.

METHODS. Eight healthy volunteers received 2 ng/kg E. Coli endotoxine (O:113). Multiple blood samples were drawn. Plasma of a selection of these samples was added to a monolayer of human umbilical venular endothelial cells (HUVEC) cultured on semipermeable membrane inserts (Transwells) and incubated for 6 hrs, after which FITC-labelled bovine serum albumin permeability was determined. Concentrations of various mediators (TNF-a, IL-1β, IL-8, IL-10, IL-12, IFN-γ, Vascular Endothelial Growth Factor, leptine, and activation of the complement system: TCC)were correlated with the measured permeability.

RESULTS. Human endotoxemia resulted in marked plasma elevations of TNF-a, IL-1β, IL-8 and IL-10, whereas no relevant increase in IFN-γ and IL-12, and no increase in TCC and leptin was found. A 6 hr incubation of the endothelial monolayers with the plasmas that were drawn 2 and 4 hours after endotoxin administration resulted in an increase in a relative endothelial permeability of 41% and 47% respectively after 6 hrs of equilibration, compared to a relative permeability of 29% after incubation with unstimulated plasma. The level of VEGF and IL-10 demonstrated a significant but moderate correlation with the increase in endothelial permeability ($r=0.47$ and $r=0.43$ respectively). No significant correlation was found with other cytokines. Incubation for 45 min was enough to establish an increase in permeability of the endothelial cells.

CONCLUSION. Incubation of monolayers of endothelial cells with plasma derived from endotoxin exposed subjects results in an increased permeability of these monolayers. This increase is moderately correlated to VEGF and IL-10 levels and not to other mediators that are increased during endotoxemia. The main induction of permeability takes place in the first 45 min of incubation of the monolayer with the sample.

Grant acknowledgement. PP is a recipient of a Clinical Fellowship grant of the Netherlands Organisation for Scientific Reseach (ZonMW)

040

THE EFFECT OF SERUM ON LPS-INDUCED CHANGES OF PIG CORONARY ARTERY & HUMAN NEUTROPHILS IN VITRO

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INTRODUCTION. The action of LPS on Toll-like 4 receptors in myeloid cells involves a complex interaction with serum-derived soluble CD14 and lipopolysaccharide-binding protein (LBP) 1. In contrast, much less is known about the interaction of LPS with non-myeloid tissue. In the case of isolated blood vessels, high concentrations of LPS (> 10mug/ml) are often required in vitro to induce the hyporesponsiveness of the vasculature characteristic of septic shock. The aim of this study was to investigate the effect of foetal calf serum (FCS) on the action of low concentrations of LPS in a myeloid (neutrophil) and a non-myeloid (vascular) tissue.

METHODS. Leukocyte-enriched blood was prepared from volunteers and exposed to LPS (1ng/ml to 10mug/ml) for 30 min in the presence or absence of 2% FCS. Activation of neutrophils was measured by assessing changes in forward scatter using Flow Cytometry. Segments of the porcine coronary artery were prepared for isometric tension recording as previously described 2 following overnight exposure to 1 mug/ml LPS in the presence or absence of 10% FCS. Preparations were exposed to 60 mM KCl followed by a cumulative concentration response curve to U46619.

RESULTS. In four separate experiments LPS caused a concentration-dependent increase in forward scatter of human isolated neutrophils (-log EC50 6.10+0.18 g/ml) which was increased four-fold by the presence of 2% FCS (-log EC50 6.73+0.14 g/ml). LPS (1mug/ml) caused a small but significant ($p<0.05$ paired Student t-test*) reduction in the sensitivity of the artery to U46619 (-log EC50 7.81+0.04 vs 7.67+0.05, n=20; 1.4-fold), but this was not further enhanced by the presence of 10% FCS (-log EC50 7.72+0.05 vs 7.48+0.05, n=16; 1.7-fold). Similarly, a higher concentration of LPS (100mug/ml) caused a 2.5-fold reduction in the potency of U46619 (-log EC50 7.73+0.14 vs 7.36+0.08, n=8) which was not affected by the presence of 10% FCS (-log EC50 7.81+0.10 vs 7.49+0.06, n=8; 2-fold).

CONCLUSION. The interaction between LPS and serum factors differs between myeloid and non-myeloid tissues. Neutrophils are sensitive to low concentrations of LPS and serum factors (possibly LPB and soluble CD 14) enhance this action. In contrast, serum factors do not appear to enhance the ability of low concentrations of LPS to induce hyporesponsiveness of coronary arteries.

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041

CAROTID BLOOD FLOW DURING HYPOTENSION AND LOW-DOSE ENDOTOXEMIA

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INTRODUCTION. Endotoxemia modifies vascular reactivity. We evaluated the effect of hypotension induced by prolonged anesthesia with and without endotoxin on carotid blood flow.

METHODS. 11 pigs were anesthetized with continuous thiopental and fentanyl. All animals underwent laparotomy and cannulation of the major splanchnic vessels. Cardiac output (CO, thermodilution), carotid arterial pressure (BP) and flow (Qcar, Doppler ultrasound)were measured. After surgery, baseline measurement were taken and the animals randomized to infusion of endotoxin (E; 0.4 mcg*kg-1*h-1, n=5) or placebo (P;n=6) both combined with continuous infusion of thiopental/fentanyl. Cardiac filling pressures were maintained constant.

RESULTS. Results are expressed as mean (SD). MANOVA for repeated measurements: effects: time,group,time-group for all variables. While the fractions of cardiac output of superior mesenteric artery, trunk, hepatic artery and portal vein flows remained stable over time, fractional renal blood flow decreased in both groups.

TABLE 1.

		BD (mmHg)	CO (L/min)	Qcar (ml/min)	Qcar/CO
Baseline	E	68 (6)	3.1 (0.7)	140 (37)	0.05
	P	76 (20)	3.0 (0.4)	112 (23)	0.04
6 h	E	70 (18)	3.9 (0.5)	131 (53)	0.03
	P	69 (7)	3.5 (0.6)	128 (36)	0.04
18 h	E	56 (9)	4.5 (0.5)	161 (35)	0.04
	P	67 (12)	4.3 (0.7)	160 (38)	0.04
28 h	E	41 (10)	4.0 (0.9)	158 (33)	0.04
	P	42 (13)	4.5 (0.9)	186 (91)	0.04

CONCLUSION. 1) In contrast with renal blood flow both, absolute and fractional carotid blood flow was maintained, even when blood pressure dropped to very low values at the end of the experiment. Consequently, systemic blood flow seems to be more important for cerebral perfusion than blood pressure. 2) Preservation of carotid blood flow was independent on the presence or absence of endotoxin.

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042

RED BLOOD CELL DESIALYLATION INDUCES ALTERATIONS OF SHAPE AND METABOLISM

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INTRODUCTION. Increased red blood cells (RBCs) 2,3 diphosphoglycerate (2,3 DPG) content induces alterations of the RBC deformability (1). In rheumatoid arthritis, decrease in sialic acid (SA) RBCs membrane content is associated with decreased activities of membrane ionic pumps and transketolase (2). We have observed that RBCs from septic patients showed a more spherical shape with a decreased SA membrane content (3). We therefore hypothesized that the loss of SA RBC membrane content as observed in septic patients could alter the 2,3 DPG concentrations of the RBC.

METHODS. Washed RBC from 10 volunteers were incubated with 0.125 U/mL of the degrading SA enzyme (neuraminidase from Clostridium perfringens, Sigma ®). The RBC shape was estimated by flow cytometry after 10 hours of neuraminidase incubation. Normal RBC show a bimodal distribution related to the biconcave form (1). On this histogram, we calculated the second Pearson Coefficient of Dissymmetry (= 3 x (mean-median)/SD) (PCD). The normal PCD value is around - 0.8 whereas a value of zero represents a perfect spherical shape. 2,3 DPG and lactate RBCs concentrations were measured after 10 hours of neuraminidase incubation. Control groups were constituted of RBCs incubated 10 hours with RPMI. Data are presented in mean ± SD and were evaluated by a Student's test. Correlation was evaluated by the Spearman test.

RESULTS. Neuraminidase altered the RBCs shape and their metabolism. Moreover, we observed a significant correlation between the PCD and the 2,3 DPG concentration ($r = 0.61$; $p = 0.008$)

TABLE 1.

	Control	Neuraminidase	P value
PCD	-0.80 ± 0.48	-0.69 ± 0.14	0.006
2,3 DPG (µmol/ml)	0.19 ±0.05	0.46 ±0.25	0.006
Lactate(mmol/L)	0.66 ±0.05	0.81 ±0.07	0.002

CONCLUSION. The loss of SA RBC membrane content induces a RBC sphericity and a increases in RBCs concentrations of lactate and 2,3 DPG. This latter phenomenon could contribute to the RBC rheology alterations observed in septic patients

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043

MUSCLE METABOLIC MODIFICATIONS IN SEPSIS CHRONIC MODEL

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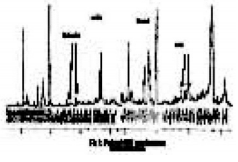
INTRODUCTION. In normal circumstances, there is a reciprocal relationship between the availability of free fatty acids and glucycemia. The metabolic modifications observed in certain situations induce a mobilization of energetic substrates. The aggression generates metabolic responses which mobilize substances stored for the support of vital organs. The aim of our study was to evaluate metabolic muscular modifications generated chronic sepsis due to caecal ligation and puncture.

METHODS. Two groups of 5 Wistar rats were submitted to a chronic peritonitis (septic group), or no surgical procedure (control group). After 14 days the extensor digitorum longus (EDL, fast muscle) and the soleus (SOL, slow muscle) are dissected and immediately frozen in liquid nitrogen then stored at -80°C. The samples are analyzed in NMR spectroscopy.

RESULTS. For muscle EDL the energy metabolism is comparable between both groups. For the soleus, in the group S, there is an tendency towards oxidation of free fatty acids and phospholipids, disappearance of the polyunsatured fatty acids (PUFA), and reduction in phospholipids (fig 1.) and of the production of the essential amino acids (increase in the peak of the glutamine and glutamate) to detriment of the metabolic glucose pathway.



CONCLUSION. The energy muscular adaptation induced by a chronic sepsis is translated in a preferential pathway within the slow muscles by a probable increase of oxidation of the acids of the free fatty acids and of a production of amino acids essential with the detriment of glucose metabolism. At the time of a severe aggression the slow muscles could play an important part in the energy production for vital organs.

044

IMPACT OF TIME ON SYSTEMIC AND LOCAL EVALUATION OF PERFUSION/OXYGENATION DURING SEPTIC SHOCK

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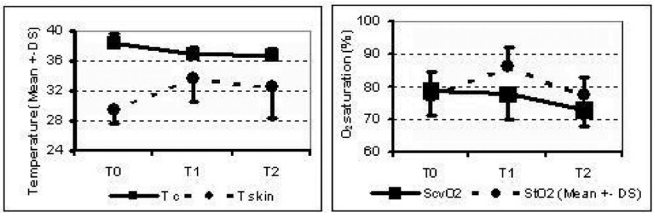
INTRODUCTION. We study the relation between systemic and local perfusion indexes in septic shock patients.

METHODS. 7 consecutive septic shock patients were studied (mean SOFA score: 11,5 [8 - 16]). Systemic parameters: BPsyst; BPdiast, SvO2 central (ScvO2), central temperature (Tc); local parameters: thenar skin temperature (Tskin), static tissue oxygenation of thenar skeletal muscle (StO2), dynamic tissue oxygenation (NIRS) following forearm arterial occlusion: the slope of the decrease in StO2 during occlusion as an index of local tissue oxygen consumption. Measurements at T0: ICU admission; T2: after 24hrs; and T3: ICU discharge.

RESULTS. from T0 to T1, systemic parameters did not change with a large gradient between Tc and thenar Tskin (9°C) which decreased at T1 to 3°C ($p<0.05$). The slope of StO2 during occlusion was slower at T1 than T0 ($p<0.05$) and StO2 baseline value was higher at T1 than T0 ($p<0.05$) suggesting a reduction in local O2 consumption.



CONCLUSION. the association between reduction in temperature gradient and an occlusion slower slope of StO2 decrease suggests an improvement in tissue perfusion after resuscitation (temp gradient reduction) associated with a reduction in tissue O2 consumption after 24 hrs. Local modifications along time were more pronounced than systemic modifications in acute phase.

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045

ENDOTHELIAL OXIDATIVE STRESS INDUCED BY SERUM FROM PATIENTS WITH SEPTIC SHOCK

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INTRODUCTION. During septic shock (SS) endothelial cells are one of the first target of reactive oxygen species (ROS). However, endothelial cells are also source of ROS. The hypothesis of the present study is that serum from patients in SS has a potency to activate endothelial cells which then become a source of ROS thus potentially participating with circulating cells to the subsequent increase of oxidative stress and development of organ dysfunction. The questions addressed were the following 1/ Is oxidative imbalance effective during SS in adults? 2/ Does serum from patients with SS induces ROS production when infused on naive endothelial cells? 3/ Is this production related to the severity of the SS ?

METHODS. After approval by institutional ethic committee blood samples were collected from patient in septic shock (SS) within the first day of admission (D1) and at day 3 (D3) and day 5 (D5) and from healthy volunteers. Oxidative stress was studied in vivo by measuring lipid peroxydation products, enzymatic antioxidant (superoxide dismutase, catalase, gluthatione peroxydase) and non-enzymatic oxidant (vitamin A and E). Fluorescent microscopy (DCFH fluorescent probe) was used to study radical oxygen species (ROS) production by perfused HUVEC. Corralation between fluorescence intensity and patient severity parameters (SAPS II, SOFA score, survival) was observed.

RESULTS. Lipide peroxidation was significantly increased during septic shock and catalase and gluthatione peroxidase activities were significantly decrease at 3 days of observation. Vitamine A was significantly decrease at D3 and D5.
Serum of SS patients induced significant rise of DCFH fluorecence compared to HV. Intensity of fluorescence was significantly corralated to SOFA score and SAPS II and to survival.

CONCLUSION. Septic shock is associated with an increase in lipidic peroxidation products associated with an imbalance in antioxidant status. In addition, serum from patients treated in ICU for septic shock induces ROS formation in naive endothelial cells, and that the magnitude of this production is correlated with the septic shock severity. This study support the hypothesis that endothelial cells potentially participate with circulating cells to the subsequent increase of oxidative stress and development of organ dysfunction in septic shock.

046

MITOCHONDRIAL BIOENERGETICS OF PERIPHERAL BLOOD MONOCYTES IN PATIENTS WITH SEPTIC SHOCK

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INTRODUCTION. Septic shock is characterized by an impaired oxygen extraction despite evidence of apparent tissue hypoperfusion. A mitochondrial dysfunction has been observed in septic animals or patients, which could be explained by the presence of reactive oxygen or nitrogen species, or by inhibition of the mitochondrial respiratory chain complexes. The aim of this study was to investigate the mitochondrial oxidative phosphorylation in peripheral mononuclear cells (PBMC) from patients with septic shock.

METHODS. PBMC were isolated from whole blood using a Ficoll gradient. Mitochondrial oxidative phosphorylation was investigated after permeabilization of the plasmic membrane by digitonin. The optimal concentration of digitonin was determined by measuring the differential release of the cytoplasmic lactate deshydrogenase and the mitochondrial enzyme citrate synthase. Patients were recruited in a medical ICU, through a period of 4 months with informed consent obtained. PBMC were isolated from control non-septic patients and from patients with septic shock. Oxygen consumption rate (VO in nmol O/min/mg proteins) were measured using a Clark-type electrode on various substrates. In the same time, mitochondrial ATP synthesis rate (VATP, in nmol ATP/min/mg proteins) was determined by bioluminescence (luciferine-luciferase system). Data were analyzed using Student t-test, with $p<0.05$ as significant.

RESULTS. Eight patients with septic shock were compared with eight control patients. In the septic shock group, there were 4 women and 4 men, with a mean age of 64 years, an IGS II of 49 and a SOFA score of 11. With glutamate as substrate (for complex I), VO decreased in septic patients with a statistically significant decrease in VATP (3.30 ± 0.48 vs 1.74 ± 0.51 nmol ATP/min/mg proteins). With succinate as substrate (complex II), no differences were found between both groups.

CONCLUSION. This preliminary study confirm the feasibility of this technique exploring mitochondrial respiration and ATP synthesis on a non-invasive material compared to muscle biopsy. As other authors we found a mitochondrial dysfunction in septic shock patients, characterized by an alteration of the complex I of the respiratory chain.

047

INCREASED NA+-K+-ATPASE ACTIVITY AND HYPERLACTATEMIA IN SHOCK STATE

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INTRODUCTION. We recently demonstrated (1) in hyperkinetic septic shock that muscle produced lactate and that ouabain a selective inhibitor of Na+-K+-ATPase totally inhibited that muscle overproduction. We hypothetised that in low flow state such as hemorragic shock or non resuscitated septic shock, endogenous epinephrine in increasing Na+-K—ATPase activity through β2 adrenoreceptor activation increased lactate level through an increase in aerobic glycolysis.

METHODS. We investigated 3 rodents models of shock : normokinetic endotoxinic shock, an hypokinetic peritonitis model and hemorrhagic shock. 3 microdialysis probe were inserted in the muscle and perfused at 2 µl/min with Ringer free lactate plus Ethanol (50 mmo/l) and Propanolol (10-4 mol/l) or ouabain (10-7 mol/l) or ICI 118551 (10-8 mol/l)(β2 blocker). Abdominal and femoral blood flow were measured. Lactate and pyruvate were measured both in blood and muscle

RESULTS. Both drugs decreased blood flow around the probe as estimated by ethanol ratio. Despite that decrease, both drugs in all models decreased lactate and pyruvate production by the muscle
In both septic model, muscle lactate was always higher than blood lactate. In hemorrhagic shock, blood and muscle lactate were equal.

CONCLUSION. The activation of Na+-K+-ATPase through bêta-2 stimulation is an ubiquitous phenomenon in shock state. Nevertheless, in both models, ouabain or ICI did not abolish muscle lactate production evocating the presence of others mechanism.In hemorrhagic shock, others organs than muscle are involved in lactate formation

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048

APOPTOSIS AND REGULATION OF THE BCL-2 FAMILY IN LYMPHOCYTES DURING SEVERE SEPSIS

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INTRODUCTION. Apoptosis was shown to be increased in murine models of sepsis (1) as well as in septic patients (2). The bcl-2 family of proteins controls the mitochondrial release of pro-apoptotic factors. Inhibition of apoptosis by adoptive transfer of lymphocytes overexpressing the anti-apoptotic bcl-2 improved survival in septic mice (1). The aim of our study was to investigate the contributions of bcl-2 family members to lymphocyte apoptosis during sepsis.

METHODS. 16 Patients were enrolled as soon as they fulfilled the criteria of severe sepsis. Informed consent was obtained. Blood samples were drawn on days one, three and five after enrolment. 11 healthy volunteers served as control. Enzyme activation and antigen expression were meassured by flow cytometry after immunophenotyping. mRNA expression was quantified by real-time polymerase chain reaction.

RESULTS. Caspase-3 was activated in CD4+ T-cells, CD8+ T-cells and B-cells. This was reflected in an increased phosphatidyl-serin externalisation indicating increased early apoptosis. The antiapoptotic mitochondrial protein bcl-2 was clearly decreased in lymphocytes. On the transcriptional level bcl-2 mRNA expression was down regulated. The mRNA expression of the pro-apoptotic bax instead remained unchanged. Moreover, the mRNA expression of the anti-apoptotic bcl-xl dropped significantly.

CONCLUSION. These results demonstrate an imbalance between the anti-apoptotic bcl-2 and bcl-xl on the one hand, and the pro-apoptotic bax on the other hand. It is likely, that this mitochondrial imbalance contributes to the observed increase in lymphocyte apoptosis during severe sepsis.

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DECREASED IN-VITRO SENSITIVITY TO NOREPINEPHRINE AFTER ENDOTOXIN-EXPOSURE AND FAECAL PERITONITIS

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INTRODUCTION. In septic shock, high doses of nor-epinephrine are frequently used to maintain sufficient blood pressure. This may decrease hepato-splanchnic blood flow. The aim of this study was to assess the sensitivity of splanchnic blood vessels to nor-epinephrine after 24 hours of severe sepsis and septic shock.

METHODS. In 5 pigs, E. coli lipopolysaccharide was infused for 24 hours, and in 3 pigs, autologous faeces was inoculated intraperitoneally and kept for 24 hours. A group of 8 animals served as controls (observation period 12 hours). All animals underwent laparatomy for vessel localization at the beginning of the experiment. Hepatic (HA) and superior mesenteric (SMA) arteries were sampled at the end of the experiment, and vascular rings (HA, n=48; SMA, n=42) were prepared for norepinephrine (NEP, 10-8M to 10-5M) dose-response contraction studies, using organ chamber technique. Contractility is expressed as maximal force (Fmax, gr) to NEP.

RESULTS. Animals exposed to endotoxin-infusion and faecal peritonitis developed hyperdynamic shock (mean arterial pressure <60 mm Hg), while the control animals remained hemodynamically stable.

TABLE 1.
FMax (gr)

	HA	SMA
Controls	9.9 ± 5.4	13.2 ± 6.6 p=0.049, vs. HA
Endotoxin/faecal peritonitis	4.6 ± 3.6 p<0.001, vs. controls	6.2 ± 4.0 p<0.001, vs. controls

CONCLUSION. Endotoxemia and faecal peritonitis result in decreased in-vitro sensitivity to nor-epinephrine in both HA and SMA. While the maximal response in SMA is higher as compared to HA in non-septic conditions, decreased in-vitro sensitivity to vasopressors in sepsis does not seem to be restricted to specific vasculatures.

REFERENCE(S). 1. Wakabayashi I et al. Eur. J. Pharm. 1987; 141: 117-22.; 2. Beasley D. Am. J. Phys. 1990; 259: R38-44.; 3. Fleming I et al. Brit. J. Pharm. 1991; 103: 1047-52.

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Poster Sessions
Cardiovascular dynamics 050-058

050

COMPLICATIONS OF HEPARIN INDUCED THROMBOCYTOPENIA (HIT) IN A MEDICAL INTENSIVE CARE UNIT.

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INTRODUCTION. HIT is an immune mediated disease that leads to thrombocytopenia.Is associated with hypercoagulability and may cause life threatening complications(arterial and venous thromboembolisms,hemorrhagic complications,skin lesions and acute systematic reactions.We investigated the incidence of complications in our HIT(+) critically ill pts.

METHODS. Prospective study in a 6 bed University Hospital ICU. Time period 18 months.28 pts with HIT were included in the study. HIT was identified using the platelet aggregation test (PAT) and in turn verified with ELISA test and flow cytometry. Pts with HIT were treated with continuous infusion of Lepirudin.There was only one surgical patient in the HIT group.There were no orthopedic or cardiothoracic patients.All patients of the HIT group had previously taken either unfractionated or low molecular weight heparin. The control group consisted of 28 consecutive ICU patients without HIT.Apache II scores were calculated for both groups.All pts that were included in the study had a conventional vessel color flow duplex sonography upon admission and were followed up when HIT was verified or with clinical indication.

RESULTS. 18 female and 14 male pts aged between 39-89 were included the HIT group.APACHE II scores were similar for both groups Thrombocytopenia developed between days 5-14. Minimum platelet count varied from 12000-62000 and improved gradually during lepirudin anticoagulation therapy. In 4 pts (14,3%) the thrombocytopenia resolved within 6-10 days after discontinuation of the heparin therapy.Twenty pts (71,4%)of the HIT group developed hemorrhagic complications as opposed to 6(21,4%) in the control group and were controlled with discontinuation of lepirudin therapy for a few hours and subsequently verifying the infusion rate at a more acceptable level and with transfusions of blood and plasma. Totally 27 units of blood and 58 units of plasma were transfused.Four patients (14,3%) had a thrombo-embolic complication as opposed to none in the control group.11 pts (39.3%) died. There were 2 pts(7,14%) with skin lesions and there was none with acute systemic reaction.

CONCLUSION. There is a higher incidence of thromboembolic complications either arterial or venous in the HIT group.Hemorrhagic complications were significantly higher among the HIT group pts.

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DOPEXAMINE INDUCES CONTRACTION IN PIG CORONARY ARTERY IN VITRO

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INTRODUCTION. Dopexamine has been proposed as a selective peripheral vasodilator in the treatment of sepsis and septic shock. As a catecholamine it may have large spectrum of effects, including the effects on coronary arteries, which has not been examined.

METHODS. We investigated in-vitro the effects of dopexamine and partly compared to dopamine, on the isometric tension of the rings of the left anterior descending coronary artery of pig. The preparations were isolated from freshly taken hearts obtained from the local abattoir and its tension examined in presence or absence of moderate pretension (KCl 20mM, or PGF2-alpha, 5x10-6M) or/and after pre-incubation with various agents.

RESULTS. Dopexamine elicited concentration dependent contractions in the KCl pre-contracted preparations (given as EC50, means ±SEM) (4.38 ±0.23; n=7); whereas dopamine produced a relaxation (6.61 ±0.26; n=6). Dopexamine induced contractions were endothelium (ENDO) dependent (-ENDO vs. +ENDO: 3.78 ±0.38; n=5, vs. 4.38; ±0.23; n=7; P=0.0002). Pre-incubation with adrenergic alpha-receptor antagonist prazosin (10-5M), beta-receptor antagonist propranolol (10-6M), or dopamine DA1 receptor antagonist SCH23390 (10-7M) displaced dose-response-curves of dopexamine to the right, as compared to the controls. (respectively 4.07 ±0.40, n=7; 4.10 ±0.27, n=7; and 3.95±0.19, n=8; all P<0.001). Pre-incubation with verapamil only partially inhibited dopexamine elicited contractions (verapamil vs. controls: 2.54 ±1.68; vs. 4.38 ±0.23; n=7, P <0.001) while in Ca2+ free solution (+ EDTA, 5x10-4M) dopexamine elicited contractions of coronary arteries that were weakly pre-contracted with KCl (control vs. Ca2+ free solution: 4.30 ±0.36 vs. 3.96 ±0.30; n=7, P<0.001). The incubation with the cGMP-inhibitor ODQ (10-4M) or phosphatase inhibitor cantharidin (10-6M) both partially inhibited contractions caused by dopexamine (respectively: 3.87 ±0.18; n=6; P=0.004; and 3.65 ±0.28; n=6; P=0.028).

CONCLUSION. It was found that dopexamine contracted coronary artery of the pig, probably as a result of adrenergic and dopaminergic (DA1) receptors stimulation, but also by some unidentified extra cellular Ca2+ independent mechanism.

051bis.

NOREPINEPHRINE PLUS DOBUTAMINE VERSUS EPINEPHRINE ALONE FOR THE MANAGEMENT OF SEPTIC SHOCK

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INTRODUCTION. Catecholamines infusion is a major component of septic shock management. International guidelines recommend that norepinephrine should be preferred to epinephrine, though phase III trials are lacking. The present study aimed at comparing the efficacy and safety of norepinephrine plus dobutamine to that of epinephrine in adults with septic shock.

METHOD. This was a prospective, multicenter, randomised, double-blind study conducted in septic shock patients who received either epinephrine or norepinephrine plus dobutamine. Drugs were titrated to maintain mean blood pressure over 70 mmHg. Main outcome was 28-day mortality.

RESULTS. 330 patients were enrolled (epinephrine: 161; norepinephrine plus dobutamine: 169). The two treatment arms were well balanced at baseline except that, in the epinephrine group, patients were older (m±SD, 63±15 vs. 59±16 years, p=0.03), had lower heart rate (112±23 vs. 118±22 bpm, p=0.01) and higher haematocrit level (32±6 vs. 31±6%, p=0.02). At 28 day, there were 65/161 (40.4%) deaths in the epinephrine group and 58/169 (34.3%) deaths in the norepinephrine plus dobutamine group (p=0.26, RR=0.85, 95%CI, 0.64-1.13). There was also no significant difference between the two groups for mortality rates at ICU (46.6 vs. 44.4%, p=0.69, RR=0.95, 95%CI, 0.75-1.21) or hospital (52.2 vs. 48.5%, p=0.51, RR=0.93, 95%CI, 0.75-1.15) discharge. There was no evidence for a difference between the two groups in terms of systemic hemodynamics, time on vasopressors, time on ventilator, and adverse events (i.e. stroke, coronary events, arrhythmia, and limb ischemia).

CONCLUSION. There is no evidence for the superiority of norepinephrine plus dobutamine on epinephrine alone for the management of adults with septic shock.

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IN VIVO MEASUREMENT OF MYOCARDIAL ENERGY-RELATED METABOLITES

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INTRODUCTION. Microdialysis allows the in vivo biochemical analysis of interstitial fluids. We investigate the dynamic changes of myocardial metabolism in patients with ischemic heart disease and low left ventricular ejection fraction (EF < 40%).

METHODS. In 17 patients undergoing coronary artery bypass grafting (CABG) a microdialysis catheter was directly inserted in the left anterior wall into an area with abnormal ventricular contraction identified by MRI. Contrast-enhanced MRI was performed to detect reversible myocardial dysfunction. A second catheter was placed in the normokinetic anterior wall of the right ventricle as a control. Microdialysis measurement was performed at time intervals before, during and up to 24 hours after cardiopulmonary bypass (CPB). Microdialysis samples were analysed for lactate, pyruvate and glycerol. Lactate-pyruvate-ratio (LPR) was calculated as an direct marker of myocardial cell damage.

RESULTS. The postoperative course of all patients was uneventful. No complications were seen due to catheter implantation and explantation. During aortic cross clamping the myocardial LPR significantly increased in the ischemic region of the left heart from 28 (10-49) to 66 (25-167) (P<0,05) at the end of CPB, while the ratio in the right ventricle rose from 24 (10-58) to 38 (10-98). After CPB the LPR decreased to normal range in both areas at the end of observation (8-16, P<0,05). The glycerol concentration as marker of membrane damage increased in both ventricles significantly (P<0,05) and declined to low values after removal of the cross clamp until the end of observation.

CONCLUSION. Myocardial microdialytic measurement is feasible and can be performed safely in a clinical setting. It was possible to reveal data about the metabolic changes of ischemic and nonischemic myocardium during and after CPB as a bedside monitoring. LPR and glycerol values as markers of the onset and amount of anaerobic metabolism and cell membrane desintregity respectively showed signs of rising in both ventricles during cardioplegic arrest, but were significantly higher in the left ventricle due to underlying ischaemic coronary disease. Myocardial microdialysis is an useful tool in rapid intraoperative detection of ischemia.

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EFFECTS OF EXOGENOUS NITRIC OXIDE ON K-ATP CHANNEL POTENTIATION IN VASCULAR SMOOTH MUSCLE.

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INTRODUCTION. Activation of the ATP-sensitive potassium (KATP) channel via the inducible NO pathway contributes to the vascular hyporeactivity seen to catecholamines in sepsis. Moreover, relaxation to the KATP channel opener levcromakalim is potentiated in models of sepsis, both in vivo and in vitro . The mechanism of this potentiation is unknown, but we examined the hypothesis that it could be mimicked by NO.

METHODS. Rat mesenteric arteries were pre-contracted with phenlyephrine (3 muM). Isometric tension studies were used to examine levcromokalim-induced (10-9-10-5M) relaxation in the presence of DetaNO (10 muM or 1mM) at 4 hr and 20 hr timepoints. Nitrite levels (a marker of NO production) were measured using the Griess assay.

RESULTS. Relaxation to levcromokalim was not potentiated by preincubation with DetaNO for 4 hr (10 muM) or 20 hr (10 muM or 1 mM) (table 1). Paradoxically, 20 hr incubation with 1 mM DetaNO partially inhibited relaxation. Incubation in DetaNO (10 muM) for 20 hr is associated with an eight-fold increase in levels of nitrite formation compared to controls (n = 5, P < 0.005), while an in vitro model of sepsis (LPS, 1.0 mug.ml-1) doubled nitrite levels (n = 7, P < 0.05).

TABLE 1.

	4 hr Control	4 hr DetaNO (10 muM)	20 hr Control	20 hr DetaNO (10 muM)	20 hr DetaNO (1 mM)
EC50 M	7.2.10-8	1.10-7	2.07.10-7	1.63.10-7	4.47.10-7
n	6	5	4	4	4
P value		0.1		0.57	0.005

CONCLUSION. Exogenous NO failed to potentiate levcromakalim-induced relaxation. This suggests that either intracellular is important or that LPS produces potentiation through additional pathways.

REFERENCE(S). O'Brien et al (2005). Brit J Pharm. 144:367-75.

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DIAGNOSIS USING A MINIMAL CARDIAC MODEL INCLUDING REFLEX ACTIONS

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INTRODUCTION. Heart disease is difficult to diagnose due to often confusing clinical data. This paper uses integral based model parameter identification [1] to identify two disease states using the pressure waveforms through the aorta (Pao) and pulmonary artery (Ppa), the flows through the ventricles and their max and min volumes, available from a Swan-Ganz Catheter.

METHODS. The pericardium dead space volume V0,pcd is decreased by 20 ml every 8 heart beats for 40 beats to simulate pericardial tamponade. The resistance through the pulmonary circulation Rpul is increased by 20% every 8 beats to simulate pulmonary embolism. Reflex actions take effect every beat. For each disease state, the measured outputs are discretized with 10% uniform noise. The model parameters are identified in each period of 8 beats.

RESULTS. Table 1 shows the results for pericardial tamponade. For pulmonary embolism, Rpul was identified with errors ranging from 2.4% to 8.5%. Mean errors including all model parameters ranged from 5.6% to 8.95%, with no false parameters found.

TABLE 1.

	True value (ml)	Optimized value	Error (%) V0,pcd	Mean (all parameters)
1st change	180	176	2.22	5.60
2nd change	160	158	1.25	8.03
3rd change	140	138	1.43	6.84
4th change	120	117	2.50	8.95
5th change	100	100	0	8.58

CONCLUSION. Integral based optimization successively identified each disease state as it developed and in the presence of significant measurement noise. These results demonstrate the potential of using this model in a clinical setting to assist medical staff in diagnosis in clinically useful time (3-5 minutes).

REFERENCE(S). [1] Hann CE, Chase JG, Shaw GM, and Smith BW. Identification of Patient Specific Parameters for a Minimal Cardiac Model. Proc 26th IEEE EMBS 2004, p. 813-816

055

LOW-DOSE RECOMBINANT ACTIVATED FACTOR VII (NOVOSEVEN) IN CARDIAC-SURGERY

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INTRODUCTION. Excessive bleeding requiring transfusion of blood components is one of the most common complications in cardiac surgery patients. In the recent years, there has been an increased use of recombinant activated factor VII (rFVIIa) for the treatment of refractory bleeding in several patient populations1.

METHODS. From January 2004 to February 2005, 20 cardiac surgery patients with intractable bleeding were enrolled in the study. Each patient undergone a complete step-by step transfusional protocol (TP). At the end of the TP 10 patients, the Study Group, were treated with a low-dose (1.2 mg) rFVIIa and 10 patients who did not receive rFVIIa, represented the Control Group. Outcome evaluation included clinical settings, blood loss, need for red blood cells (RBCs), fresh frozen plasma (FFP) and platelets (PLT) transfusions, and coagulation laboratory findings.

RESULTS. Median, 25th –75th 24-h blood loss percentiles were 1685, 1590-1770 ml vs. 3170, 2700-3850 ml in Study Group and Controls, respectively (p=0.0004). Median, 25th –75th of red blood cells (RBCs), fresh frozen plasma (FFP), and platelets (PLT) units transfused in Study Group and Controls were: 6, 4-8 U vs. 21.5, 13-23 U, p=0.001; 7.5, 6-11 U vs 11, 9-15 U, p= 0.003;0,0-4 U vs. 9, 6-13 U, p=0.001. In addition, a significantly improvement of PT (p=0.01), INR (p=0.006), aPTT (p=0.01) and PLT count (p=0.003) was detected in the Study Group vs. Controls. Furthermore Study Group patients showed a lower ICU Length of Stay (LoS; $\chi 2$=15.9, p=0.001) and experienced a low surgical re-exploration rate ($\chi 2$=16.2, p<0.001).

CONCLUSION. In our experience, low-dose rFVIIa showed satisfactory results in cardiac patients with intractable bleeding. Further larger randomized series are necessary to confirm our findings

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056

PERIPHERAL VENOUS BLOOD GAS SAMPLES IN PATIENTS WITH ACUTE PULMONARY EDEMA

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INTRODUCTION. Arterial blood gas (ABG) samples are useful in the management of patients with acute pulmonary edema (APE) for assessing the severity and indications for some mechanical ventilation forms. However, the value of venous blood gas (VBG) samples in this setting has not been analyzed.

METHODS. Thirty-four consecutive patients with severe acute pulmonary edema were studied during the first hours of admission, obtaining simultaneous peripheral arterial and venous blood gas samples at different intervals: on arrival, after 60, 120, 180, 240 and 600 minutes. Oxygen saturation by pulse-oximetry (SpO2) was also simultaneously registered.

RESULTS. One-hundred seventy nine paired samples were obtained. Mean values and Pearson correlation coefficients between arterial and venous parameters are shown in Table 1. (p<0.0001)VBG could fairly identify arterial acidosis (pH<7.35), either metabolic (BE < -2) and respiratory (PaCO2>46mmHg). The cutoff for these imbalances with greater area in ROC curves were: venous pH 7.32 (Area 0.968); venous Base excess: –0.95 (Area 0.931); venous PCO2 51.3mmHg (Area 0.870), respectively (p<0.0001). The test accuracy of these cutoff were 92%, 88% and 68% respectively.

TABLE 1.

Correlation of ABG and VBG

	ABG	VBG	Pearson Correlation
pH	7.346	7.318	.915*
pO2	114.6	48	.441*
pCO2	46.1	51.2	.860*
Bicarbonate	25.3	26.3	.837*
Base Excess	-0.05	0.11	.903*
Oxygen Saturation	95.1	75.38	.297*

*mean values. * p<0.001*

CONCLUSION. Peripheral VBG samples are useful to identify acid base disturbances in patients with APE. Introducing some corrections, VBG samples may provide similar information than ABG samples, making arterial puncture unnecessary in many of the cases.

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CEREBRAL ISCHEMIA DURING LOW-PRESSURE CARDIO-ULMONARY BYPASS IN PIGLETS

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INTRODUCTION. Neurologic dysfunction after cardiopulmonary bypass (CPB) has been related to cerebral embolism and hypoperfusion. The cerebral perfusion pressure necessary to avoid hypoperfusion is not well established. We studied intracranial pressure (ICP) and markers of cerebral energy metabolism in groups of anesthetized piglets with high and low mean arterial pressure (MAP) during CPB.

METHODS. A group of piglets (LP)(n=6)were given low MAP by nitroprusside and compared with another group (n=6) with high pressure (HP) by norepinephrine during 60 min of normothermic followed by 90 min of hypothermic CPB. ICP, MAP, markers of cerebral energy metabolism (microdialysis), hematocrit, s-osmolality and acid-base parameters were measured. Total tissue water of the study groups and of a non-CPB group (n=7) were determined.

RESULTS. MAP of HP and LP was 67.3 (2.5)(mean (SEM))and 41.3 (1.0)mm Hg, respectively, after 30 min CPB (P<0.001). ICP increased during CPB in both groups with higher values in HP. Cerebral perfusion pressure decreased to 21.3 (3.1) mm Hg in LP. Intracerebral levels of glucose decreased in LP (P>0.05) and levels of lactate and glycerol increased(P<0.05). Lactate/pyruvate ratio was elevated (Table 1). Cerebral water content was similar in LP and HP, but higher than in the non-CPB group (P<0.001).

TABLE 1.

Results from cerebral microdialysis during CPB. Values as mean (SEM).

	Pre-CPB values (n=12)	HP, 90 min CPB (n=6)	LP, 90 min CPB (n=6)
Glucose (mmol/L)	2.5 (0.4)	2.5 (0.7)	1.7 (0.6)
Lactate (mmol/L)	3.8 (0.4)	4.5 (0.6)	9.6 (1.5)***
Glycerol (micromol/L)	41.8 (7.3)	48.2 (15.8)	119.2 (15.0)*
Lactate/pyruvate	15.7 (1.8)	19.0 (3.3)	64.5 (35.8)

*: p<0.05; ***:p<0.001 (compared with pre-CPB.

CONCLUSION. Intracranial pressure increased during CPB and contributed to a reduction in cerebral perfusion pressure. A MAP of 40 mm Hg may lead to cerebral hypoperfusion, ischemia and cerebral injury. Our results may have implications for hemodynamic management during CPB.

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COMPARING ANESTHETIC REGIMENS FOR NON-INVASIVE STUDIES IN MICE: IMPACT ON CARDIAC PERFORMANCE

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INTRODUCTION. Non-invasive techniques allow for functional analysis of cardiac phenotypes in intact animals. High sensitivity imaging requires immobility to obtain technically adequate images. We compared cardiac performance under light levels of 2 commonly used anesthetic regimens and with addition of xenon to isoflurane.

METHODS. 3 groups of C57-Bl/6 mice (n=7 each) were anesthetized with 0.85% isoflurane (Iso), ketamine 60mg/Kg + acepromazine 1.3mg/Kg (Ket/ace), or 0.35% isoflurane + 35% xenon (Iso/xe) and imaged using a high-resolution ultrasound system (30Mhz scan-head). Cardiac performance was measured at baseline (B), after dobutamine, 2mg/Kg ip (D) and after esmolol 40mg/kg ip (E). Stroke volume (SV, muL) was assessed by aortic outflow tract Doppler, fractional shortening (FS, %) by M-mode in the short axis view, and cardiac output (CO, mL/min) was calculated as SV*HR.

RESULTS. Both Iso and Iso/xe reduced induction and recovery time. Baseline function was better with Iso and Iso/xe than Ket/ace. After D, CO was comparable, but HR was higher in Iso/xe compared to Iso and Ket/ace, and SV was lower.

TABLE 1.

	HR	FS	SV	CO
Iso B	515±15	43±5	56±8	28.6±4.0
Iso D	540±18	57±3 a	58±8	31.5±4.6
Iso E	351±17 ab	27±3 ab	50±9	17.5±2.3 ab
Ket/ace B	363±154 #	38±9	48±9	17.5±9.5 #
Ket/ace D	451±138	57±4 a	57±10	25.1±7.2
Ket/ace E	294±64 b	35±6 b	55±6	16.0±2.7
Iso/xe B	498±81	30±4 #*	49±9	22.2±3.9
Iso/xe D	647±29 a*	57±3 a	48±5	31.2±3.0 a
Iso/xe E	435±96	29±4 b	48±7	18.5±6.1 b

*a p<0.05 vs B; b p<0.05 vs D; # p<0.05 vs Iso; * p<0.05 vs Ket/ace*

CONCLUSION. Compared to Ket/ace, Iso and Iso/xe have less impact on cardiac function and allow study of animals at shorter intervals. Higher HR with xenon after dobutamine injection suggests reduced impact on adrenergic receptors.

Poster Sessions
Ventilation strategies in acute lung injury
059-072

059

THE ROLE OF THE PULMONARY RENIN-ANGIOTENSIN SYSTEM IN VENTILATOR-INDUCED LUNG INJURY

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INTRODUCTION. Mechanical ventilation is essential for the treatment of critically ill patients, but at the same time may cause lung injury (ventilator-induced lung injury; VILI). One of the mechanisms contributing to VILI is biotrauma, consisting of a local inflammatory response and alveolar epithelial cell apoptosis. The exact mechanism by which mechanical ventilation can initiate these processes is still poorly understood. The renin-angiotensin system (RAS), with angiotensin-converting enzyme (ACE) as one of its key components, might play a pivotal role herein. All of the components of the RAS system can be generated locally in the lung tissue, as well as systemically. We hypothesized that injurious mechanical ventilation will activate this pulmonary RAS inducing biotrauma.

METHODS. Male Sprague-Dawley rats were randomly allocated to three ventilation groups: group I Pinsp 16 cmH_2O, PEEP 5 cmH_2O, group II Pinsp 26 cmH_2O, PEEP 5 cmH_2O, group III Pinsp 36 cmH_2O, PEEP 5 cmH_2O. After 4 hours of ventilation we collected broncho-alveolar fluid (BAL) and blood for the determination of ACE activity and pro-inflammatory cytokines (MIP-2 and IL-6). Lungs were studied immunohistologically for apoptotic cell death by activated caspase-3 antibody staining. Non-ventilated animals served as controls.

RESULTS. Ventilation with increased pressure amplitudes showed a significant increase in BAL ACE-activity (control group 804 RFU/ml, group I 2175 RFU/ml, group II 5258 RFU/ml, group III 34319 RFU/ml, $p<0.05$). Interestingly, mechanical ventilation with increasing pressure amplitudes caused a significant progressive decrease in serum ACE-activity (control group 42063 RFU/ml, group I 48276 RFU/ml, group II 28181 RFU/ml, group III 16523 RFU/ml, $p<0.05$). Preliminary results indicate that the increased BAL ACE-activity is correlated with increased BAL cytokine levels and enhanced activated caspase-3 staining.

CONCLUSION. Injurious mechanical ventilation activates the pulmonary RAS leading to local production of ACE, accompanied by an inflammatory response and apoptosis. Serum ACE activity decreases with increased pressure amplitudes. The significance of the concomitant rise of ACE in BAL and decline in serum has to be determined further. We are currently investigating whether blocking the RAS attenuates inflammation and apoptosis

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PEEP SELECTED BY BEST RESPIRATORY COMPLIANCE PRESERVES EFFECTS OF RECRUITMENT MANEUVERS

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INTRODUCTION. Respiratory mechanics has been proposed to set open-lung PEEP after recruitment maneuvers (RMs) although has not been studied in clinical setting. We designed this study to assess effects of PEEP selected by best respiratory compliance (Crs) after RMs on respiratory function, supportive therapies requirements (including vasopressors, needing for sedation or neuromuscular blockade), urine output, fluid balance and incidence of barotrauma.

METHODS. We retrospectively analysed data of 40 consecutive patients with bilateral infiltrates and acute hypoxemia (PEEP ≥ 10 cmH2O and inspiratory oxygen fraction (FiO2) ≥ 0.6), whom were ventilated with open lung strategy. A stepwise RM was applied consisting of 3-min steps of tidal ventilation with fixed 15-cmH2O pressure control and progressive PEEP levels (16, 20, 24, 28, 32 and 36 cmH2O). The post-RM PEEP was selected evaluating the change in Crs as PEEP was decreased. Patients were ventilated on pressure control mode. Data were recorded at baseline, after RM and 96 following hours.

RESULTS. After RM, Crs increased from 24.42 ± 8.14 to 32.82 ± 11.31 ml/cmH2O ($p < 0.0001$) and changes in ventilatory parameters extended to 96 hrs (table 1). There was no increase in supportive therapies requirements, fluid balance and urine output (p: n.s.). Three patients (7.5%) had radiographic evidence of barotrauma after one RM. There were no differences between patients with pneumonia and other causes for respiratory failure (p: n.s.).

TABLE 1.

	Before RM	After RM	Day 1	Day 2	Day 3	Day 4
Tidal volume	501±128	453±108*	465±100	463±93	484±94	492±90
PEEP	12.6±3.1	19.17±3*	18.7±3.1*	18.1±2.7*	17±3.1*†	16.3±3.3*†
Peak Pressure	33.9±5.5	33.6±4.2	33.2±4.6	32.7±4.6	31.2±4.6*†	31±5.8*†
Presset Pres.	21.3±4.5	14.5±3.2*	14.5±3.4*	14.5±4*	14.1±4*	14.7±4.5*
FiO2	0.8±0.16	0.59±0.16*	0.55±0.12*	0.51±0.11*	0.5±0.16*†	0.49±0.15*†

**p < 0.05 compared with BeforeRM.. † p < 0.05 compared with AfterRM.*

CONCLUSION. PEEP selected by best Crs preserved effects of RMs on respiratory function without increasing supportive therapies requirements nor rate of barotrauma.

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061

CHANGES IN PAO2/FIO2 AND SHUNT RATIOS DURING O2 TREATMENT OF ACUTE LUNG INJURY CAUSED BY PHOSGENE

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INTRODUCTION. Phosgene is a common chemical widely used in the plastics manufacturing industry and with the potential for warfare use. Using a previously described pig model(1) the changes in the oxygen index (PaO_2/FiO_2) and oxygen shunt (Qs:Qt) following treatment with various concentrations of oxygen over time was studied.

METHODS. 30 pigs were terminally anaesthetised, instrumented and entered into the study. They were exposed to phosgene (Ct 2430 mg.min.m-3). Intermittent positive pressure ventilation was started 30 min post exposure – tidal volume 10ml/kg, respiratory rate 20 breaths/min with 3 cm of PEEP. Pigs were randomly placed in the following groups: group 1. FiO2 0.24, 2. FiO2 0.80 started immediately; group 3 at 6 h; group 4 FiO2 0.40 at 6h and group 5 FiO2 0.40 at 12 h. Pigs were studied for up to 24 hours with physiological parameters taken throughout.

RESULTS. All pigs from groups 3,4 and 5 survived to 24 hrs compared to 30% from group 1 ($p<0.05$). In group 2 one pig died at 23 h and another showed severe cardiorespiratory derangement. Significant improvement in PaO2/FiO2 ratio was only seen in group 3 animals. All oxygen treatment groups showed decreased Qs:Qt ratio when compared to Group 1 animals. Pigs in groups 3,4 and 5 had significantly lower lung wet weight/body weight ratios compared to group 1 ($p<0.05$). Histologically all animals showed areas of neutrophilia, oedema and congestion. This was greater in groups 1 and 2. As reported previously(2) increasing the FiO2 resulted in an improved PaO2, in the case of Group 3 animals a significant improvement in the oxygen index and shunt was also noted. All treatment groups also showed a decreased mortality, except when high FiO2 is started immediately.

CONCLUSION. The results suggest that treatment with O_2 FiO2 of 0.8 when given at 6 hours post exposure was the most beneficial not only in maintaining PaO_2 but reducing oxygen shunt and increasing the oxygen index. This was reinforced by histological findings suggesting that giving high FiO2 early is detrimental in the treatment of inhaled phosgene.

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062

HIGH PEEP DURING OPEN LUNG VENTILATION DOES NOT INCREASE RIGHT VENTRICULAR AFTERLOAD

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INTRODUCTION. Open lung ventilation (OLV) has been associated with an increment of RV afterload due to the use of high PEEP levels. This ventilation strategy, however, did improve in a previous study, functional residual capacity and oxygenation after extubation in cardiac surgery patients1. To assess RV afterload, Doppler echocardiography can be used, allowing in- and expiratory measurements of a number of parameters which reflects right ventricular afterload2. We hypothesize that high PEEP levels during OLV do not increase right ventricular impedance during expiration.

METHODS. On 28 patients scheduled for cardiac surgery, two ventilation strategies were applied in a cross-over design; the sequence of the applied ventilation strategy was randomized by envelope. The CMV group was ventilated with a tidal volume of 6-8 ml/kg with 5 cm H2O PEEP. During OLV, recruitment maneuvers were applied until PaO2/FiO2 >50 kPa was achieved (reflecting an open lung) and maintained by the use of sufficient levels of PEEP. The OLV group was ventilated with low tidal volume of 4-6 ml/kg. Acceleration time (Acmean) of the pulmonary artery was measured with transesophageal echocardiography in a long axis view of the pulmonary artery during end-inspiration and end-expiration.

RESULTS. Acmean during expiration was comparable between groups. Acmean during inspiration was significantly higher in the OLV group compared to the CMV group. Inspiration caused a significant decrease in Acmean compared to expiration in the CMV group, but not in the OLV group. Total PEEP in the OLV group was 14+4 compared to 5+1 cm H2O in the CMV group.

CONCLUSION. High PEEP during OLV does not increase RV afterload during expiration in cardiac surgery patients. OLV with low tidal volume does decrease RV afterload during inspiration compared with conventional ventilation.

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063

THE RELATIONSHIP BETWEEN SOFA SCORE AND PROGNOSIS IN THE PATIENTS WITH SIVELESTAT

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INTRODUCTION. Sivelestat (SIV) is a inhibitor of neutrophil elastase, and has been reported to prevent the development of lung injury. Sequential organ failure assessment (SOFA) score is to describe quantitatively and as objectively as possible the degree of organ dysfunction/failure. The present study was carried out to assess SOFA scores in the patients diagnosed as acute lung injury (ALI)/ acute respiratory distress syndrome (ARDS) and administrated SIV, and to determine the relationship between the scores and the prognosis of the patients.

METHODS. The following information was obtained retrospectively from the medical chart of each patient: a) PaO2/FiO2 (P/F) ratio and SOFA score before and after SIV administration; b) prognosis. Group L included the patients whose SOFA score before SIV administration was 8 or lower, and group H included the patients whose SOFA score before SIV administration was 9 or higher. Statistical analyses were performed using Mann-Whitney U test, Wilcoxon signed-ranks test and Fisher's exact probability test, respectively.

RESULTS. P/F ratio was significantly improved after SIV administration in both groups. SOFA score was significantly improved after SIV administration in group L but not in group H. Mortality rate of group L (14%) was significantly lower than that of group H (67%).

TABLE 1.

SOFA score, P/F ratio and mortality in groups L and H.

	Group L (n=23)	Group H (=9)
SOFA score before SIV administration	5.3 +/- 1.5	11.4 +/- 1.9#
SOFA score after SIV administration	2.4 +/- 1.5$	9.4 +/- 5.0#
P/F ratio before SIV administration	151 +/- 48	140 +/- 53
P/F ratio after SIV administration	288 +/- 79$	262 +/- 110$
mortality(%)	14	67#

 # p< 0.01, compared with group L. $ p< 0.01, compared with before SIV ad.

CONCLUSION. SOFA score but not P/F ratio predicts the effectiveness of SIV in ALI/ARDS patients. SIV would be effective for the ALI/ARDS patients who had lower SOFA scores.

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HIGH-FREQUENCY OSCILLATORY VENTILATION IN PEDIATRIC PATIENTS WITH ACUTE RESPIRATORY FAILURE

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INTRODUCTION. High-frequency oscillatory ventilation (HFOV) is frequently used as rescue treatment of pediatric patients with acute respiratory failure (ARF). The aim of this study was to evaluate the effectiveness of HFOV in pediatric patients with ARF, failing conventional ventilation (CV).

METHODS. Twenty consecutive pediatric patients (ages 12 days to 5 years) with ARF and diffuse alveolar disease (pneumonia : 14; sepsis with acute respiratory distress syndrome : 3; severe upper airway obstruction with pulmonary oedema : 2; salicylate intoxication with acute respiratory distress syndrome : 1), failing CV (PaO2/FiO2 ratio of 62.6±13 mmHg, alveolar-arterial oxygen difference (P(A-a)O2) of 559±79.6 mmHg, Oxygenation index (OI) of 26.3±7.3) were managed with HFOV and prospectively evaluated. Mean length of CV, prior to instituting HFOV, was 24.7±13 hours. Seven patients had a severe pulmonary air leak prior to HFOV. ventilator settings, arterial blood gases, OI, P(A-a)O2 and PaO2 / FiO2 ratio were prospectively recorded prior to HFOV (0h) and at predetermined intervals throughout the course of the HFOV protocol and compared using the one-way Friedman rank-sum procedure and a two-tailed Wilcoxon matched-pairs test.

RESULTS. Nineteen patients (95 %) responded to HFOV. There was an overall improvement in gas exchange on HFOV. After one hour of HFOV, mean PaCO2 decreased from 70.7±41 to 41.5±10 mmHg (p=0.002) and remained within the target range thereafter. There was a significant increase in mean PaO2/FiO2 ratio as early as one hour (p = 0.003) and a significant decreases in P(A-a)O2 and OI as early as one and 4 hours, respectively (p= 0.001 for both). All these improvements were sustained during the first 12 hours of HFOV (p<0.05). One patient, who had evidence of pulmonary interstitial emphysema, prior to HFOV, developed pneumothorax on HFOV. No significant others complications associated with HFOV were detected. Fifteen patients (75%) survived to hospital discharge. Length of mechanical ventilation, HFOV and supplemental oxygenation in the survivals were 10±7 days, 8±5 days and 11±7 days, respectively. Among the 5 patients died, only one died from respiratory failure.

CONCLUSION. In pediatric patients with ARF, failing CV, HFOV improves gas exchange in a rapid and sustained fashion and provide a good outcome.

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NEGATIVE PRESSURE VENTILATION WITH THE CHAMBER ESPIRATOR IN 6 INTUBATED PATIENTS WITH ARDS

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INTRODUCTION. In patients with acute lung injury continuous negative pressure has been applied with cuirass and Poncho wrap systems during positive-pressure ventilation. In contrast to these devices tankrespirators are effective for ventilation but patient care is very limited as numerous lines and connections cannot be led out of a tankrespirator. Therefore, we constructed the chamberrespirator to apply continuous external negative pressure ventilation (CENPV) in critically ill adult patients and studied the effects and the practicability of the device in a pilot study.

METHODS. The pyramidal chamber consists of transparent acrylic glass. Gull-wing doors at both sides and one at the head side enable rapid access to the patient who is placed completely inside the chamber. Three outlets at each side and two at the top enable rapid introduction of respiratory circuits, central venous, arterial and other lines, ECG, pulseoxymetry, urine catheters, wound drainages and connections to chest tubes and various devices. CENPV was combined with pressure support ventilation (PSV) triggered by CENPV. We gained first clinical experiences on the applicability and efficiency of the chamberrespirator in 6 ARDS-patients. CENPV in combination with PSV was compared to continuous positive pressure ventilation (CPPV) in each patient using equivalent treatment time intervals.

RESULTS. The chamberrespirator was used 51 times for a total time of 356 h. The device was applied in 1 to 18 intervals for a total time of 7 to 133 h in each patient. During CENPV the median chamber pressures varied between -28 and -35 cmH2O at inspiration and between -14 and -19 cmH2O at expiration. Median positive airway pressures applied in addition to CENPV varied from 10 to 21 cmH2O at inspiration and from 0 to 14 cmH2O at expiration. These values were lower compared to the plateau pressures (30 to 41 cmH2O, p<0.05) and PEEP-values (16 to 23 cmH2O, p<0.05) during CPPV. In 5 patients the mean interval paO2/FiO2-values improved in all 43 applications of the chamber-respirator compared to the prior CPPV-interval. The median paO2/FiO2-values improved 39 to 95 mmHg (p<0.05 in 4 patients). After changing from CENPV to CPPV the paO2/FiO2-values decreased in 42 of 51 applications.

CONCLUSION. The chamberrespirator enabled to apply efficiently CENPV in intubated ARDS-patients during routine intensive care. These first clinical experiences provide the basis for controlled studies on CENPV in ARDS-patients.

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SELECTIVE RECRUITMENT OF A LOBE COLLAPSE IS EFFECTIVE AND HAS NO CIRCULATORY SIDE EFFECTS

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INTRODUCTION. Left lower lobe atelectasis is common after cardiac surgery. Lung recruitment maneuvers (LRM) may be used to inflate the atelectasis and improve PaO2. However, this patient category may not tolerate the circulatory depression caused by a general LRM. We hypothesized that a selective LRM (S-LRM)of the affected lobe would improve PaO2 equally well as a general LRM (G-LRM) but only have minimal circulatory side-effects.

METHODS. 10 anesthetized pigs were tracheotomized and ventilated with VCV, FiO2 1.0, PEEP 10 cmH2O, VT 8ml/kg. A bronchial blocker (BB)was inserted in the right lower lobe by the use of a bronchoscope and the cuff was inflated and the air of the isolated lobe exsufflated and measured ("lobe volume"). Thereafter the lobe was selectively lavaged (with a "lobe volume" of 37C 0.9% NaCl) 15 times. The inner lumen of the BB was connected to -10 cmH2O pressure. The pigs were randomized into 2 orders of LRMs (40 cmH2O,30 s); either 1st, a S-LRM, in which the isolated lobe was inflated via the inner lumen of the BB (with the cuff of the BB inflated) and 2nd, after the lobe had again been deflated, a G-LRM via the ET-tube with the cuff of the BB deflated, or vice versa. Before and after each procedure end-expiratory lung volume (EELV), Crs (compliance), blood gases,shunt,left ventricular end-diastolic area (LVEDA), cardiac output (PiCCO) and vascular pressures were obtained. Statistics:Wilcoxon.

RESULTS. The changes in the variables (mean±SD) by the LRMs are indicated as + = increase, - = decrease. EELV, PaO2 and shunt are obtained 3 min after the LRM while MAP, CO and LVEDV at the end of theLRM. * p < 0.05 compared with baseline, § <0.05 S compared with G. S-LRM vs G-LRM: EELV (ml) 99±47 * vs. 120±56 *, Crs (ml/cmH2O) 6±3 * § vs. 11±3 *, PaO2 (kPa) 19±14 * vs. 17±12 *, Shunt (%) -8±6 vs. -6±8, MAP (mmHg) 0±4 § vs. -33±11*, CO (L/min) 0±0.5 § vs. -2.0±0.7 *, LVEDA (cm2) -0.5±1.2 § vs. -4.3±1.4 *.

CONCLUSION. A selective recruitment of a collapsed lobe is in this model as effective as a general LRM, but has no circulatory side-effects.

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067

DOES CLAMPING OF THE ENDOTRACHEAL TUBE PRESERVE PEEP LEVELS?

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INTRODUCTION. When the patient is disconnected from the ventilator the positive end expiratory pressure (PEEP) is lost and there is a risk of lung collapse. Clamping of the endotracheal tube are sometimes used to preserve PEEP levels and to avoid loss of lung volume. Routines and implementation of clamping varies between hospitals and within hospitals, and depends on the managing staff. The aim of the study was to investigate the effects of clamping and whether the clamping should be made at end-inspiratory or end-expiratory.

METHODS. In six anaesthetised pigs the endotracheal tube was clamped with a surgical forcep and the ventilator was disconnected for 15 seconds. Measurements were done both at end-expiratory and end-inspiratory at three PEEP levels, +5, +10 and +15 cm H2O. Monitoring of tracheal pressures, hemodynamics and lungmechanics were done during clamping. End-expiratory lung volume (EELV) was measured in three pigs with N2 washout/washin technique.

RESULTS. It could be seen from the tracheal pressure measurements that there was a reduction of PEEP level and high peak pressure when the ventilator was reconnected to the endotracheal tube after clamping. This was dependent on when in the breathing cycle the reconnection appeared. The mean arterial pressure (MAP), at a PEEP level of 15 cm H2O, decreased from 59±3 to 56±2 mmHg during inspiratory clamping and was unchanged during expiratory clamping, 60±3 mmHg (p=0.02). The mean pulmonary arterial pressure (MPAP) increased from 23±2 to 28±2 mmHg during inspiratory clamping and was unchanged during expiratory clamping 22±2 mmHg (p<0.001). Resistance and compliance did not change by the clamping procedure. The EELV increased with increasing PEEP; 5 cm H2O 602±95 mL, 10 cm H2O 757±116 mL and 15 cm H2O 1024±85 mL (p<0.001), but was not affected by the clamping procedure.

CONCLUSION. Clamping of the endotracheal tube should preferable be done end-expiratory, since clamping end-inspiratory resulted in significant changes in pulmonary and systemic blood pressures. However, clamping can not guarantee a maintained PEEP level.

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IS CORRECT TO SET THE TIDAL VOLUME ON THE IDEAL BODY WEIGHT?

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INTRODUCTION. The tidal volume during mechanical ventilation in ALI/ARDS patients is usually set based on the ideal body weight (1). The "rationale" should be a good correlation between the ideal body weight and the volume - weight of the lung. It has been suggested that by maintaining a tidal volume between 6-8 ml/Kg the lung stress / strain should be reduced.We evaluated the relationship between the ideal body weight and the degree of lung inflation during controlled mechanical ventilation.

METHODS. 39 intubated, sedated and paralyzed ALI/ARDS patients (mean age 56±18 years, body mass index 23.5±3.5 Kg/m^2, PaO2/FiO2 191±80 mmHg, PEEP 11.7±3.2 cmH2O, tidal volume 571±149 ml resulting in a tidal volume per body weight of 8.9±1.9 ml/Kg) were studied A lung CT scan was performed during an end expiratory pause at 5 cmH2O of PEEP (140 mA, 120 Kv). The lung was manually drawn and the quantitative analysis to asses the volume – weight of the lung was made using dedicated software (Softefilm, University of Milan, Italy).

RESULTS. We did not find any relationship between the ideal body weight and the inflated lung volumes (p<0.001, r=0.12).

CONCLUSION. This might explain the contradictory results obtained by the most recently clinical trials which evaluated the possible benefits of a low tidal volume ventilation strategy.

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069

SEVERE HYPOXEMIA IN MECHANICALLY VENTILATED PATIENTS. IS EXTRACORPOREAL MEMBRANE OXYGENATION MANDATORY?

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INTRODUCTION. The prognosis of patients with severe hypoxemia is controversial. Some authors report a mortality of > 80%, which has led some centres to propose non-conventional treatments such as extracorporeal membrane oxygenation (ECMO).

OBJETIVE: To analyse the prognosis of patients with severe and sustained hypoxemia who meet the criteria usually accepted for the application of ECMO.

METHODS. Prospective observational study of all consecutive patients requiring mechanical ventilation in a neurotrauma intensive care unit during a 12-month period and who fulfilled ECMO criteria under optimal treatment, summarized as: 1) fast-entry criterion: Po2/fio2 below 50 for > 2 h; 2) slow-entry criterion: Po2/fio2 below 150 for more than 12 h. Further inclusion criteria were lung compliance below 30 ml/cmH2O, age below 60 years and absence of advanced multiple organ failure and terminal disease.

RESULTS. Out of 254 patients requiring mechanical ventilation from 1/11/2003 to 31/10/2004, 13 met slow-entry criteria and four of these also met fast-entry criteria for ECMO application. The duration of severe hypoxemia was 159+113h in patients with slow-entry criteria and 3, 4, 4 and 12h, respectively, in patients with fast-entry criteria. Four patients died, 30% of the total. The mean age of the survivors was 34.1 years, with a mean duration on mechanical ventilation of 33 days and mean ICU length of stay of 44.2 days.

CONCLUSION. The mortality of patients who meet ECMO criteria is lower than previously reported and does not justify the application of non-convencional treatments.

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070

THERE IS A NEED OF EARLY LUNG RECRUITMENT AFTER ENDOTRACHEAL SUCTION

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INTRODUCTION. Patients mechanically ventilated need to have mucus cleared by suction but this can negatively affect lung function. To limit the risk of complications a post-suction recruitment manoeuvre (PS-RM) was investigated in an experimental animal model. Our hypothesis is that suction induces lung volume loss which results in gas exchange impairments, and a PS-RM prevents these side effects.

METHODS. Healthy pigs were anaesthetised, ventilated in pressure controlled ventilation with a PEEP of 3 cmH_2O and pressure level set to achieve tidal volume 14 mL kg^{-1}. Open endotracheal suction followed by a PS-RM at 1 and 120 minutes were compared (n=5). Measurements were obtained before suction, before and after PS-RM. PS-RM comprised of an increase of airway pressure to 15 cmH_2O above inspiratory pressure for 10 sec. Lung volume was measured with nitrogen washout/washin method (n=4).

RESULTS. Open endotracheal suction caused decrease of lung volume from 617±104 to 511±190mL (p<0.05) and increased by PS-RM at 1 minute to 579±57 mL. In the 120 minutes period, suction decreased lung volume from 561±124 to 495±110 mL (p<0.05) and was increased by PS-RM to 547±117 mL. Suction induced gas exchange impairment that was restored by PS-RM at 1 minute, but not at 120 minutes. See Table 1.

TABLE 1.
Post-suction recruitment manoeuvre (PS-RM) at 1 and 120 minutes after suction.

	before suct.	1 minute before PS-RM	after PS-RM	before suct.	120 minutes before PS-RM	after PS-RM
Crs mL/cmH2	29 ± 5	23 ± 4*	28 ± 5	28 ± 6	20 ± 4*	25 ± 4*
VT mL	354 ± 52	310 ± 62	354 ± 65	356 ± 48	282 ± 41*	344 ± 30
$ETCO_2$	5.1 ± 0.2	5.4 ± 0.2	4.8 ± 0.2	4.8 ± 0.3	6.8 ± 1.1*	6.0 ± 0.8*

*Mean SD *different from before suction ANOVA p<0.05*

CONCLUSION. These findings indicate that endotracheal suction induces lung volume loss and gas exchange impairment that can be restored by PS-RM immediately after suction.

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IMPACT OF A STUDY ON MECHANICAL VENTILATION WITH PEEP ON CLINICAL PRACTICE IN ARDS PATIENTS

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INTRODUCTION. As our Unit participates to a clinical trial on mechanical ventilation comparing high and classical level of PEEP (ExPress), we assess the impact of this trial on the practice of mechanical ventilation in ARDS patients

METHODS. from 01/01/2003 to 01/01/2005, patients who were not included in ExPress study were collected in screen log. Using clinical charts, we retrospectively recorded the maximal and minimal tidal volume and respiratory rate and the maximal FiO2 and PEEP. The study population was separated in two periods that were compared using t-test + Fisher's exact test and Kruskal-wallis test. A $p < 0.05$ was considered significant.

RESULTS. 60 patients were included. Non inclusion criteria in ExPress study were : low hope of survival (n=17), inclusion in another trial (n=10), a missed inclusion (n=10), discreepancy in family members (n=8), pneumothorax (n=8), liver disease Child C (n=4), cardiogenic edema (n=1), pregnancy (n=1), Guillain-Barré syndrome (n=1). Sex ratio, age, SAPS II, ODIN score and mortality rate were similar. Table shows the main results

TABLE 1.

	1st period (n=30)	2nd period (n = 30)	p
PaO2/FiO2	118 [42-230]	111 [54-271]	0.47
PEEPmax	8 [2-16]	7 [3-15]	0.74
Vtmin (IBW)	7.3 [5.5-11]	5.1[5.3-9.9]	0.20
Vtmax (IBW)	8.6 [6.8-11.2]	8.0 [6.0-11.2]	0.10
Vtmin (weight)	6.3 [4.8-8.0]	5.6 [4.2-7.2]	0.03
Vtmax (weight)	7.5 [5.3-9.0]	6.6 [4.7-8.5]	0.03
FRmin 14	[11-20]	16 [12-22]	0.01
Frmax 20	[15-30]	24 [17-33]	0.02

CONCLUSION. ExPress study led us to increase respiratory rate and decrease tidal volume measured according to actual weight. Despite an evident impact, our practice should be improved in measuring tidal volume using IBW based on patient's height.

072

RELATIONSHIP BETWEEN COMPLIANCE CURVE AND COMPUTED TOMOGRAPHY IN ACUTE RESPIRATORY FAILURE

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INTRODUCTION. Computed tomography (CT) in acute respiratory distress syndrome (ARDS) does not always show uniform finding in spite of its simple difinition of chest radiograph. We examined the relationship between the morphological pattern of CT and property of compliance curve in ARDS.

METHODS. We examined chest CT and static pressure volume (P-V) distribution in 22 ARDS pts in the last four years. P-V distribution?was measured just after tracheal intubation with muscle relaxant. Under controlled ventilation, respiratory freqency was set at six per minute and inspiratory time was set over four second in order to ensure sufficient plateau time. We got scattergram of plateau pressure and volume by changing tidal volume every 100 to 200 ml. Static compliance curve was induced by differentialtion of the P-V curve led by polynomial approximation of scattergram of plateau pressure and tidal volume. We compared compliance at zero cmH2O (C0), maximal compliance (Cmax) and pressure at Cmax (Pcmax) between the three morphological patterns (diffuse, patchy and back) of CT.

RESULTS. C0 in diffuse group was lowest and C0 in back group(28.2±18.7ml/cmH2O) was higher than other two groups. Pcmax in diffuse group was one and a half times higher than that in back group (p=0.008). There was no difference between Cmax of each group.

TABLE 1.

CT and compliance

	C0 (ml/cmH2O)	Pcmax (cmH2O)	Cmax (ml/cmH2O)
diffuse	5.5±15.0	23.1±4.8	43.6±16.9
patchy	6.3±22.7	20.9±4.9	55.3±21.8
back	28.2±18.7	14.5±4.5	56.0±22.0
p	0.058	0.008	0.420

CONCLUSION. Elastic property of respiratory system in ARDS vary depend upon the morphological pattern of CT. The patients with diffuse attenuation may need aggressive PEEP, On the other hand, patients with infiltration in dependent lung should be treated in prone position in stead of high PEEP.

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COBATRICE SURVEY OF PATIENTS AND RELATIVES IN INTENSIVE CARE MEDICINE

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INTRODUCTION. CoBaTrICE (Competency Based Training in Intensive Care Medicine in Europe) is a project aimed at developing an internationally accepted minimum standard of competency (knowledge, skills and attitudes) for specialists in Intensive Care Medicine. As part of the project, a postal survey was carried out to harness patients' and relatives' views on what competencies a doctor in Intensive Care should possess.

METHODS. A postal survey by self-completion questionnaire was carried out in seven European countries: the Czech Republic, Denmark, Italy, the Netherlands, Poland, Spain and Switzerland. Respondents were asked to rate twenty-one discreet competencies.

RESULTS. 1086 responses were obtained. Formal response rates could not be calculated and the eventual sample was dominated by strong responses from Spain (22% of all responses), Italy (21%)and Poland (19%). 66% of respondents were relatives, and 55% were women. Competencies most frequently rated 'essential' or 'very important' were: decisiveness (99%), clinical knowledge (99%) and ability to act calmly (98%). Competencies most frequently rated 'not so important' or 'not important' included: finding out what patients think and feel (34%), giving patients full information (32%) and involving patients in decisions (29%). Patients were more inclined than relatives to describe fully informing patients ($p<.02$), involving patients in decision-making ($p<.01$) and explaining in ways patients can understand ($p<.02$), as essential. Relatives were more inclined to see giving bad news in a caring way ($p<.02$), and treating patients as individuals ($p<.01$) as essential competencies. Women were more likely than men to describe giving patients the opportunity to ask questions ($p<.01$), discussing fears and anxieties ($p<.01$), and involving patients and relatives in decisions ($p<.01$), as essentail. The data furthermore suggested regional differences in the weight patients and relatives ascribe to competecies relating to information giving and patient involvement in decision-making.

CONCLUSION. Patients and relatives find ICU doctors' clinical competence more important than behavioural and communication competencies. However, this survey showed significant variation in the response from patients and relatives, and differences across gender and geographic regions.

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074

PROLONGED MECHANICAL VENTILATION PATIENTS: MORTALITY AND QUALITY OF LIFE IN 6 MONTHS FOLLOW-UP

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INTRODUCTION. Patients requiring 14 or more days of mechanical ventilation consume lots of resources.We used to focus on ICU or in-hospital mortality but we do not know how our patients do after hospital discharge. Mortality and quality of life after 6 months of ICU discharge are studied.

METHODS. During 3 years, we analyzed all the patients requiring 14 or more days of mechanical ventilation in a 8-beds polyvalent ICU of a teaching hospital without cardiac surgery and neurosurgical wards. We assessed in-ICU,in-hospital and 6-months mortality. In survivors, we formulated, by telephone call, a validated quality-of-life questionnaire, EQ-5D (EuroQol five-dimension), Spanish version. 3 levels of severity were differentiated (1: no problems; 2: moderate problems; 3: extreme problems) in 5 variables: mobility, self-care, usual activities, pain/discomfort and anxiety/depression.

RESULTS. 1414 patients were admitted from 1st January 2001 to 31st December 2003; 40 patients (64+/-14 yrs, 67%M, APACHE II 25.5+/-8.6) were admitted for 14 or more days. 14 patients(35%) died in the ICU and 6 before hospital discharge. After 6 months, 4 more patients had died and 1 was not found. The resulting 15 patients (9M) answered the EQ-5D questionnaire (see Table 1). Of those 15 patients, 8 were medical, 5 were surgical and 2 were multiple trauma. No differences between gender or age. Surgical and multiple trauma patients were more likely to have disability.

TABLE 1.

	Level 1 no problems	Level 2 moderate problems	Level 3 extreme problems
Mobility	11(73.3%)	4(26.7%)	0
Self-care	10(66.7%)	3(20%)	2(13.3%)
Usual activities	10(66.7%)	3(20%)	2(13.3%)
Pain/discomfort	9(60%)	5(33.3%)	1(6.7%)
Anxiety/depression	7(46.7%)	6(40%)	2(13.3%)

CONCLUSION. Mortality was as expected according to APACHE values and the results of other series. Quality of life after six months was acceptable. More than 50% had anxiety or depression after 6 months discharge. Psychological support should be provided in these kind of patients.

075

ARE WE ABLE TO PREDICT THE QUALITY OF LIFE 1 YEAR AFTER ICU ?- PRELIMINARY RESULTS

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INTRODUCTION. Research on the outcome of critically ills was mainly focused on mortality. However patients are more concerned about their future quality of life (QOL). Caregivers are often asked by patients or their families to describe how their QOL would be. This question is central in the decision making. We tested the ability of patients, families, nurses and physicians to predict the QOL of the patient after 1 year.

METHODS. We included all adults admitted to our surgical ICU, who stayed >36h in the unit and consented to participate. We collected patient's demographic, admission data and the QOL before ICU measured by the Euro-QOL visual analogue scale (EQ-VAS). This is a scale from 0-100 anchored at one end by 0 (worst imaginable QOL) and at the other end by 100 (best imaginable QOL). At ICU discharge we asked the patient, the family, the attending nurse and the senior physician, to predict the EQ-VAS of the patient at 1 year after ICU. After 1 year we re-contacted the patient to obtain his actual EQ-VAS.

RESULTS. From 10/2002 to 11/2003 we included 283/1400 patients. We analyzed 208 patients (33 died, 5 could not and 32 refused to respond). The mean (SD) age was 55 (18), 67% were males. Causes of admission were 41% cardiovascular, 22% trauma, 17% gastrointestinal , 11% neurosurgical and 9% miscellaneous. ICU length of stay was 3d (median). They were mechanically ventilated 5.3h (median). Patients had a mean (SD) EQ-VAS of 71 (26) before ICU admission and 72 (20) (p=NS) at 1 year after ICU. The interclass correlations between the EQ-VAS at 1 year and the prediction by the patient (0.212), the family (0.217) and the nurse (0.256) were bad, and even worse by physicians (0.105). The agreement (by Bland and Altmann) between the EQ-VAS at 1 year and the predictions by the patient, nurses and physicians was poor (-7±47,-3±49,+3±53 respectively), slightly better by families (-4±23). Correlations and agreements were not significantly affected by types of diagnosis or degrees of QOL at 1 year.

CONCLUSION. Correlations between measured and predicted QOL were bad. Agreements showed a great dispersion. The ability of caregivers a well as of families or the patient himself to predict the QOL at 1 year after ICU was poor. Caregivers should be very careful when informing patients or families about the expected future QOL of patients or when they try to integrate this dimension in therapeutic decisions.

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076

SEVERE SEPSIS IS ASSOCIATED WITH CHANGES IN HEALTH RELATED QUALITY OF LIFE

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INTRODUCTION. Despite ongoing searches to improve treatment modalities severe sepsis remains a leading cause of death in ICU patients. Although patients may survive sepsis, health related quality of life (HRQOL) may remain impaired. We hypothesized that severe sepsis and intensive care (IC) treatment result in long-term impairment of HRQOL.

METHODS. We performed a prospective study in patients with severe sepsis admitted to a 10-bed mixed IC unit. Patients were included if they met predefined criteria of severe sepsis and were admitted to the IC unit for >48 hours.The SF-36, a generic instrument for measuring HRQOL in eight dimensions was used. Patients or proxies completed the SF-36 in the first 48 hours of admission [1]. Patients completed the SF-36 at IC and hospital discharge, and 3 and 6 months after IC discharge. Demographic data and severity of illness were obtained. Statistical comparisons were done with t-tests and multivariate analysis of variance.

RESULTS. Data from 95 out of the 170 patients with severe sepsis could be evaluated 6 months after IC discharge. HRQOL changed significantly over time in all dimensions of the SF-36 (P<0.05). A distinct pattern of a sharp decline during IC treatment and gradual improvement at six months after IC discharge was found. However average scores at 6 months compared with baseline were significantly lower in the physical functioning and general health dimensions (P<0.05). Average SF-36 scores of survivors of severe sepsis were lower in six of the eight dimensions six months after IC discharge compared to a normal population (all P <0.05). Interestingly, the pre-admission HRQOL of severe sepsis survivors was already lower in three of the eight dimensions when compared to HRQOL in the normal population (all P < 0.01).

CONCLUSION. HRQOL showed a sharp decline during IC treatment and gradual improvement at six months after IC discharge. Average scores at six months compared with baseline were significantly lower in the physical functioning and general health dimensions. Pre-admission HRQOL was already lower in severe sepsis survivors than in the normal population.

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077

UNSUCCESSFUL INTENSIVE INSULIN THERAPY IS NOT ASSOCIATED WITH CHANGES IN QUALITY OF LIFE

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INTRODUCTION. Recent data showed that intensive insulin therapy (IIT) improved the mortality and morbidity in post-operative intensive care (IC)-patients. IIT, bears the risk of hypoglycaemia, which might be associated with a decreased health related quality of life (HRQOL). We determined the influence of increased hypoglycaemia on HRQOL.

METHODS. All measured blood glucose values (BGs) in all patients admitted >48 hours to a 10-bed mixed IC from 2001 – 2003 were retrospectively collected. (Severe) hypoglycemia was defined as BG < 2.2 mmol/ and < 4.4 mmol/l, respectively. Patient data were divided in two groups: „successful IIT" group: patients with >75% of BGs in normal range, and no (severe) hypoglycemia at any time during IIT; „unsuccessful IIT" group: patients that did not fulfill the former criteria. HRQOL was assessed using the Short-Form (SF)-36. Patients or proxies completed this questionnaire in the first 48 hours of admission [1]. Surviving patients completed the SF-36 also at 6 months after IC-discharge.

RESULTS. For all years, approximately 19000 BGs were collected in 331 patients. Mean BG was 6,9 ± 1,5 mmol/l in the successful group and 8,7 ± 3,2 mmol/l in the unsuccessfull group. In the successful group, the percentage of patients with severe hypoglycemia and hypoglycemia was 3,3% and 31%, respectively. In the first group, scores in the physical functioning (mean 74) and general health (mean 61) domains decreased in the 6 month evaluation period (mean 51; P = 0,003 and mean 38; P<0,001, respectively). No changes were found in the role physical, vitality, pain, social functioning, role emotional; and mental health domains. In the unsuccessful IIT group, scores in the physical functioning (mean 67), role physical (mean 60) and general health (mean 58) domains decreased in the same period to mean 54; P < 0,001, mean 39; P < 0,001, and mean 48 ; P < 0,001, respectively. No changes were observed in the vitality, pain, social functioning, role emotional and mental health domains. No differences between the groups could be demonstrated with respect to scores in the different HRQOL domains 6 months after ICU discharge.

CONCLUSION. HRQOL decreases after IC-treatment, particularly with respect to physical functioning and general health. This decrease was independent of successfulness of IIT.

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078

ELDERLY PATIENTS ADMITTED IN THE ICU–MORTALITY AND QUALITY OF LIFE AT SIX MONTHS

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INTRODUCTION. Elderly patients represent a growing amount of ICU admissions. This study aims to study mortality and HRQOL in patients older compared with those younger than 74 years.

METHODS. At 6 months after ICU discharge, EQ-5D instrument was applied. EQ-5D includes the report of problems in five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and a visual analogue scale (EQ VAS). Patients older than 74 years (OG) were compared with those between 18 and 44 years (YG) and with those between 45 and 74 years (MG), concerning background variables (age, gender, previous health state, categorized in healthy, with previous chronic non-disabling disease or with previous chronic disabling disease), ICU variables (admission diagnostic categories, APACHE II and length of ICU stay) and EQ-5D variables.

RESULTS. Between 1997 and 2001, 1230 patients were admitted from which 229(19%)were older than 74 years .In-hospital mortality in the OG was significantly higher (33%) than in the YG (20%) and MG (25%). Sixty-six survivors from the OG, 292 survivors from the MG and 145 survivors from the YG answered the questionnaire. An older age was significantly associated only with the presence of previous chronic disease. Older age was significantly associated with a higher APACHE II and with more admissions for non-scheduled surgery. Older age was significantly associated with the report of problems in all dimensions, except anxiety / depression, and with a lower EQ VAS. However, if survivors were analysed according to their previous health state, we found that, when comparing YG with MG and OG that were previously healthy or had previous chronic non-disabling diseases, significant differences could only be found on the mobility, self-care and usual activities dimensions. When comparing those that had previous chronic disabling diseases, significant differences could only be found on the usual activities and pain/discomfort dimensions.

CONCLUSION. Although exhibiting a significant higher mortality, after adjusted for previous health state, survivors with an older age reported significantly more problems only on the more physical dimensions. These reductions on their HRQOL may be more related with their previous health state rather than with their age or their capability of recovering from critical illness. These findings should encourage the admission of elderly patients into the ICU.

079

FOLLOW-UP OF CRITICALLY ILL PATIENTS AFTER INTENSIVE CARE UNIT DISCHARGE.

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INTRODUCTION. The traditional aim of Critical Care Medicine has been to reduce short-term mortality, but we don't usually know long-term outcome.Objetive:To assess the survival and health-related quality of life of critically ill patients after Intensive Care Unit(ICU) discharge.

METHODS. Prospective, descriptive study from March 1st 2004 to September 31th 2004 in a Medical-Surgical ICU of a tertiary referral hospital. We analyse epidemiological data, previous health state, diagnosis on admission, severity scores, survival and health-related quality of life using the EuroQol five-dimenssion (EQ5D) questionnaire.

RESULTS. Two hundred and thirty five patients(p.) were admitted to our ICU during the study period and one hundred and ten p. were discharged from hospital.Evaluation was not possible in 21 p(19.1%).Five p(4.8%) died after hospital discharge but before 6-months evaluation.The mean age was 52.6±16.7 years old and 63.6% (70 p) were male.APACHE II at ICU admission was 15.1±7.4.Main reasons for admission were: altered level of consciousness: 36 p(37.7%, acute respiratory failure: 24 p(21.8%), septic shock:11 p(10%), severe acute pancreatitis:2 p (1.8%), liver transplantation:21 p(19.1%) and others causes:16 p (14.5%).At 6 months after ICU discharge:59 p(70.23%) had no problems in walking about, 20 p(23.81%) had some problems in walking about and 5 p(6%) were confined to bed. Seventy one p(84.52%) had no problems with self-care.Fifty four p(64.28%) had no problems with performing their usual activities.Twelve p(14.26) had moderate-extreme pain or discomfort.Fifthteen p(17.9%) were moderately or extremely anxious or depressed and 23.8% of them were in treatment.Seventy three p(86.9%) claim to be better or the same than 6 months earlier.Five p(6.33%) were admitted to a chronic ill patients hospital.Twenty one p were actively working of 46 p that were actively working previously.

CONCLUSION. Our results about survival and heath-related quality of life at 6 months from ICU discharge confirm the experience reported in the literature. However, further studies must be made with more number of patients.

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080

PREDICTIVE FACTORS OF SHORT-TERM AND LONG-TERM MORTALITY IN (NON) PLANNED VERY ELDERLY PATIENTS ADMITTED TO AN INTENSIVE CARE UNIT

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INTRODUCTION. Few studies were undertaken to investigate the predictive factors of short-term and long-term outcomes of very elderly patients admitted at ICU. This may be partly due to the high risk of ICU or hospital mortality among these patients. The aim of this study is however to determine independent risk factors for short-term and long-term mortality in planned and non-planned very elderly ICU patients.

METHODS. In this retrospective observational cohort study we examined a patients aged 80 years and older, admitted, planned or non-planned, to a medical and surgical ICU during 1st of January 1997- 1st of December 2002 in a general tertiary university teaching hospital. Data were collected on physiological and laboratorial values derived from the first 24 hours after ICU admission. ICU and hospital mortality were recorded and survival or date of death was noted at censor date.

RESULTS. Planned (n=329) patients were compared to non-planned (n=249) patients younger, had more often a normal Glasgow Coma Scale (93% vs 61.9%, p<0.001), and received significantly less cardiopulmonary resuscitation during the first 24 hours before admission than the planned patients (18.5% vs 1.2%, p<0.001).
The ICU-mortality of non-planned patients was significantly higher (36.1% vs 10.6%, p<0.001), and the hospital mortality was also significantly higher in the planned versus the non-planned (18.1% vs 4.0%, p=0.003). However, the long-term mortality was not significantly different between planned and non-planned patients (7% vs 12.0%, p=0.335).
In the multivariate analysis were the Glasgow Coma Scale, the SAPS II score, the length of ICU stay, the lowest urine output over 8 hours, and the arterial blood oxygenation index independent risk factors for ICU mortality. Creatinin and haemoglobin were independent risk factors for hospital mortality, and a cerebrovascular event, length of ICU stay, albumin, creatinin and haemoglobin were independent risk factors for long-term survival.

CONCLUSION. Mortality in non-planned very elderly ICU patients is higher than in planned patients. Independent risk factors associated with ICU mortality, hospital mortality or long-term survival are different.

081

THE QUALITY OF LIFE AFTER PROLONGED ICU STAY

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INTRODUCTION. Despite morbidity correlates better with in-Intensive Care Unit (ICU) postoperative length of stay (PLOS) it does not allow to estimate the effects of cardiac operation on long term patient outcome and satisfaction (quality of life, QOL). Among the commonly used measures of long-term outcome is the Short Form-36 General Health Status Survey (SF-36). We used the SF-36 to evaluate the general health status of patients who had in-ICU PLOS.

METHODS. 2,183 consecutive adult patients who underwent cardiac surgery were analyzed. In-ICU PLOS was defined >5 days. The physical and mental functional health in PLOS patients was assessed using the SF-36 which includes a multi-item scale assessing eight health domains. The SF-36 was administered 12 months after the discharge from ICU. The original database of Italian standard population (normal people, Norms) was also analyzed in order to compare Norms to our cardiac surgical patients.

RESULTS. PLOS patients were 282/2183 (12.9%). The overall 30-day mortality was 3.9% (n =85), and 19.5% (55/282) was in PLOS group. One year mortality for PLOS patients was 1.8%. Age, left ventricular ejection fraction, myocardial infarction within 7 day from operation, and reoperation resulted associated with PLOS. Patients aged 55-64 (11.6%) had a SF-36 score similar to Norms. Patients aged 65-74 (43.4%) had higher values of SF-36 than Norms for physical and mental status. In the over 75' (44.8%) higher scores than Norms for all the SF-36 items were found. The SF-36 score adjusted for gender showed higher scores for PLOS male group than Norms. PLOS-female group had similar items to Norms.

CONCLUSION. QOL seems to be influenced by gender, as well as by age. Our findings suggest that differences of QOL related to sex are less important in patients over 75 years. Despite age is an independent risk factor, cardiac surgery can be performed in elderly with acceptable morbidity and mortality. Among patients currently referred for cardiac operation age does not appear to influence or limit the improvement in QOL. The elderly patient seems to benefit from improved functional status and QOL after surgical procedures than younger.

082

MORBIDITY, MORTALITY AND QUALITY OF LIFE OF ICU PATIENTS. PRELIMINARY RESULTS

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INTRODUCTION. Assessment of Quality of Life (QOL) is now accepted as a relevant measure of ICU outcome. The ideal outcome is that these patients will attain their previous or a similar QOL to a person of the same age, gender and medical condition. The aim of this study was to assess the long-term QOL before & 18 months after ICU discharge

METHODS. Prospective observational study using patient or close family member interviews before, 6, 12 & 18 months after ICU discharge in a 7-bed mixed ICU in a 700-bed university affiliated hospital. All 262 consecutive patients >18 yrs old admitted to the ICU for 2 yrs for >24 hrs were eligible. Age, gender, length of ICU stay (LOS), illness severity, mortality and death probability was recorded prospectively. Primary outcomes included 18 months survival, functional status and health-related QOL. Values are expressed as X±SD. Comparisons were performed using Wilcoxon test

RESULTS. Of 261 pts (M/F 182/79) LOS was 15.1±23 days, age 58.38±20.8 yrs and APACHE II score 18.61±8. LOS of the 80 non-survivors was 16.29±26.2 days, age 64.52±16.8 yrs and APACHE II score 24.72±5.8. LOS of the 181 survivors was 14.63±21.4 days, age 55.46±21.9 yrs and APACHE II score 15.91±7.4. Death probability was 28±0.23, ICU & hospital mortality was 30% & 5% respectively. Among the 149 pts who discharged from hospital 117 were available for follow-up. Sixty-seven pts completed the 18 months follow-up and responded the questionnaire. Pre-ICU QOL score was 2.95. Follow-up revealed no significant changes in the overall QOL score from 6 (5.34) to 18 months (4.91) (p=0.27). The subscales basic physiological activities BPA (p=0.0002), normal daily activities NDA (p<0.0001) & emotional state ES (p=0.002) showed a significant deterioration 6 months after ICU discharge. A sign. improvement was noted for the BPA (p=0.0078) & NDA (p<0.0001) from 6-18 months. No sign. improvement was noted for the subscale ES (p>0.99)

CONCLUSION. QOL score changes between preadmission & 18 months post ICU discharge showed that most survivors had regained most of their preadmission QOL status. Emotional domains seem to improve slowly. Further studies focusing on the effect of time on various domains of QOL are warranted

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083

OUTCOME OF LONG-TERM INTENSIVE CARE TREATMENT. EXPERIENCE OF A MEDICAL INTENSIVE CARE UNIT

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INTRODUCTION. Patients receiving long-term intensive care treatment are generally believed to have a poor outcome. However, data on outcome and rehabilitation of long-term intensive care patients are scarce.

METHODS. Patients discharged after more than 29 days of ICU treatment were followed by telephone interviews. Survival times and karnofsky indices (KI) were calculated from data acquired during interviews. Medical records were analysed for parameters reflecting the course of intensive care treatment.

RESULTS. From 1992 to 2002 84 patients (m 45; w 39; age 57 ± 16 years) had courses of more than 29 days (mean: 51 ± 23) of intensive care treatment. Most frequent diagoses were sepsis n= 14; pneumonia n=14; pancreatitis n=6; variceal haemorrhage n= 6; liver failure n=5. APACHE II score on admission was 24 ± 7. 59 Patients were on mechanical ventilation (MV) for 37±19 days, 24 patients received haemodialysis for 33±16 days, vasopressors were given to 53 patients for 40±23 days. 36 patients received 17±16 units of packed red blood cells. 24 patients (28,6%) died in the ICU. Of the survivors, 5 were lost to follow up. Of the remaining 55 patients, 15 (27%) died during the first 6 months after discharge, 23 (42%) patients were alive at 24 months. Functional status at 6 months to 1 year after discharge from ICU was obtained for 49 patients. KI was 59 ± 32, reflecting a 28-point decrease from an average of 87 ± 19 before admission. 15 patients had no decrease in KI and a median of survival of 24 months. ICU survivors had a significantly shorter duration of MV (p = 0,004) and a higher KI before admission (p = 0,014) than non-survivors. There was no significant difference in the analysed therapeutic interventions or initial APACHE II-scores. The only factor weakly correlated with deterioration of the KI was age on admission (Spearman rho corr. = 0,416; p = 0,002). Prevalence of chronic medical conditions before admission was similar for survivors and non-survivors and for those with a small or with a larger (>20 points) decline in KI.

CONCLUSION. Only age and functional status before admission had a detectable influence on outcome. There was functional impairment in many patients, a substantial number, however, were fully rehabilitated. Decisions concerning withdrawal of critical care treatment and medical futility should not be based on the duration of critical care therapy.

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HOSPITAL FOLLOW-UP OF CRITICALLY ILL PATIENTS AFTER INTENSIVE CARE UNIT (ICU) DISCHARGE.

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INTRODUCTION. The traditional goal of Intensive Care has been to decrease short-term mortality, but we don't frequently know long-term outcome. Objetive: to assess the hospital morbidity and mortality of critical care patients after ICU discharge.

METHODS. Prospective, descriptive study from March 1st 2004 to March 31th 2005 in a Medical-Surgical ICU of a tertiary referral hospital. We analyse epidemiological data, previous health state, diagnosis on admission, hospital complications and mortality after ICU discharge.

RESULTS. Three hundred and sixty nine patients (p.) were admitted to our ICU during the study period, 95 p. (25.7%) died in ICU. Two hundred and seventy four p. were discharged from ICU, the mean age was 52.8 ± 17.2 years old and 57.1% (156 p.) were male. The Acute Phisiology And Chronic Health Evaluation II (APACHE II) at ICU admission was 15.4± 6.9. Main diagnosis on admission were: altered level of consciousness: 81 p. (29%), acute respiratory failure: 66 p. (24%), septic shock: 31 p. (11%), multiorgan failure: 2 p. (7%), severe acute pancreatitis: 5 p. (2%), liver transplantation: 49 p. (18%) and others causes: 38 patients (14%). The mean length of ICU stay was 9.05 ± 10.6 days and the mean length of hospital stay was 31.3 ± 29.7.
Eighteen p. (6.6%) died in hospital. Expected mortality was 33.3 % (6 p). The causes of mortality were: neurological complications in 2 p., multiorgan failure in 2 p., shock in 3 p., respiratory complications in 5 p. and sepsis in 6 p. Several complications appeared during hospital stay after ICU discharge: shock in 9 p. (3.3%), acute respiratory failure in 20 p. (7.3%), neurological complications in 12 p. (4.4%), acute renal failure in 6 p. (2.2%), infection in 37 patients (13.5%), 9 p. presented mild infection. Twenty p. (7.3%) presented critically ill polineuropathy after ICU discharge. Thirty two patients needed rehabilitation. Fourteen p. (5.1%) were readmitted to ICU.

CONCLUSION. Our results about mortality confirm the experience reported by others. However, further studies must be made with more number of patients. Follow-up of patients discharged from the ICU is recommended to improve the quality of critical care practice performance.

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EPIDEMIOLOGY OF SEVERE SEPSIS AND SEPTIC SHOCK IN GERMANY – THE PROGRESS REGISTRY

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INTRODUCTION. Since sepsis is the major cause of multiorgan failure and death on non-coronary ICUs, surveillance of epidemiological data is important. The purpose of this study is to describe epidemiological data from Germany in comparison to other countries by using a registry.

METHODS. PROGRESS is an international internet-based sepsis registry. From Dec. 2002 until March 2005, patients with severe sepsis or septic shock were enrolled by 13 German hospitals and 260 hospitals worldwide.

RESULTS. In Germany, 1,436 patients with a median age of 66.0 (65.0, 67,0) have been enrolled into the study. 60.3% of the patients suffered from nosocomial infections. 10,457 patients, 62.0 (61.0, 62.0) years of age, have been entered into the register outside of Germany. In most cases (55.7%), the infection was community acquired.

TABLE 1.

	Germany	Global (without Germany)
APACHEII-Score	27.0 (26.0, 27.0)	22.0 (22.0, 22.0) *
SOFA-Score (1st day)	11 (10, 11)	9 (9, 9) *
Gram+ Infection	45.3% (42.7, 48.0)	30.4% (29.5, 31.3) *
Gram- Infection	35.4% (33.0, 38.0)	42.7% (41.8, 43.7) *
ICU mortality	37.7% (35.2, 40.2)	40.0% (39.1, 40.2)
Hospital mortality	43.8% (41.2, 46.4)	50.7% (49.7, 51.7) *
ICU LOS (days)	13.0 (13.0, 14.0)	9.0 (9.0, 9.0) *
Hospital LOS (days)	28.0 (27.0, 29.0)	18.0 (18.0, 19.0) *

*median or frequencies (95% confidence intervals), *: p<0.05, LOS: length of stay*

CONCLUSION. There are considerable differences in the type of underlying infection between the countries. Despite of a higher severity of illness in Germany, ICU mortality was not different to other countries. However, outside of Germany patients were released earlier from the ICU.

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OUTCOME OF CRITICALLY ILL "OLDEST OLD" PATIENTS (AGE ≥ 90 YEARS) ADMITTED IN THE ICU

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INTRODUCTION. As our population ages, the incidence of elderly patients necessitating admission to the ICU has been increasing. Our objective was to assess the outcome of 90 years) compared to younger≥critically ill oldest old patients (age patients.

METHODS. In a prospective cohort study performed in a general ICU of a tertiary care hospital in Athens, Greece we examined in hospital and ICU mortality and stay, demographics, comorbidity, complications in the oldest old (age ≥ 90 years) group of patients.

RESULTS. Of 5505 consecutive patients admitted to ICU, 60 (1.1%) were in the "oldest old" group (range 90-98 years). Their mean (SD) length of ICU and hospital stay was 5.3 (6.8) and 23.3 (35.7) days, respectively. ICU mortality was 20%. Total in-hospital mortality was 40%, compared to 8.9% (p=0.001) of younger patients. Of 24 oldest old patients who died, 22 (91.7%) died either in the ICU or in the ward within 30 days following ICU discharge.

CONCLUSION. All cause in-hospital mortality was higher in the oldest old group compared with younger patients. However, the mortality of our cohort of patients did not reach a figure that would make physicians, relatives and health care administrators to decide against ICU care in this population.

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AMINOGLYCOSIDE DOSING IN ICU-PATIENTS-VARIABILITY OF DISTRIBUTION - VOLUME AND SERUM CONCENTRATIONS

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INTRODUCTION. Key to a successful aminoglycoside therapy is a reliable achieved serum concentration within the therapeutic range. (6-10 mg/l) (1). There is a high risk of ineffective low or toxic high serum levels. Concentrations above 20 mg/l must be avoided strictly (2). Goal of our study, based on a pharmacokinetic controled aminoglycoside dosing regime, was to demonstrate the variability of distribution-volume and serum level calculated after a fixed single dose of Gentamycin.

METHODS. In altogether 1677 treatment days 331 ICU-patients received gentamycin according to the following pattern: After determing a base value (C1) patients were given 160 mg of gentamycin over a time course of 20 minutes. 10 minutes (C2) and 100 minutes (C3) after cessation of the infusion samples were taken (Enzym-Immunoassay EMIT, Dade-Behring, Analyser aca-star, Dade-Behring). We used a one-compartment model in order to calculate the volume of distribution, half-life and clearence from which the subsequent two-point dosage schedule was calculated (3). At a calculated time the fourth sample (C4) was drawn to control the target peak level.

RESULTS. Volume of distribution (Vd) after a single dose of 160 mg Gentamycin was calculated as 23,2 l (7,6 l SD; min. 6,9 l; max. 80,0 l). 68,5 % of cases were within desired range of concentration (serum level 7,7 mg/l; 2,3 mg/l SD). After individual calculated pharmacokinetic dosage 88,6 % of cases reached therapeutic levels (8,4 mg/l; 2,3 mg/l). There were no toxic levels of concentration.

CONCLUSION. The narrow therapeutical range limits the use of aminoglycosides for ICU-patients. Volume of distribution for Gentamycin varies strongly inter- and day to day intraindividual. While applying a fixed dosage scheme there is an increasing risk of ineffective low or toxic high concentrations. This pharmacokinetic controlled dosing regime has proven to achieve therapeutic concentrations reliably under avoidance of toxic serum levels.

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NEBULIZED AMPHOTERICIN B DOES NEITHER PREVENT TRACHEAL COLONIZATION WITH CANDIDA NOR CANDIDEMIA

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INTRODUCTION. Amphotericin B (Ampho B) is nebulized as part of selective digestive decontamination (SDD) to decrease fungal colonization and infection. Primary tracheobronchial and pulmonary infections with candida, however, are regarded as overdiagnosed entities.

METHODS. Approved by the ethical committee of the University of Münster a prospective observational study was conducted. Over 6 months, colonization and infections of surgical ICU patients were documented during routine microbiological monitoring (2x/week) in patients, who inhaled Ampho B desoxycholate. Then, Ampho B prophylaxis was abandoned, and data were collected in patients with SDD entering the ICU during the next 6 months (Control). P<0,05 was defined as statistically significant using Chi square tests.

RESULTS. 86 patients, in whom Ampho B was nebulized > 48hrs, and in whom at least 2 cultures of tracheal secretions were available, qualified for analysis in the Ampho B group versus 103 patients in the Control group. In 21% of the patients, who were begun on Ampho B (n=149), the drug was stopped for side effects (in 90% bronchospasm).

TABLE 1.

Parameters with/without amphotericin B

	Ampho B	Control	
Tracheobronchial candida (first vs. final culture)	45% vs. 36%	52% vs. 50%	Change ns. in both groups
Purulent tracheal secretion	28% (24/86 patients)	28% (29/103 patients)	ns.
Candida in tracheal secret. (purulent vs. clear)	92% vs. 44%	93% vs. 58%	p<0,05 in both groups
Systemic antimycotics	29% (25/86 patients)	14% (14/103 patients)	p<0,05
Candidemia	1% (1/86 patients)	1% (1/103 patients)	ns.

CONCLUSION. The presence of candida in the tracheobronchial tree may play a role in the development of purulent tracheobronchitis. Termination of routine nebulization of Ampho B did neither increase the incidence of tracheal candida nor the incidence of candidemia, while causing severe side effects. Routine nebulization of Ampho B can therefore not be recommended as part of the SDD concept.

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CONTROL OF MRSA ENDEMIA ADDING ORAL VANCOMYCIN TO SELECTIVE DIGESTIVE DECONTAMINATION

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INTRODUCTION. MRSA has become an epidemiological problem,its prevalence has increased worldwide as both a nosocomial and, more recently, a community-associated pathogen. The usual recommendations to control MRSA endemia have often failed. We describe the control of two MRSA endemias, adding oral vancomycin to usually administered selective digestive decontamination (SDD).

METHODS. During the first term of 2003 and at the end of 2004,a loud number of MRSA infections was detected in our ICU. The traditionally recommended methods were applied: hygiene, isolation, in order to reduce the spread of this pathogen. In spite of the aforementioned procedures, new cases of MRSA were identified. Trying to control the endemia, oral vancomycin (oropharynx 4% paste) was administered, added to SDD (gentamycin, colistin and amphotericin B) to all admitted patients.

RESULTS. With the introduction of oral vancomycine, the number of MRSA infections was reduced and finally disappeared. In the first period, vancomycin was given until two months after the last case of infection occurred. During the nine following months, only one new case was isolated.

TABLE 1.

MARS INFECTIONS

	January-03	February-03 Vancomycin	March-03 Vancomycin	Nov-2004	Dec-2004	Jan-2005 Vancomycin	Feb-2005 Vancomycin
Respiratory	3	5	1	2	4	3	1
Bacteremia	0	1	0	0	0	2	0
Others	0	0	0	1	1	0	0

CONCLUSION. The administration of oral vancomycin is effective in the control of MRSA endemia.
This administration is not associated with the apparition of antibiotic resistance.

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AMFOTERICIN B CONCENTRATIONS IN SERUM AND PERITONEAL FLUID OF ICU PATIENTS WITH CANDIDA PERITONITIS

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INTRODUCTION. The treatment of fungal infections has evolved from conventional amfotericin B (AmB) to recently developed antifungal drugs. Previously, AmB in combination with flucytosin was the first choice for all candida infections. However, studies concerning the treatment of candida peritonitis in critically ill patients with AmB are not available. The main reason not to treat with conventional AmB is the incidence of toxic effects, mainly renal failure. If it would be known what serum levels of AmB result in sufficient intraperitoneal levels, AmB treatment might be optimised. We studied the AmB levels in serum and peritoneal fluid.

METHODS. Consecutive patients with candida peritonitis, treated with AmB with or without flucytosin were included provided that abdominal drains were in situ. Both AmB and flucytosin were administered by continuous infusion over 24 hours. Serum and peritoneal fluid were simultaneously collected for analysis. AmB level was determined by HPLC. APACHE II score, SOFA score and outcome were recorded.

RESULTS. 12 patients were included. Serum AmB levels ranged from 0.10 to 0.52 mg/l, mean 0.21 mg/l. Peritoneal fluid amfotericin B levels were significant lower (p=0.001, Wilcoxon rank sum test) and ranged from 0.0 to 0.36 mg/l. Amfotericin B levels greater than zero in peritoneal fluid were found when serum levels were above 0.12 mg/l. The mean gradient from serum to peritoneal fluid was 0.13 mg/l. SOFA scores ranged from 1 to 17 but did not have a relation with serum AmB level. Peritoneal AmB levels were correlated with SOFA (r2=0.22). The serum to peritoneal gradient showed a weak correlation with SOFA.

CONCLUSION. Amfotericin B levels in peritoneal fluid during candida peritonitis are significantly lower compared to serum levels. To obtain levels in peritoneal fluid above the minimal inhibitory concentration (MIC) serum levels should exceed 0.50 mg/l.

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ORAL VANCOMYCIN TO REDUCE CARRIAGE OF AMOXICILLIN RESISTANT ENTEROCOCCI (ARE)

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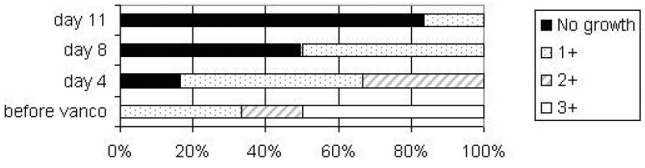
INTRODUCTION. ARE are low pathogens like other enterococci. However, it has been reported that ARE endemicity is associated with evolution to carriership of vancomycin resistant enterococci (VRE). ARE can be acquired by cross contamination in the ICU or other hospital wards. We investigated, during an ARE outbreak, if ARE carriage could be eliminated by gut decontaminating tract with oral vancomycin in a sticky paste and by nasogastric tube.

METHODS. Six ICU patients with identical strains of ARE were simultaneously treated with oral vancomycin 1 gr bid for 10 days. The ARE was susceptible for vancomycin by E-test. In addition, defaecation was actively promoted and patients were washed with chloorhexidin on the 2nd and 9th day of treatment. All disposable tubes (nasogastric, urinary, tracheal, drains) were changed on the second treatment day. Surveillance cultures for ARE and VRE were taken from throat/rectum, sputum, urine, wounds, drains and colo/ileostomies before treatment and on the 4th, 8th and 11th day.

RESULTS. VRE was not found before or after treatment with vancomycin. Figure shows percentage of patients with growth of ARE from throat and rectum.



CONCLUSION. In an increasing number of patients ARE decontamination was succesfully achieved by oral vancomycin over 10 days and VRE did not occur. Follow up is ongoing to determine whether elimination or suppression has ocurred.

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SERUM VANCOMYCIN LEVELS DURING ORAL VANCOMYCIN ARE RELATED TO SEVERITY OF DISEASE

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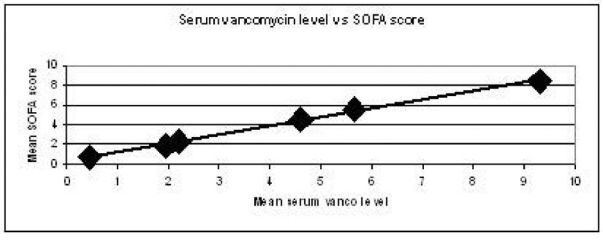
INTRODUCTION. Oral vancomycin (Va) is occasionally used for Clostridium infections or in gut decontamination in case of MRSA. Va is regarded to be not absorbed from the gut. However, critically ill patients may have increased gut permeability.

METHODS. Va was measured in serum in patients treated with oral Va 1 gr bid after 5 and 10 days.

RESULTS. In 6 patients (mean age 69 and mean APACHE II 25)mean serum Va levels were 4.3 mg/l (SD 3.9) at day 5 and 3.8 mg/l (SD 2.5) at day 10 (p=NS). Mean SOFA was 4 (SD 2.2) at day 5 and 2 (SD 1.3) at day 10. The mean Va level of day 5 and day 10 in each patient correlated well with the mean SOFA score of day 5 and day 10 in the same patient (r2=0.99).



CONCLUSION. Oral Va in ICU patients results in detectable serumlevels. Serum Va levels have a strong correlation with the SOFA score of each individual which probably represents enhanced gut permeability.

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OUTCOMES IN ICU PATIENTS WITH CLINICALLY DOCUMENTED/POSSIBLE FUNGAL INFECTION BY JAPANESE GUIDELINE

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INTRODUCTION. Japanese guidelines for the diagnosis and treatment of invasive fungal infections (IFIs) were established in 2003. According to these, clinically documented FIs (CDFIs) are diagnosed by more than 2 sites of colonization and positive serum beta-D glucan and possible FIs (PFIs) are diagnosed by one of them in critically ill febrile patients.

METHODS. The information of patients stayed in our ICU from 2000 to 2004 was investigated retrospectively by the database and documents. Between CDFIs and PFIs groups, age, gender, APACHEII score, diagnosis, length of ICU stay (LOIS), treatments, numbers of colonization sites (NOCS), beta-D glucan, administration of antifungal agents, ICU mortality were compared.

RESULTS. Twenty-five and 104 patients were diagnosed as CDFIs and PFIs, respectively. Twenty percent of the patients diagnosed as PFIs progressed to CDFIs during the stay. While 40% of PFIs patients were treated before 2003, 68% of them were treated with antifungal agents after 2003. The mean (±SD) score of APACHEII was higher in CDFIs group (22±8 vs 17±8, respectively; p=0.018). The LOIS was longer in CDFIs group (38±32 vs 25±23, respectively; p=0.003). The patients in CDFIs group were more frequently ventilated (88% vs 65%, respectively; p=0.027) and performed tracheotomy (32% vs 13%, respectively; p=0.027). The NOCS and beta-D glucan level were higher in CDFI group (3±1 vs 1±1, respectively; p<0.001 and 66.9±89.2 vs 33.4±82.1 pg/ml, respectively; p<0.001). Those in CDFIs group were more frequently treated with antifungal agents (84% vs 47%, respectively; p<0.001). There was no difference in ICU mortality between the two groups. The shorter LOIS and utilization of ventilator and continuous hemodiafiltration were risk factors of death after adjusting for APACHEII, fungal diagnosis, use of antifungal agents and other factors (odds ratio [OR], 1.1; 95% confidence interval [CI], 1.1 to 1.2; p<0.001, OR, 7.2; 95% CI, 1.5 to 34.5; p=0.014 and OR, 4.1; 95% CI, 1.3 to 12.4; p=0.013, respectively).

CONCLUSION. The prognosis of critically ill patients with CDFIs or PFIs is not related with early diagnosis and antifungal therapy.

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CEFAZOLIN AS PARENTERAL COMPONENT OF SELECTIVE DIGESTIVE DECONTAMINATION

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INTRODUCTION. Selective decontamination of the digestive tract (SDD) using parenteral and enteral antimicrobials reduces mortality in intensive care patients. Usually a 3rd generation cephalosporin, cefotaxime is given intravenously during the first 4 days combined with enteral polymyxin, tobramycin and amphotericin (PTA) in throat and gut throughout ICU treatment. We assessed whether cefotaxime could be replaced by cefazolin, a 1st generation cephalosporin.

METHODS. The unit is a 10-bedded closed format surgical-medical ICU run by intensivists. ICU patients expected to be ventilated for more than 48 hours were eligible for SDD. The introduction of SDD in the unit was preceded by a 6-month period in which cultures were taken from all SDD eligible patients, without administration of neither PTA nor any intravenous antibiotic unless clinically indicated. The next six months SDD with PTA and cefazolin were administered to all eligible patients. Cultures of throat, tracheal aspirate and rectum were taken from all patients on admission and then twice weekly. Cultures from day 0, 1 and 2 after admission were defined as 'admission' cultures and were pooled together from both groups. Cultures from day 3 and beyond were defined as 'late' cultures.

RESULTS. The non-SDD group comprised of 39 ICU episodes in 39 patients, median age 70 years, median duration of mechanical ventilation 6,0 days. The SDD group comprised of 74 ICU episodes in 72 patients, median age 68 years, median duration of mechanical ventilation 5,5 days. At admission aerobic Gram negative bacilli (AGNB), excluding P aeruginosa, were cefazolin-resistant in 31 patients, cefuroxime-resistant in 10 patients, cefotaxime-resistant in 2 patients. SDD patients had less AGNB and fungi in late cultures. S aureus or enterococcal carriage was not different. Hospital mortality was 14 out of 39 (35,9%) in the non-SDD group and 19 out of 74 (25,7%) in the SDD group (RR 1,40, 95% CI 0,70-2,47).

CONCLUSION. In our patient population cefazolin as parenteral component was inadequate as one third of patients carried AGNB cefazolin-resistant but cefotaxime sensitive on admission.

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THE MOST SUITABLE REGIMEN OF CIPROFLOXACIN IN PATIENTS WITH CONTINUOUS RENAL REPLACEMENT THERAPY

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INTRODUCTION. Critically ill patients are often complicated with acute renal failure and are treated with continuous renal replacement therapy (CRRT). However, there is no universality in the pharmacokinetics of drugs during CRRT. ciprofloxacin(CPFX) is often administered for critically ill patients with various severe infections. The influences of CRRT on the pharmacokinetics of CPFX are suspected to depend on the various combinations of CRRT. The aims of this study were to estimate CPFX clearance during CRRT, and to determine appropriate regimens of CPFX in patients during CRRT.

METHODS. CPFX clearance by CRRT (CPFX CL_{CRRT}) was calculated based on circuit models. CPFX clearance in vivo (CPFX CL_{vivo}) was estimated using data from previous reports. CPFX total clearance (CPFX CL_{tot}) during CRRT was the sum of CPFX CL_{CRRT} and CL_{vivo}.
In the clinical study, CPFX pharmacokinetic values were measured in 3 patients during CRRT. Based on the results, the appropriate regimen of CPFX on each predictive CPFX CL_{tot} is shown.

RESULTS. CPFX CLtot during CRRT is follows:
CPFX CL_{tot} (L/hr) = CPFX CL_{vivo} + CPFX CL^{CRRT} = (0.29 x CL_{cre} + 6.41) + 0.89 x (Q_D+Q_F), where CL_{cre} is creatinine clearance, Q_D is dialysate flow, and Q_F is ultrafiltrate flow.
The appropriate dosages of CPFX based on the predictive CPFX CL_{tot} are follows:
1) CPFX CL_{tot} < 10 (L/hr) 300 mg every 12 hr
2) CPFX CL_{tot} 10-20 (L/hr) 400 mg every 12 hr
3) CPFX CL_{tot} 20-30 (L/hr) 400 mg every 8 hr

CONCLUSION. A predictive CPFX CL_{tot} formula was established. This predictive formula can be applied to patients under various conditions of CRRT. The recommended CPFX regimens to achieve effective concentrations were shown on the basis of PAPM CLtot.

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AMPHOTERICIN B TISSUE DISTRIBUTION AFTER TREATMENT WITH LIPID-FORMULATED AMPHOTERICIN B

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INTRODUCTION. Amphotericin B (AMB) is the standard drug for treatment of proven or suspected invasive mycosis. Its clinical use, however, is restricted by its side-effects, above all its nephrotoxicity. Therefore, in critically ill patients systemic fungal infections are frequently treated with less toxic AMB lipid formulations as liposomal AMB (LAMB) and AMB colloidal dispersion (ABCD). These lipid-formulations display remarkable differences in their plasma pharmacokinetics which can be attributed to the different clearance of their lipid moiety.

METHODS. AMB levels in different tissues of patients, who had been on treatment with lipid-formulated AMB, were measured in samples obtained from routine autopsy of 17 patients. All patients had been on vasopressor therapy and mechanical ventilation. Ten patients had been treated with ABCD, seven patients with LAMB. Antimycotic therapy had been initiated for suspected or proven invasive fungal infections. AMB tissue levels were assessed by extraction of homogenized tissue samples, purification by solid phase extraction and measurement of AMB by HPLC.

RESULTS. In ABCD treated as well as in LAMB treated patients, highest AMB concentrations have been found in the liver (104.6 ± 63.16 \mug/g for ABCD vs. 102.81 ± 68.72 \mug/g for LAMB treatment [mean ± standard deviation]) and spleen (74.49 ± 50.11 vs. 60.32 ± 29.75 \mug/g), followed by lung (31.8 ± 24.77 vs. 11.63 ± 7.7 \mug/g), kidney (37.47 ± 38.00 vs. 11.89 ± 12.77 \mug/g) and heart (4.56 ± 2.99 vs. 3.18 ± 3.18 and \mug/g). Very low amounts were achieved in the brain (1.08 ± 0.58 vs. 0.98 ± 0.75 \mug/g). Thus AMB-tissue levels in liver, spleen, heart and brain were similar after LAMB- and ABCD therapy. However, in lung and kidney AMB concentrations of ABCD treated patients exceeded those of LAMB treated. This difference was significant (p = 0.025 for lung tissue and p = 0.030 for kidney).

CONCLUSION. Lipid-formulated AMB accumulates in liver and spleen. ABCD displays a favourable lung penetration and a higher penetration into the kidneys, while LAMB blood concentrations exceed those of ABCD. Thus the choice of AMB lipid-formulation should probably be guided by the location of fungal infection (e.g. in pulmonary manifestation ABCD might be advantageous, in fungemia LAMB).

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EVALUATION OF THE ADMINISTRATION OF VANCOMYCIN TREATMENT IN ICU PATIENTS WITH FEBRILE NEUTROPENIA

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INTRODUCTION. We performed a retrospective analysis to analyze the management and the appropriate use of vancomycin in the strategy of systematically adding vancomycin as second-line empirical treatment in MICU febrile neutropenic patient.

METHODS. Data were collected on neutropenic patients with a hematologic malignancy who were admitted to the Pellegrin Hospital MICU between January 1998 - January 2004. Standard medical treatment for treating patients with febrile neutropenia was to institute broad-spectrum antibiotics at the first sign of fever and to add vancomycin (VCM)at day 3, if neutropenia persisted. The first-line treatment was a blactam (monotherapy). Serum VCM concentrations were monitored by the physicians as one wants. If VCM concentrations were monitored, the VCM doses should be adjusted to obtain optimal concentrations of 25-40 µg/ml.

RESULTS. 320 episodes of febrile neutropenia occurring in 238 patients requiring an ICU admission or occurring into the MICU were analysed. Most of the patients were already neutropenic and febrile at the admission into the MICU. It was the case for 188 patients (79 %). For the other 50 patients, the episode of neutropenia with fever has occurred during the MICU hospitalisation. 59 and 23 patients have presented respectively a second and a third episode of febrile neutropenia. A total of 224 episodes of fever + neutropenia have been treated by at least VCM. Finally, 38 patients had an infection due to Gram-positive cocci. This result corresponds to 17 % of the episodes of prescription of VCM, 16% of the enrolled patients or 12% of all the 320 episodes of neutropenia + fever. In 37% and 89% of the cases, the serum concentration was respectively inferior to 12,5 and 25 µg/ml. When treatment with VCM was started at the time and/or after the MICU admission (99 episodes), the mean time to obtain the objective of serum concentration (> 25 µg / mL) was 5 days.

CONCLUSION. Adequate vancomyin therapy occurred in a very small percentage of neutropenic patients with persistent fever and deteriorated clinical state requiring an MICU admission. Furthermore, the objective of serum concentration was achieved with difficulties in a mean delay of 5 days. Despite the results, it seems difficult to recommand a restriction of the vancomycin use as a second-line empirical treatment in critically ill neutropenic patients.

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MYOCARDIAL DEPRESSION IN SEPTIC SHOCK: WHY NOT ISOPROTERENOL?

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INTRODUCTION. During septic shock, a myocardial depression, which is generally treated with dobutamine, is observed in 10 to 20% of patients. Our hypothesis is that isoproterenol is an alternative drug to improve hemodynamics of these patients.

METHODS. We assessed data prospectively collected in 13 septic shock patients (ACCP/SCCM) receiving norepinephrine, which developed an acute heart failure with a mixed venous saturation (SvO2) < 70% and a pulmonary capillary wedge pressure (PCWP) >14mmHg. In these patients, isoproterenol was administered to increase SvO2. Data at each time were compared to baseline. A value of P<0.05 was considered as significant. Results are expressed as mean ± SD.

RESULTS. Cardiac index (CI) and stroke volume (SV) increased significantly during isoproterenol infusion, as well as left ventricular work (LVW). Mean arterial pressure (MAP) was stable over the study period. The increase in heart rate and SvO2 did not reach a significant level. One patient developed arrythmia. Mortality rate was 66%.

TABLE 1.

Isoproterenol in 13 patients

	Baseline	2 h	8 h	12 h
Heart rate (b/min)	112±21	115±22	126±25	121±25
MAP (mmHg)	74±24	76±17	80±14	80±12
PCWP (mmHg)	15±3	14±4	14±4	16±5
SV (mL)	47±3.7	63±5.8*	55±5	65±6.2*
LVW (gm.m/batt)	41±3.5	60±5.3*	52±4.6	62±5.8*
CI (L/min/m²)	3.1±0.6	4.1±1.9*	4.0±1.1*	4.4±1.6*
SvO2 (%)	67±10	68±25	71±9	70±11

**P<0.05 compared to baseline*

CONCLUSION. Isoproterenol improved SvO2, although non statistically significant, via a significant increase in CI due to the combination of a significant elevation of SV and a moderate acceleration of heart rate. Isoproterenol may be considered as a potential alternative to dobutamine in septic shock patients without myocardial ischemia.

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ARE NORWEGIAN ANAESTHESIOLOGISTS INTERESTED AND EXPERIENCED IN CLINICAL NUTRITION?

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INTRODUCTION. Undernutrition is prevalent in hospitalised patients and may cause increased morbidity and mortality. Despite simple screening methods and algorithms, nutritional goals are difficult to achieve. The aim of the present study was to evaluate knowledge, interest and use of clinical nutrition among anaesthesiologists in Norway.

METHODS. 1999 doctors from different specialities were randomly selected from hospitals in Norway to receive a questionnaire about knowledge, interest and use of clinical nutrition. The random sample comprised 327 anaesthesiologists (18% of the doctors asked).

RESULTS. Twenty-nine percent of the doctors (n=579) and among these 104 anaesthesiologists (49% working in university hospitals and 62.5% working as consultants) answered the questionnaire. Questions concerning knowledge of the importance of nutrition were correctly answered by more than 90 % of the anaesthesiologists. More then ninety percent stated that nutritional assessment should be performed on admission, but only 20 percent claimed that it was a routine procedure in their department. Only 13.5% of the departments registered body weight in all patients on admission, while 88% claimed that it should be routinely performed on admission. Ninety-eight percent stated that energy-demand should be routinely evaluated on a day to day basis, but only 51.5% performed this as a routine. Fifty-five percent of the anaesthesiologists believe that their education has prepared them to deal with nutritional matters. Despite this ninety-four percent wanted guidelines to identify patients that require nutritional therapy, and sixty-seven percent claimed that national guidelines are missing. Twenty-two percent reported that inadequate nutrition in their department caused complications and increased morbidity, and 20% stated that nutritional matters have low priority in their department.

CONCLUSION. According to our results knowledge in nutritional matters seems adequate, but there is a discrepancy between ideals and realities. Effort should be put into interdisciplinary educational programmes and the development of simple national guidelines.

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EFFECT OF ENTERAL VS PARENTERAL NUTRITION ON OUTCOME OF MEDICAL PATIENTS ON MECHANICAL VENTILATION

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INTRODUCTION. Early enteral nutrition in patients on mechanical ventilation has commonly been advocated, based mainly on the studies conducted in mixed populations of trauma and surgery patients. Our aim was to compare ventilator-associated pneumonia rates and outcomes in medical ICU patients receiving enteral versus parenteral nutrition.

METHODS. All patients fulfilling the inclusion criteria who needed mechanical ventilation for more than 48 hours, during the period between 01.02.04 and 31.3.05 were included. Enteral (e) or parenteral (pe) nutrition was started within 48 hours of intubation after randomization. The day feeding goal was attained, was defined as the first day patient received full dose nutritional support without any interruption. Development of ventilator-associated pneumonia, the day feeding goal was attained, ICU and hospital lengths of stay, duration of mechanical ventilation, ICU and hospital mortality rates were recorded. The results are expressed as median [interquartile range] or n(%) where applicable.

RESULTS. Out of 160 evaluated patients, 54 patients were included in the study, and 22(41%) were randomized to receive enteral nutrition. There was no difference when groups were compared for age (e:59[37-71], pe:60[44-71]; p=0.73), sex (e:8 males, pe:18 males; p=0.15), body mass index (e:25[21-27], pe:22[21-25]; p=0.10), and admission APACHE II scores (e:18.5[15-24], pe:22[15-28]; p=0.44). Ventilator-associated pneumonia rate (e:4(18.2%), pe:10(31.3%); p=0.35), ICU mortality rate (e:6(27.3%), pe:14(43.8%); p=0.22), and hospital mortality rate (e:9(42.9%), pe:15(50%); p=0.62) were not different in both groups. Length of ICU stay (e:12[9-17] days, pe:14[9-26]; p=0.25), and hospital stay (e:28[13-46] days, pe:28[20-47]; p=0.53) were similar in both groups. However, duration of mechanical ventilation was longer in the parenterally fed group (11[6-19] days vs. 8[4-10]; p=0.05). Yet, the day feeding goal was attained was earlier in the parenterally fed group (3rd[3-4] day vs. 4th[4-5]; p=0.02).

CONCLUSION. Although enteral support is commonly recommended in the critically ill, these results reveal that in medical ICU patients, outcome of mechanically ventilated patients receiving parenteral nutrition is not significantly different than patients receiving enteral nutrition, and feeding goals can effectively be attained by parenteral nutrition.

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PARENTERAL NUTRITION USAGE WITHIN CRITICAL CARE

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INTRODUCTION. The use of Parenteral Nutrition (PN) within the Critical Care Directorate (CCD) has increased, although still less than in 1997. The Canadian guidelines recommend that PN be used only when all strategies to maximise enteral feeding have been attempted, and that PN be supplemented with glutamine(1). The aim of this review was to assess the CCD compliance with the guidelines, and to quantify use of PN.

METHODS. All patients referred to the Nutrition Support Team (NST) for PN over a 12-month period were reviewed.

RESULTS. 32% of all patients who received PN originated from the CCD. 33 referrals for PN were made (26 patients,31 episodes of PN). The majority of patients (96%) were peri-operative (9 resections, 7 fistulae, 4 pancreatitis, 5 misc.). Enteral nutrition was either contra-indicated or had failed following enteral tube feeding. Patients who had more than one episode had resumed successful enteral tube feeding of at least 7 days duration between episodes. All patients received glutamine, either within the PN regimen or as a separate infusion. 40% of all lines used for PN were used within the CCD (66). All lines were multi-lumen central venous catheters, the majority (94%) inserted by medical staff within the CCD. There were a total of 369 PN patient days within critical care. The mean duration was 14 days/patient (range 2-74 days), and 11.5 days/episode (range 2-58 days). There were only 2 incidences (3%) of proven and 5 (7.5%) suspected catheter-related infections (12% proven and 10% suspected CRI outside the CCD). Overall, 12 patients resumed enteral nutrition whilst still within the CCD, 9 patients died whilst on PN and 5 patients transferred to the ward on PN.

CONCLUSION. PN is used appropriately within CCD. PN is given to the majority (94%) of patients referred from critical care, compared with that overall (65%), and CRI's are relatively low. The recent increase is possibly a result of increased complex surgical cases, and a reduction in surgical jejunostomy tube placement(2). An evidence-based enteral feeding protocol and NST help achieve the recommendations.

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SEVERE ACUTE PANCREATITIS: ENTERAL NUTRITION VERSUS PARENTERAL NUTRITION

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INTRODUCTION. Severe acute pancreatitis (SAP) represents 20% of overall pancreatitis. These patients are at high risk of lethal outcome (20-40%). Around 80% mortality is related to pancreatic infection, usually caused by gram negative bacteria, colonizers of gastrointestinal tract. The gold-standard treatment is pancreatic rest.This can be achieved by feeding SAP beyond the Treitz's angle using a nasojejunal tube (NJT), with the aim of preventing gut bacterial translocation.

METHODS. Retrospective study of 55 ICU patients with SAP (january/00-april/05).Inclusion criteria:pancreatitis D/E(Balthazar),>5 days stay in ICU,admision abdominal CT and no initial surgery. We first used parenteral nutrition (PN) and from 2003 also enteral nutrition (EN). We analized both groups: age, sex, SAPS,APACHE II, Ranson, Imrie criteria, abdominal CT index (CT), multiple organ failure(MOF),C-reactive protein, pancreatic infected necrosis, abscess, pseudocyst, days of PN, ICU and hospital stay and mortality

RESULTS. SAP (55): No NJT (37/55) and NJT group (18/55). Initial necrosis(24/55): No NJT (13/24)and NJT (11/24). Mean age 58 for the four groups. See table 1. During the stay in ICU, APACHE II score decreases more quickly in the enteral feeding group than in the parenteral nutrition group; as well as the evolution of C-reactive protein in the enteral feeding group with SAP and necrosis.

TABLE 1.

	SAP (55) No NJT (37/55)	SAP (55) NJT (18/55)	SAP+necrosis (24) No NJT (13/24)	SAP+necrosis (24) NJT (11/24)
SAPSII/APACHE II	8,7 / 11,2	9,9 / 10,6	8,8 / 11,7	9,4 / 9,8
Ranson/Imrie/CT	5,2 / 4,8 / 5,1	5,1 / 4,7 / 6,1	5,2 / 4,6 / 6,9	5,6 / 4,9 / 7,2
Inf necros/Abscess	5 / 4	1 / 0	3 / 0	1/ 0
Pseudocyst / MOF	4 / 2,2	2 / 2,5	1 / 2,1	1 / 2,25
Days ICU/Hospital	16,3 / 38,8	10,7 / 21,9	21,5 / 43,5	11,5 / 21,7
Death	8	3	4	1

CONCLUSION. Patients afected of SAP, early feeded in jejunum by NJT show a decreasing tendency in the number of septic complications, ICU and hospital length of stay. The C-reactive protein (inflammatory marker) also decreases more quickly.

Grant acknowledgement. To the residents and nurses of the ICU

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CLINICAL EFFECTS OF LIPID EMULSIONS IN SEPTIC PATIENTS

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INTRODUCTION. Poly-unsaturated fatty acids display immunomodulatory properties in certain contexts, but clinical impact of low-lipid parenteral nutrition in septic subjects has not been often demonstrated. Two populations receiving respectively high and low-fat intravenous (TPN) mixtures were compared, aiming to analyse changes in hematological and biochemical variables

METHODS. Septic patients submitted to TPN (n= 96) were investigated on the 1st and the 7th day of treatment. Both glucose-based (Group I, n= 29) and lipid-based (Group II, n= 67) prescriptions were employed. Mean fat intake in Group I was 3.3 -/+ 1.2% and in Group II 25.8 -/+ 9.2% of total calories. Only soybean-oil-based emulsions were used.

RESULTS. Mean age was 55.5 -/+ 14.7 vs 59.0 -/+ 14.1 years (NS) , females represented 55.2% in both groups , and total intake was 1120 -/+ 376 vs 1352 -/+ 550 kcal/day (NS). Glucose concentration was equivalent without changes along the period. Initial serum albumin was lower in Group I (29 -/+ 6 vs 33 -/+ 6 g/L, $p<0.05$) but it recovered to similar final values (34 -/+ 4 vs 33 -/+ 6 g/L, NS). Preliminary white blood cell count (WBC) was comparable (12624 -/+ 7320 vs 13781 -/+ 11165/mm3), but final WBC tended to diverge (12118 -/+ 6317 vs 15561 -/+ 8038/mm3, NS). Thus, more patients in Group I displayed reduction in this count than in Group II (58.6% vs 40.3%, $p<0.05$).

CONCLUSION. Low-lipid TPN was associated with diminished WBC count and better response of serum albumin than high-lipid formulations. A reduced inflammatory response is consistent with those findings.

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VASCULAR EROSION BY CENTRAL VENOUS CATHETERS USED FOR TPN

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INTRODUCTION. Vascular erosion due to central venous catheters (CVC) is a rare, but potentially fatal complication. The incidence is not established, but has been postulated from small studies to be 0.5%(1). Although the risk is proposed to be higher in left-sided CVCs, this has not yet been proven.

METHODS. A retrospective review of the Total Parenteral Nutrition (TPN) service records of 1512 patients (2974 CVCs) receiving TPN via central access over a 15-year period in the Mater Hospital was undertaken. Data was entered into a spreadsheet and analysed. Fisher exact test was used to determine statistical significance.

RESULTS. Five cases of CVC erosion occurred, giving an overall incidence of 0.168%. Four followed left subclavian CVC insertion; one followed a left internal jugular CVC. No erosion occurred in patients with right-sided CVCs. Two of the patients who suffered CVC erosion died as a result. Erosion occurred between 3-7 days following insertion. Data from a 13-year period was used to determine the risk of CVC erosion in left versus right CVCs. This incorporated 2600 CVCs. The incidence of CVC erosion from left-sided catheters was 0.44% (4/889). This compared with 0% in right-sided CVCs. (n=1701). The relative risk of erosion occurring in a left sided CVC as compared to right sided is 2.9 (95% Confidence Interval 2.751 to 3.06), p value = 0.026. There was no statistically significant increased risk of CVC erosion of left subclavian line (incidence 0.62% 3/487) when compared to left internal jugular CVC (incidence 0.24% 1/412). Relative risk 1.5, p value = 0.62.

CONCLUSION. Although this complication is rare, there is a statistically significant increased risk of CVC erosion occurring when a left-sided approach is used. We recommend that: 1.Right-sided approach for CVC insertion should be used where possible. 2. This complication can occur within seven days of CVC insertion, and therefore a high index of suspicion should be maintained, enabling early diagnosis and management.

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DELAYED FEEDING IN INTENSIVE CARE; DISTRIBUTION WITHIN SUBGROUPS & ILLNESS SEVERITY

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INTRODUCTION. Nutritional support in critically ill patients has been well established but it is unclear how widely current guidelines are applied. We examined feeding practices in our 13 bed mixed medical and surgical Intensive Care Unit (ITU). We aimed to quantify inadequate feeding and to explore potential reasons for such.

METHODS. Data from all admissions over an 8-week period was collected. Patients were divided into those established on target enteral nutrition by 48 hours after admission (group 1) or those not fed enterally at such time (group 2). Each group was studied for diagnosis, outcome and possible reasons for delayed enteral feeding.

RESULTS. During the study period 80 patients were recruited, 65 into group 1(early feeders) and 15 into group 2. Mean ages were 59.2 years (+/- 15.0) and 64.2 years (+/- 16.7), respectively. Reasons for delayed feeding were severity of illness (5), early extubation (3), delayed discharge (2), oesophageal balloon (2), bowel anastomosis (1), non-invasive ventilation (1) and return to theatre (1). The proportion of patients not being fed early was significantly higher in the AAA groups when compared with overall patient numbers -15/80 -(Chi squared test, $p < 0.05$). There were no differences in mortality between groups 1 and 2.

TABLE 1.

Diagnostic Subgroups

	Early Feeding	Delayed Feeding
Abdominal Aortic Aneurysm (AAA)	6	8
GI Medicine	3	2
GI Surgery	10	1
Cardiothoracic	11	2
Respiratory	15	0
Other	20	2
Mortality	13	4

CONCLUSION. In this small sample of heterogenous critically ill patients those having AAA surgery were at higher risk of not receiving appropriate enteral nutrition. It is unclear whether delayed feeding was a cause or an effect of severity of illness. Some ITU patients may benefit from specifically targeted strategies to implement early enteral nutrition.

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THE IMPACT OF INTRODUCTION OF A PROTOCOL FOR PREVENTION OF CONSTIPATION IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Management of constipation can be overlooked in critically ill patients in intensive care units [ICUs]. We reported that its incidence in ICUs was high and it could cause failure to wean patients from mechanical ventilation [1]. We therefore introduced a protocol for prevention of constipation in our patients. We present the results of our second audit after protocol introduction and compare it with our historical reported audit to ascertain its impact on our patients.

METHODS. Constipation was defined as 'failure of bowel to move for >3 consecutive days'. Only ventilated patients admitted to the ICU for >3 days were included in the study. Those who had recent bowel surgery were excluded. Patient's age, sex, APACHE II score, length of stay in ICU [LOS], diagnosis and the incidence & duration of constipation were recorded. The volume of gastric aspirates, ability to enterally feed or wean patients from mechanical ventilation, and bowel care [e.g. use of laxatives] were noted.

RESULTS. Data were prospectively collected over a 3 months period. Group I, after protocol introduction, comprised 42 patients [24 male] who were included in the study. Constipated patients were 17 [40%], 4 [24%] of whom failed to wean from controlled ventilation. Only 3 out of 25 [12%] non-constipated patients failed to wean. No significant differences between constipated and non-constipated patients with respect of gender, median age [63 (range 32-78) versus 58 (23-76) years], APACHE II score [17 (9-29) versus 19 (9-34)] or median LOS in ICU [10 (4-56 days) versus 10 (4-71) days] respectively. A significantly higher incidence of constipation was noted in our patients before the protocol was introduced [Group II] [40 out of 48 patients (83%)] compared with Group I, p <0.0001]. The incidence of failure to wean from controlled ventilation in constipated patients in Group II was 42.5%.

CONCLUSION. The introduction of the protocol reduced the incidence of constipation in ICU. This audit also confirmed previous finding that more constipated patients fail to wean from mechanical ventilation than non-constipated patents. These findings highlight the need for further investigations.

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A SINGLE DOSE OF INTRAVENOUS FISH OIL MODULATES THE RESPONSE TO ENDOTOXIN IN HEALTHY SUBJECTS

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INTRODUCTION. Lipopolysaccharide (LPS) mimics the physiological response to acute inflammation in critically ill patients. This study assessed the effects of intravenous fish oil (FO) in healthy volunteers challenged with i.v. LPS.

METHODS. 2 groups of 8 healthy subjects were randomised to receive 2 infusions of FO (Omegaven®10%) or no treatment. 2ng/kg of LPS was injected as a single bolus on the investigation day at time T0. The FO group received twice 0.5g/kg of FO 2 and 1 day before the investigations. Heart rate variability (HRV) and baroreflex sensitivity (BRS), temperature, metabolic rate (indirect calorimetry) were recorded. Blood was sampled for thrombocyte membrane phospholipid composition (EPA & DHA). Statistics: ANOVA for repeated measurements with a significance-level of p≤0.05.

RESULTS. tables 1&2. Basal EPA and DHA content in thrombocytes membrane was low (0.28% and 2.54% respectively) but was significantly increased by FO (1.68% and 3.32%). The response to endotoxin was blunted by FO, particularly the rise of temperature, plasma ACTH, norepinephrine and TNF-α. LF power decreased markedly and significantly after endotoxin. HF power decreased significantly at T360. LF/HF ratio, a surrogate of the sympatho-vagal balance significantly increased over time. BRS decreased significantly.

Time (min)	Temp.(°C)		ACTH(ng/l)		NE (pg/l)		TNF-α (pg/ml)	
	control group	FO group	control	FO group	control	FO group	control	FO group
T0	36.8±0.3	36.7±0.2	23.3±6.6	28.6±17.3	186±51	195±77	6±8	7±8
T120	38.0±0.5	37.3±0.3	151.5±66.3	109±79.9	653±276	266±78	687±555	255±222
T240	38.7±0.3	38.1±0.2	347.4±203.5	110.4±98	169±35	179±56	96±42	48±29

Time (min)	BRS (ms/mmHg)	LF (ms²)	HF (ms²)	LF/HF
T30	12.25±3.67	1499±1486	797±845	2.0±0.8
T120	11.23±4.61	2134±1226	753±517	3.7±1.5
T360	5.78±2.04	627±538	144±117	4.7±1.6

CONCLUSION. Intravenous FO modified the phospholipid composition of platelets membrane and blunted fever and the neuroendocrine and inflammatory responses to endotoxin. They also affected the sympatho-vagal balance.

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ANTIOXIDANT SUPPLEMENTS MODULATE CLINICAL COURSE AFTER COMPLEX CARDIAC SURGERY, AND MAJOR TRAUMA

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INTRODUCTION. Oxidative stress and alterations of endogenous antioxidant (AOX) status characterise severe critical illness. Small size trials suggest that AOX supplementation may result in clinical benefits. This study aimed at testing influence of early AOX supplements on organ failure and outcome in a large patient population

METHODS. Prospective, randomised, placebo controlled trial in patients admitted to ICU after major cardiac surgery, myocardial infarct, trauma or subarachnoid haemorrhage (SAH). Randomisation to either AOX (Se 270 ug, Zn 30 mg, Vit C 1600 mg, Vit E 310 mg, Vit B1 100 mg : double dose on days 1 and 2) or vehicle IV within 24 hours, for 5 days. Variables: organ failure, infections, hospital stay (LOS), and 3 months-outcome. Trends at p<0.25

RESULTS. 205 patients (median SAPS II= 36) were included; 24 patients died (Table 1). Severity of disease was evenly distributed except in trauma patients: brain injury was more severe (p=0.02) in AOX patients with more early deaths (6 vs 2: p=0.01). Cardiac patients were elder (n=113; 70±10 yrs) than trauma (n=66; 40±19 yrs) and other groups. Outcome did not differ in infarct and SAH patients (n=26). There was trend to less acute and persistent renal failure in cardiac patients (3 in AOX versus 76; p=0.17). In trauma patients LOS was shorter in AOX (29 vs 40; p=0.09)

CONCLUSION. Se containing AOX supplements are associated with lower numbers of acute renal failure and shorter hospital stay (trends). Cardiac surgery and trauma patients appear best candidates for AOX intervention

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TEMPORAL CHANGES IN WHOLE BLOOD GLUTATHIONE IN ICU-PATIENTS WITH MULTIPLE ORGAN FAILURE

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INTRODUCTION. Glutathione is quantitatively the main scavenger of oxygen derived free radicals in humans and is depleted in whole blood in the early phase of critically illness. Tissue glutathione depletion is associated with bioenergetic failure and also mortality in the early phase of septic shock. Erythrocytes make a major contribution to scavenging mainly by glutathione depended enzyme systems. We have previously shown that the concentration of muscle glutathione resituates within one week in the same category of patients. The aim of this study was to characterize the time dependence of the glutathione status in whole blood of ICU patients with multiple organ failure and thereby investigate if whole blood would be representative of changes occurring in skeletal muscle.

METHODS. The protocol was designed as a prospective descriptive pilot study. Critically ill patients with multiple organ failure (n=11) were studied with repeated determination of whole blood glutathione every 72 hours. For reference purposes one group of healthy individuals and one group of patients with chronic obstructive lung disease (COPD) were sampled. HPLC technique was used for the analyses. The patients were studied for 6 to 15 days. No specific intervention was performed during the study. Nutrition was supplied according to routines to supply basal needs including glutamine.

RESULTS. The concentration of glutathione in whole blood was substantially decreased and remained at low concentration during the whole study period, as compared to a reference group consisting of patients with chronic obstructive lung disease (n=21). The concentration of glutathione in the reference group is in accordance with values obtained from healthy volunteers (n=10).

TABLE 1.

	Day 0 n=11	Day 3 n=11	Day 6 n=11	Day 12 n=7	Day 15 n=7	COPD n=21	Contr n=10
tGSH	674 ± 134	631± 163	623 ± 101	670 ± 121	668 ± 116	1213 ±187	1203 ± 198

CONCLUSION. This study demonstrates that the concentration of glutathione in whole blood is depleted in ICU patients with multiple organ failure and remains at a decreased level, as opposed to muscle glutathione. The whole blood glutathione depletion might be the result of an ongoing supply of glutathione to other tissues for antioxidant protection.

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SAFETY OF FISH OIL CONTAINING PARENTERAL NUTRITION AFTER ABDOMINAL AORTA ANEURYSM SURGERY

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INTRODUCTION. Fish oil (FO) has been shown to have anti-inflammatory properties both in vitro and in vivo. Abdominal aortic aneurysm (AAA) surgery constitutes a model of ischemia-reperfusion with an intense inflammatory reaction, which might be modulated by FO. The study aimed at testing the safety and the clinical impact of a FO containing TPN after elective AAA surgery

METHODS. Randomized double blind trial. Patients admitted after AAA surgery received 4 days of either standard (STD: Lipofundin MCT ®: LCT50%-MCT50%) or FO containing TPN (FO: Lipoplus ®: LCT40%-MCT50%-FO10%). Energy requirements were set at 1.3 times the preoperative resting energy determination by indirect calorimetry. Blood sampling on days 0, 2, 3, and 4. Clinical data: length of ICU stay, of hospital stay, organ failure

RESULTS. 24 patients, aged 70±7 years, with a body mass index of 26±3, and with SAPSII score of 22±7 were investigated, and discharged alive. Both solutions were clinically well tolerated. There were no differences in laboratory safety parameters, inflammatory, metabolic data, nor in organ failures. Tocopherol increased similarly; DHA and EPA were unchanged in the STD group but increased significantly by day 4 in the FO group versus baseline (EPA: 4.2±1.8 à 28.2±8.2 mg/l, DHA: 25.0±12.4 à 46.7±12.1 mg/l). MDA was higher on day4 in the FO group (p<0.05). Postoperative T° increased in both groups, with a trend to lowed values in the FO group (p= 0.09). There was a trend towards shorter ICU stay in the FO group (1.6±0.4 versus 2.3±0.4: p=0.18), and hospital stay (9.9 ±2.4 versus 11.3±2.7 days: p =) respectively

CONCLUSION. Both lipid emulsions were safe after AAA surgery: FO enhanced the plasma PUFA content. Trends to lower body temperature and length of stay were observed in FO patients, despite an only minimal difference in lipid composition (10% fish oil). The absence of significance is attributed to the limited power of the study, and to the small differences in the 2 lipid solution compositions

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EFFECT OF PARENTERAL ALANYL-GLUTAMINE ON GLUTAMINE PRODUCTION RATES

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INTRODUCTION. Glutamine supplementation to ICU patients improves morbidity and mortality. More knowledge on glutamine production and utilisation rates are needed to better understand the mechanism behind the glutamine depletion and the effects of supplementation. Existing methods to assess glutamine kinetics utilising tracers are complicated by difficulties to obtain a tracer steady state. Here we used of a bolus injection of labelled glutamine in combination with non-compartmental analyses to overcome these potential problems and measure the effect of parenteral glutamine supplementation on glutamine production rates in healthy volunteers.

METHODS. Healthy volunteers (n=9) received an iv bolus of 1-13C-glutamine (3mg/kg) after which sixty arterial plasma samples were obtained during 90 minutes. Five of these subjects received a continuous infusion of glutamine (115 µmol glutamine/kg/h as alanyl-glutamine) 4 hours before and 90 minutes following the tracer injection. Tracer/tracee ratio of glutamine was determined by gaschromatograhy-massspectrometry. Whole body rate of glutamine production was calculated as bolus dose devided by the area under the curve for the glutamine tracer/tracee ratio.

RESULTS. Basal rate of glutamine production was 390±135 µmol/kg/h. Infusion of extra glutamine in the form of alanyl-glutamine did not effect the endogenous glutamine production (393±83 µmol/kg/h).

CONCLUSION. Intravenous glutamine supplementation of about 1.3g/hour for 4 hours does not influence the endogenous glutamine production in healthy volunteers. A bolus injection of labelled glutamine is a useful technique to study whole body glutamine production without the need of a prolonged tracer infusion or a tracer steady state.

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EFFECTS OF GLUTAMINE PARENTERAL NUTRITION IN PREVALENCE OF NOSOCOMIAL INFECTION IN ICU PATIENTS

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INTRODUCTION. Glutamine (GLN) is the most abundant free amino acid in the human body, defined in critically ill patients as a conditionally essential substrate. Several studies showed a relationship between GLN depletion and the increased nosocomial infection in ICU patients. The purpose of the present study is to investigate the effects of glutamine supplemented parenteral nutrition on lymphocyte subpopulations and correlate it with the infectious morbidity in critically ill patients.

METHODS. We performed a blind randomised, controlled study of GLN enriched parenteral nutrition (GLN-PN). Twenty-eight critically ill patients were randomly assigned to 2 groups of nutrition therapies, as either Dipeptiven® (0.40 gr/Kg/day) supplemented parenteral nutrition (GLN group n=16) or an isocaloric and iso-nitrogenous standard parenteral nutrition (STD group n=12). Blood samples were obtained for lymphocyte subpopulations at begining and at 5th and 10th day after standard TPN. Flow cytometry analysis was performed immediately. Nosocomial infections from entry to discharge from ICU were determined.

RESULTS. Baseline data were similar in standard and glutamine groups. CD4/CD8 ratio and CD25 showed an increase from 1st to 5th day in the GLN group. GLN-PN treated patients had less nosocomial infections ($p < 0.05$). From 1st to 10th day after start parenteral nutrition (Table 1), the markers of infection (leucocytes) and inflammation (CRP) decrease in GLN-PN ($p < 0.05$). The mortality in ICU is decreased in GLN group (12,5 vs 25%).

TABLE 1.

GLN vs STD group (day 1 vs 10)

	GLN 1 / GLN 10	STD 1 / STD 10
Leucocytes	16,5 ± 6,6 / 11,6 ± 2,2	14,7 ± 6,8 / 16,7 ± 7
CRP	14 ± 4,9 / 7,3 ± 3,5	16,7 ± 7,1 / 13,6 ± 6,4

CONCLUSION. This pilot study showed that GLN-PN supplemented improved not only lymphocyte activation, but also regulatory mechanisms of lymphocyte proliferation, illustrated by increased lymphocyte expression surface marker CD25. This effects can apparently decrease nosocomial infections and mortality in ICU patients.

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NURSING ACTIVITY SCORE – NAS. OUR EXPERIENCE WITH THE SYSTEM IN A GENERAL ICU. PART I

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INTRODUCTION. Nurses workload computing systems have different design problems (physician oriented designs, need for periodical updating, ...). that represented a little acceptance when compared to other management tools. Our ICU began in 1998 to use NEMS as a system to express nursing workload, and since 2004 we introduced NAS 1. Our aim is to describe our experience with NAS and the change process.

METHODS. During the last four months of 2004 we have used NAS on a daily basis to all patients admitted to our multidisciplinary 19 beds ICU. NEMS 2 was simultaneously applied. An acceptance survey on NAS usefulness and its use has been carried through ICU nursing personnel. NAS was calculated for every day of ICU stay of every patient enrolled in the study. Special interest have been focused in first day, last day before ICU discharge, total NAS score for the whole stay and average day NAS score. NEMS was estimated for the first day and for the whole length of stay. A correlation study between NAS and NEMS has been performed.

RESULTS. A total of 366 patients were enrolled in the study. That means 1880 days of NAS / NEMS scores. First day NAS scores was 39,2 ± 11,7 and NEMS first day score was 35,45 ± 7,8. Total stay NAS scores rise to 237,2 ± 379,9 and total NEMS score was 127,4 ± 225,1. The range for daily values was narrower for NEMS (18 to 45 vs. 22,4 to 84, 50). Correlation between NEMS and NAS daily scores showed an R2 value of 0,1634 and this value is still poorer if estimated on a shift basis. The performed opinion survey on 36 nurses of the 43 working in out ICU (57,1 ± 53,4 months of experience) estimated time for fulfilling NEMS forms in 1,3 ± 0,8 minutes in front of 4,1 ± 2,7 minutes used for NAS records. 95 % of the responding nurses consider that NAS reflects better the nursing workload.

CONCLUSION. NAS is a better accepted system for quantifying workload, with a better expression of real patients attendance activities, and does not represent a heavy overload of nursing time for being fulfilled.

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A STRUCTURED PROGRESSIVE INTRODUCTION OF AN I.C.U. GLUCOSE PROTOCOL

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INTRODUCTION. Intensive insulin therapy (IIT) for critically ill patients is now considered necessary. For it to be feasible this therapy should be enacted by the ICU nursing staff, this nurse driven therapy is a new way of working for nurses in most hospitals. The challenge is then: how to introduce this nurse driven protocol on a 30 bed ICU of a tertiary teaching hospital. What proof can be presented about the effectiveness of the introduction: the accuracy of it's use and acceptability to the nursing staff?

METHODS. Based on the Planned Change model for innovations, the demands for IIT on the ICU were drawn up. It had to be enacted with an acceptable accuracy. An first protocol was made. A lecture was presented to a (small) group of ICU nurses. In a 4 bedded 'pilot' room these nurses started with the IIT with the nurse leading the project present. After a evaluation, the protocol was amended. Lectures were offered to all nurses and the IIT was started on two rooms. All nurses were thus given the opportunity to work with the protocol with help of the nurse leading it. This phase was evaluated and (minor) changes in the protocol were made. The protocol was subsequently started on all 30 beds. The evaluations were qualitative for problems encountered and quantitative for: frequency of serious deviations from the protocol and number of hypoglycaemic events. The acceptability of the protocol for the nursing staff was assessed at the end by means of a questionnaire.

RESULTS. In the quantitative assessments were 1890 measurements of 100 patients. The mean glucose value obtained was 7,2 mmol/l (SD 2,3) this is comparable with Kinsley [2].The protocol was enacted by the nursing staff with 95% accuracy (deviations with immediate patient consequences). Three patients had glucoses below 2,5 mmol/l. The introduction was perceived as effective and acceptable by the nurses.

CONCLUSION. A structured, progressive introduction of a intensive insulin therapy on the ICU has resulted in acceptation of the protocol by the nursing staff and a low percentage of deviations from the protocol, while still reaching the target on glucose values. This form of introduction can well be of use in other hospitals and for other major changes in working

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INITIAL DEVELOPMENT OF A PAIN ASSESSMENT TOOL FOR UNCOMMUNICATIVE INTENSIVE CARE PATIENTS

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INTRODUCTION. Pain is an unpleasant somatic sensation which arise from many situations in the intensive care setting, such as routine patient care, trauma, immobility, presence of endotracheal tubes or other monitoring devices. Critical care patients are at particular risk for unrelieved pain when they are unable to communicate. One of the barriers to effective pain management in critical care is the lack of methods for assessing pain. The purpose of this study was to investigate the factors to be taken into consideration when assessing pain of an uncommunicative intensive care patient and also the factors with which the pain can be assessed.

METHODS. The study was carried out by applying the Delphi method, which is based on gathering information from experts and reaching a consensus. Two Delphi rounds were used. Nurses and physicians, who had experience of intensive care, knowledge of the pain of the intensive care patients and a wide view of intensive nursing, were chosen to the study. 31 (67 %) experts participated in the first Delphi round and 23 (79 %) experts in the second round, representing 12 different intensive care units in Finland. The experts evaluated the factors with which the pain of an uncommunicative intensive care patient can be assessed. The study data was analyzed by means of content differentiation, and consensus level was set at 51 %.

RESULTS. As a result of this study a pain assessment tool was developed for an uncommunicative intensive care patient. Both physiological and behavioral factors were included. Physiological factors included hypertension, increased heart rate and sweating. Behavioral factors included body movements/position and facial expressions. These factors constituted a tool, which had a five-step numerical scale and a three-step verbal scale. The study also indicated that when assessing the pain of an uncommunicative intensive care patient, it is important to locate the pain and to know whether the pain is caused by internal or external factors. Furthermore, the family members and their opinions should be taken into consideration when assessing the pain of an uncommunicative intensive care patient.

CONCLUSION. The study showed that it is necessary to have a tool for assessing pain of an uncommunicative intensive care patient. In the future this tool should be tested.

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SURVIVAL AFTER INTENSIVE CARE WITH A TRACHEOSTOMY - OPTIMISED WITH OUTREACH?

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INTRODUCTION. The discharge of tracheotomised patients from ICU to the ward is associated with risk1. The critical care outreach team (CCOT)reviews ICU discharges on the ward daily, weaning CPAP therapy and tracheostomy tubes (including decannulation) using CCOT guidelines. Study aims were to audit hospital survival rates, bed day use, ward areas involved, incidence of, and time to, decannulation by CCOT and adverse events.

METHODS. A retrospective audit of discharges from ICU to wards (January 1st –December 31st 2004) from a 20 bedded ICU in a tertiary referral teaching hospital. Data were collected using the ICNARC case mix programme and CCOT records.

RESULTS. 1053 patients were admitted to ICU in this period. 883 (83.8%) survived to discharge from ICU. 122 (13.8%) patients were discharged with a tracheostomy, 90 (73.7%)on CPAP therapy. Of these 122 patients, 95 (77.9%) survived to discharge from hospital (Table 1) utilising 3170 bed days in 20 ward areas. Of survivors, 67 (70.5%) were decannulated by CCOT with average days to decannulation being 22.9 days. Adverse events were minimal.

TABLE 1.

Tracheostomy Patient -Outcomes

	Number	Percentage
Survival to discharge from hospital	95	77.9
Deaths on ward (DNAR status)	19	15.6
Deaths on ward (no DNAR status)	2	1.6
Deaths following readmission to ICU (subsequent DNAR status)	2	1.6
Remain inpatients	4	3.3
Total	122	100

CONCLUSION. This model of tracheostomy management appears successful with 116 patients (95%) either surviving to discharge from hospital or having death preceded by DNAR decisions. 2 patients' deaths (1.6%) were not preceded by DNAR decisions. Bed day usage was high. Decannulation was achieved by CCOT in 67 (70.5%) patients.

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BENEFIT OF INTEGRAL TREATMENT IN PATIENTS ADMITTED IN ICU AFTER A SEVERE ISCHEMIC STROKE (SIS)

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INTRODUCTION. To study the efficiency for patients admitted in the ICU of a global treatment, ICU plus intensive, integrated and multidisciplinary post-ICU rehabilitation program, versus patients to whom only ICU treatment was used.

METHODS. 42 patients admitted to ICU after a SIS all under the same protocol of management were studied. A case-control design was used for this study. Group 1 (22 patients) received ICU treatment plus rehabilitation services in an outpatient rehabilitation setting, and Group 2 (20 patients) received ICU treatment without receiving this kind of rehabilitation program after discharge from hospital. The mean duration of the post-ICU rehabilitation treatment was 6 months. Both groups were homogenous in severity evaluated by GCS, Canadian Scale and The APACHE II. Major clinical (side of lesion, type of stroke, surgery, hospital length of stay, etc), and demographic (age, years of education, etc.) variables were examined to prove the homogeneity between groups. Functional recovery, measured 6 months after discharge of ICU was measured by the Functional Independence Measure (FIMTM) and the Functional Assessment Measure (FAM). The initial and the final FIM-FAM score were compared between groups using the U of Mann-Whitney test; and within groups using the T of Wilcoxon for paired samples test. Relative functional gain was calculated.

RESULTS. Patients from Group 1 showed better results in every FIM-FAM functional areas than patients from Group 2. Areas psychosocial adjustment and cognitive functions showed significant differences between groups (p-value <0.01). The functional gain was either better in Group 1, where significant differences were found in most of the functional areas as self-care, mobility, transfers (p-value <0.05); psychosocial adjustment and cognitive functions (p-value <0.01). Group 1 achieved a higher functionality than Group 2, while the first one obtained a functionality of about 70%, Group 2 only obtained a functionality of about 50%.

CONCLUSION. The ICU treatment of patients with SIS increases its efficiency if after discharging patients a specific rehabilitation treatment is applied. The treatment performed in the intensive care unit must be enhanced by providing an additional outpatient treatment that increases its efficacy and makes worthwhile the ICU intervention.

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EVIDENCE BASED PRACTICE GROUPS IN INTENSIVE CARE

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INTRODUCTION. The health care knowledge base has increased enormously in recent years.Yet, due to a time lag between conduct of research and change in practice, many patients do not benefit from results of research. At Ullevål University Hospital a project to pilot evidence based practice groups was established in the surgical intensive care units in 2002. The purpose of this presentation is to describe the improvement process.

METHODS. The small group method as described by Greenhalgh (1999) was used as a vehicle to introduce evidence based practice. The groups used the five steps process of evidence based practice described by Sackett. (2000): (1) ask a question about practice that can be answered. (2) find the best evidence.(3) appraise the evidence. (4) use the best evidence. (5) evaluate the change.

RESULTS. A total of 7 groups of 3-8 nurses have been established so far. The groups received training and subsequent facilitation by a masters prepared critical care nurse researcher. The topic for exploration was discussed in the group and a clinical question formulated. All group members participated in electronic database searching, relevant articles were selected by the group and read by all members. One member presented the article at group meetings and the group critically appraised the article in plenum. The evaluation of each individual article concluded with level of evidence, strengths and weaknesses of the study. In order to evaluate the strength of the body of research evidence for the question, articles with good quality were recorded in a schema. This summary of evidence then formed the basis for developing a procedure or guideline on the topic. which was then implemented in the unit. Examples of topics addressed include oral care for the intubated patient, prevention of postoperative lung complications, suctioning adults with an artificial airway and use of central venous catheter. Six new procedures or guidelines have been developed.

CONCLUSION. We have found that introducing evidence based practice by small group method in critical care nursing reduces the gap between research and practice.

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SUCTIONING PATIENTS WITH AN ARTIFICIAL AIRWAY

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INTRODUCTION. Suctioning the artificial airway of the critically ill patient is a common nursing procedure in the intensive care unit. We questioned whether our current procedure was based on the best available research evidence. The aim of this study was to explore the latest research related to this nursing procedure and develop a new procedure based on the latest research evidence.

METHODS. We used the evidence based process described by Sackett and a literature search was conducted in following electronic databases: CINAHL, EMBASE, OVID, PubMed, and The Cochrane Database. Following search terms were used: suctioning, artificial airway, respiration, saline and suctioning, mechanical ventilation and tracheotomy. We did a critical appraisal of the literature in order to find the best available research evidence. We found a systematic review of high quality; this paper had cited 95 studies and 350 papers had been discussed.

RESULTS. The current procedure used in clinical practise was not based on the latest research evidence. We had a routine when the patients were suctioned minimum 3 times a day. Research showed that suctioning of the patients airways should be based on a clinical assessment, not on routine. Research also showed that hyperinflation together with hyperoxygenation via the respirator could minimise suctioning introduced hypoxemia and result in less haemodynamic alteration compared to using a manual resuscitation bag. Exploring the latest research evidence lead to development of a new procedure.

CONCLUSION. By using evidence based strategies we developed and implemented a new procedure in suctioning patients with artificial airways. Hyperinflation and hyperoxygenation via the respirator were introduced in the new procedure instead of using a manually resuscitation bag. A clinical assessment is performed instead of the routine of suctioning the patient minimum 3 times a day.

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COMPARISON OF EARLY WARNING SCORE TRIGGERS IN A HAEMATOLOGY AND ACUTE MEDICAL WARD

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INTRODUCTION. Critical Care Outreach incorporating a modified Early Warning Score (EWS) based on simple bedside physiological monitoring has demonstrated reduction in cardiac arrest in general medical and surgical patients (1). In our hospital, EWS has been delivered to some patient groups for 4 years using temperature, conscious level, blood pressure, pulse and respiratory rate. Recently we have introduced EWS to the haematology unit. The aim of this study is to investigate whether EWS used in general medical wards is appropriate for haematology.

METHODS. Data were prospectively collected on the 20-bed haematology unit for 4 weeks and 2 acute general medical wards for 2 weeks. We collected all scores >or= 3 with a breakdown of contributing parameters and interventions performed by staff after each trigger. We then compared the aggregate trigger scores from each area and the trigger ratio - total triggers to the number of new trigger episodes indicating how rapidly scores are reduced. Data were analysed by \chi2 tests.

RESULTS. On the haematology unit 17 patients had EWS >or= 3 145 times. On the general wards 19 patients had EWS >or= 3 100 times. The median score in both groups was 4. The spread of aggregate EWS scores in haematology patients was not statistically different. Altered temperature contributed to 91 (63%) triggers in haematology compared to 9 (9%) on the general ward p< 0.05. 114 interventions were performed on patients in the haematology ward.

TABLE 1.

	Patients EWS >=3	Total Triggers	New Episodes	Trigger Ratio	28 day survival
Haematology	17	145	50	2.9	15
General Medical	19	100	34	2.94	12

CONCLUSION. 1. Modified Early Warning Score as part of a Critical Care Outreach service can be successfully implemented on a specialist haematology unit.2.We found no differences in the aggregate trigger scores or trigger ratios. 3 Temperature rises were more commonly associated with triggers in haematology

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NURSING DEPENDENCY OF CANCER PATIENTS IN THE CRITICAL CARE UNIT

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INTRODUCTION. Cancer patients are increasingly admitted to the critical care unit. There is concern that this development requires critical care nurses to acquire new special skills previously unfamiliar to them (1) which could potentially lead to a significant increase of their workload.
The aim of this study was to determine whether patients with solid tumours and haematological malignancies require any more nursing input than nephrology patients in whom admission to the intensive care unit is common practice and less controversial.

METHODS. We analysed the data of all cancer patients and renal patients who died in the critical care unit of a teaching hospital between February 2004 and March 2005.

RESULTS. 17 cancer patients and 15 renal patients died during the 13 months period. Table 1 shows the differences between both groups.

TABLE 1.

	Cancer patients (n=17)	Renal patients (n=15)	p - value
Average TISS score (mean, SE)	46.1 (3.3)	56.4 (3.5)	NS
Maximum TISS score (mean, SE)	54.9 (3.6)	61.4 (3.2)	NS
Day 1 mean APACHE II score (SE)	22.3 (2.3)	29.5 (2.1)	< 0.05
Ventilatory support	41%	80%	< 0.05
Withdrawal of therapy	53%	40%	NS

SE = standard error

CONCLUSION. Renal and cancer patients who died in the critical care unit required high nursing input, both technical and pastoral. Average TISS score of cancer patients was not higher than that of renal patients. Admitting an increasing number of cancer patients to the critical care unit should not cause the nurses to need new skills. In contrast, skills that already exist in the care of critically ill and dying patients are enhanced further.

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TSUNAMI VICTIMS IN HELSINKI BURN UNIT

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INTRODUCTION. On Boxing Day, December 26th 2004, a tsunami hit Thailand´s resort area. 174 Finnish tourists died or disappeared and over 200 were seriously injured.The Department of Plastic Surgery,which is a part of the Helsinki and Uusimaa Hospital District,received 25 patients. Six of them needed intensive care and were treated in the Burn Unit. Patients suffered extensive, infected soft tissue injuries and fractures. Computer tomography verified pulmonary emboli in all patients. Several patients had sinusitis and otitis.

METHODS. Patients were cohorted into two rooms because of similar bacterial infections and we wanted to avoid cross-infection with burn patients.Many of the disaster victims had lost most of their relatives.During the hospital stay effective wound care, pain management,intensive care for septic patients and crisis therapy were emphasized. Co-operation with infectious diseases consultants, orthopaedics, otolaryngologists, radiologists and physio- and occupational therapists was part of our daily procedures. Crisis therapy was carried out in co-operation with consulting psychiatrists, crisis therapist and unit staff member.

RESULTS. The injuries the patients sustained demanded especially the wound care- and operating skills that the plastic surgery unit was able to offer. By isolating the patients we avoided crossinfection with other patients.Being in the same room made possible the mutual mental support between the disaster victims.

CONCLUSION. It is suitable to treat patients with extensive soft tissue injuries and infected wounds in a Burn Unit with previous skills in plastic surgery wound care,pain management,crisis therapy and possibility to cohort patients.

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FACTORS THAT INFLUENCE REGISTERED NURSES WHEN ASSESSING WARD PATIENTS WITH CRITICAL ILLNESS

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INTRODUCTION. This research study uses a phenomenological approach to investigate the experiences of six E-grade surgical ward nurses when identifying and assessing ward patients with potential or established critical illness. Improving care of the critically ill ward patient has been prioritised by the current government and is underpinned with recent government guidelines and financial backing

METHODS. The study reviews quantitative and qualitative literature which identifies reasons for sub-optimal care on the wards, and factors that influence nurses when caring for these patients. There is a paucity of experiential research studies in this area. In the light of this, the study uses a semi-structured interview approach to investigate the lived experience of these nurses when identifying and assessing this complex group of patients.

RESULTS. Data analysis reveals four main themes: the nursing gaze, learning, use of an early warning scoring tool (EWS) and other confounding factors. It is evident from the data that the nursing gaze was a unanimous theme, with participants making reference to the „look" of the patient, use of intuition, observation of cues, and corroboration from other members of staff. Learning was perceived to be experiential, and all the participants reflected on practice. The limited sensitivity and specificity of EWS is reviewed, particularly with its applicability to the specialist surgical ward. Communication between professions was not found to be improved by EWS in this study. An unexpected finding suggests EWS is used as a tool for nurses and doctors to manipulate and achieve personal objectives rather than as a tool for nursing to optimise patient care. The participants portray frustration with other factors such as inexperience of junior doctors, increased dependency of ward patients, and lack of equipment.

CONCLUSION. This small-scale qualitative study has provided a rich source of data from which recommendations have been made to support high quality nursing and medical care of ward patients at risk of critical illness.

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THE FIRST RECEPTION OF PATIENT'S FAMILY BY THE NURSE IN THE ICU: FEELINGS AND EMOTIONS

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INTRODUCTION. Patients admit to the intensive care units are mostly people in an unstable condition with their lives in danger and with a very reserved diagnostic. There are minimized the social, professional and familiar dimensions of the person, and so nurses must care, not only the patient, but also the family. When a member become seeks there are functional and structural changes in the whole family. It is extremely important to inform the family before being with their relative. This is an human investment moment.

METHODS. The authors conducted a qualitative approach to describe the feelings and emotions of the patient's family in the first reception by the nurse in the ICU. The instrument used to data collection was a semi-structured interview.A non-selected sample whit a non-probabilistic and accidental pattern was applied. Seven patient relatives constituted it. The data treatment was based on the content analysis applied on the interviews corpus.

RESULTS. After the analysis of the seven interview corpus, it was possible to observe that the most noticeable category was the "psychological-emotional references" with 76 % of the total. The second most noticeable category was "environment references" corresponding to 19% of all citations. The last category noticeable was "physical references" with 5% of all citations.

CONCLUSION. The research findings demonstrated the need to inform the family before being with their relative in the ICU. The negative feelings and emotions may be minimized with an empathetic relation, in privacy and comfort. Instead these research limitations, we can argue that nurses in ICU must care the family, being present and answering their questions. The nurses must also respect the need to be alone with the relative, but never being so far that family don't feel supported.

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INTERNET HOME PAGES FOR THE INTENSIVE CARE UNIT IN CENTRAL FINLAND CENTRAL HOSPITAL

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INTRODUCTION. The purpose of the dissertation was to design internet home pages for the Intensive Care Unit (ICU) in Central Finland Central Hospital. The project was carried out in co-operation with the ICU and information management in Central Finland Health Care District.

METHODS. The purpose of the home pages is to respond to the needs of information about ICU and and intensive care. These needs come out from the studies about intensive care. Also the purpose is to is to increase knowledge about ICU and intensive care. The target group were patients´ relatives, health care students and employees. The use of internet is increasing. This fact supports the use of home pages as means of communication. In designing an internet publication, it was important to notice for exemple the importance of compact expression, clarity of layout and the properties of different kinds of internet browsers. The text and the pictures must together contribute to the conveying of in information. On ICU´s home pages one page was reserred to information, one for presenting intensive care and one for the patients´ relatives. The largest unit is the virtual tour in the ICU, where the ICU is presented through text and pictures. The photos, taken for the project were changed into digital form. The manuscript was made by using PowerPoint 2000- program and it acts as a model for the final electronic version; how to use the photos, the text and the links. After manuscript was accepted in ICU, it was taken to the information management for publication

RESULTS. The home pages of ICU was published on home pages of Central Finland Health Care District in February 2002 at http://www.ksshp.fi.

CONCLUSION. The pages have been in good use and they have been updated in Nov 2004.

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PROGNOSTIC VALUE OF IMMUNE ALTERATIONS IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Alterations in immune function may facilitate the development of nosocomial infection or induce organ dysfunction through overwhelming inflammatory response. We studied the relationship between changes in immune markers and mortality in ICU patients.

METHODS. Patients admitted and expected to stay in the ICU for 4 days were included (Dec 2003 - March 2004 and Sept - Nov 2004). Blood was collected every day for flow cytometry analysis of the circulating leukocytes in a lysis, no wash, direct staining technique with quantification of fluorescence using the Quantibrite kits for CD64 and HLA-DR antibody binding site enumeration on the surface of polymorphonuclear leukocytes and monocytes, respectively.

RESULTS. The study included 105 patients (40 medical, 53 surgical and 12 medico-surgical), of whom 38 were female (36%), with a mean age of 63±17 years. The overall 28-day mortality was 31% (33/105). Quantibrite CD64 was higher in the non-survivors than in the survivors on the 1st (2722±3959 vs 1581±3211) and 2nd (2683±3821 vs 1704±2099) day after admission (both p=0.03). The ROC curve of Quantibrite CD64 predicting 28-day mortality on the 1st day following admission showed a sensitivity of 85%, a specificity of 70%, with an area under the curve (AUC) of 0.70, positive predictive value of 50% and negative predictive value of 93% at the level of 2222 molecules/cell. For the Quantibrite HLA-DR, the survivors showed a higher and increasing level on the 2nd day to the 5th day after ICU admission (10569±6778 to 12557±5791 compared to non survivors (7260±3428 to 6327±3074) (p=0.03 survivors vs non-survivors 2nd day, p=0.02 survivors vs non-survivors 5th day). The ROC curve of Quantibrite HLA-DR predicting 28-day mortality on the 5th day following admission showed a sensitivity of 88% and a specificity of 73%, with an AUC of 0.81, positive predictive value of 70% and negative predictive value 89% at the level of 8253 molecules/cell.

CONCLUSION. Immune changes in the surface markers of the white blood cell can help predict outcome in ICU patients. While Quantibrite CD64 has an early predictive ability, the predictive ability of Quantibrite HLA-DR is better although a little delayed.

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INCREASED SOLUBLE TRIGGERING RECEPTOR EXPRESSED ON MYELOID CELLS PREDICTS POOR OUTCOME IN SEPSIS

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INTRODUCTION. Triggering receptor expressed on myeloid cells-1 (TREM-1) is a novel membrane molecule mainly expressed on neutrophils and monocytes stimulated by microbial products. The present study aimed to clarify differences of sTREM-1 concentrations upon evolution from sepsis to septic shock and any prognostic implications.

METHODS. Blood was sampled from 90 patients with septic syndrome (ACCP/SCCM 1992 criteria) due to ventilator-associated pneumonia on seven consecutive days after initiation of symptoms. Patients were classified in three groups: sepsis, severe sepsis and septic shock. Concentrations of tumour necrosis factor-alpha (TNFa), interleukin-6 (IL-6), IL-8 and sTREM-1 were estimated by ELISA. Serum levels of sTREM-1 were compared between the groups and between survivors and non-survivors at 28 days.

RESULTS. No differences in concentrations of TNFa, IL-6 and IL-8 were found between patients in the three groups. Patients presenting with septic shock had concentrations significantly higher than both patients with sepsis and severe sepsis in all days of follow-up. Similar findings were noted between patients who eventually survived and those who died (Table 1).

TABLE 1.

Mean+/- SE serum sTREM-1 concentrations (pg/ml) of survivors and non-survivors

	SURVIVORS	NON-SURVIVORS	p
DAY 1	144,03+/-28.82	177,30+/-31,73	NS
DAY 2	145,72+/-28,61	241,72+/-49,48	<0,05
DAY 3	144,86+/-30,11	205,69+/-48,67	<0,05
DAY 4	144,25+/-27,32	206,10+/-39,82	<0,05
DAY 5	159,89+/-24,40	291,97+/-82,44	NS
DAY 6	144,73+/-24,12	323,62+/-91,46	<0,05
DAY 7	162,78+/-32,64	235,19+/-53,40	NS

CONCLUSION. sTREM-1 is particularly increased upon evolution from sepsis or severe sepsis to septic shock. Its increase is an indication of poor outcome. The pathophysiological role of sTREM-1 for the transition from sepsis or severe sepsis to septic shock might constitute a novel target for immunomodulatory therapy.

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PLAZMA FREE APOPTOTIC DNA AS A PREDICTOR OF ORGAN DYSFUNCTION OR DEATH IN CRITICALLY ILL PATIENTS

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INTRODUCTION. The aim of the study was to estimate the trends and prognostic value of apoptotic DNA (aDNA) and necrotic DNA (gDNA) in critically ill patients.

METHODS. 94 critically ill patients (APACHE II 22,7 SD=8.8) were enrolled into the study. The following data were collected: age, gender, duration of ICU stay, SOFA score, CRP, WBC, morbidity and mortality. The blood samples for the plasma free nucleic acid analysis were taken on admission, 3rd and 5th day. Analytical method: after the extraction of interferring substance to phenol, 10 microlitres of phenol/2-butanol/chloroform deproteinized plasma was run on sequencer (ABI Prism 377). The DNA values were compared with normal values estimated in blood taken from the control group of 86 healthy volunteers (normal value = 100%). Statistical methods: ANOVA test, Fischer LSD post hoc test, Mann Whitney test.

RESULTS. The increase of plasma free aDNA and gDNA was statistically significant (p<0,001). The aDNA affected the total amount of DNA by the crucial way. The apoptotic DNA increase in median value was 16.3 times higher compared to gDNA (p<0.001). In a period of 5 days its values showed decrease contrary to the increasing levels of gDNA (p<0.001). The statistically significant correlations between the aDNA in the time of admission and SOFA score on 3rd day (p<0.05) and mortality were found (p<0.05).

CONCLUSION. Early stage of critical illness is first of all followed by the pronounced apoptosis. The increase of necrotic gDNA in plasma seems to be connected with a secondary insult.

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PROGNOSTIC VALUE OF PC AND ATIII LEVELS IN SEPSIS

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INTRODUCTION. Severe Sepsis is a devastating disorder characterized by systemic activation of the inflammatory and coagulation system in response to microbial infection. Alterations in levels of different mediators of coagulation and fibrinolysis have been reported to be associated with negative outcome in patients with severe sepsis. Lately, a large phase 3 multinational placebo-controlled randomized clinical trial demonstrated the efficacy and safety of recombinant activated protein C for severe sepsis. The aim of this study was to assess of the prognostic value of PC and ATIII levels during the first 8 days after admission on patients with sepsis.

METHODS. Prospective analysis of patients admitted with sepsis in the ICU. SAPSII and SOFA were evaluated at admission. Blood samples were obtained from all patients at days 1, 4 and 8 after the admission for the determination of protein C and antithrombin III levels (laboratory test used was the IL testTM PC/AT III kit – Instrumentation Laboratory). Data analysis and statistics were performed using SPSS 11.5.

RESULTS. 24 patients with severe sepsis were studied; (average age - 56, 79 ± 18,12; SAPS II – 39 ± 12,12 (37,5); SOFA – 9 ± 3,77 (9)). The table shows the difference between survivors and non-survivors (data expressed as median):

TABLE 1.

	Day 1 PC (%)	Day 1 ATIII (%)	Day 4 PC (%)	Day 4 ATIII (%)	Day 8 PC (%)	Day 8 ATIII (%)
Survivors (16)	53,6	68,35	73,25	79,7	86,6	95,5
Non-survivors (8)	33,5	40,7	21,85	33,8	34,6	17,4

CONCLUSION. Findings from this study showed that almost all patients had low PC and ATIII levels at admission (lower in non-survivors). In the survivors subgroup the levels tend to normalise after day 4. On the contrary, in the non-survivors subgroup the levels maintained low until the day 8. These results enforce the prognostic value of these two anticoagulants and its contribution for the decision to start treatment with recombinant human activated PC.

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SEVERE SEPSIS INDUCES SPECIFIC CHANGES IN PERIPHERAL BLOOD DENDRITIC CELLS: IMPORTANCE FOR SURVIVAL

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INTRODUCTION. The role of Dendritic Cells (DC) in sepsis is poorly understood. Our aim was to investigate the dynamic changes of peripheral blood DC (PBDC) and of their myeloid and plasmacytoid subsets (mDC and pDC) at the onset and during the evolution of severe sepsis.

METHODS. We included 27 septic pts, 10 surgical pts (elective aortic aneuirism surgery) and 20 healthy controls (HC). In sepsis samples were collected at diagnosis and at clinical resolution or before death; in surgical pts, on the 1th post-op. day. By flow cytometric analysis DC are recognized by immunoglobulin-like-transcript-3 and differentiated in mDC and pDC subsets by CD11c and CD123. Results are median and IQR of absolute DC numbers (x 106/L).

RESULTS. At diagnosis, in sepsis mDC decreased (p<0.001 vs HC) while pDC increased(p=0.03), with a reduced mDC/pDC ratio (p<0.001). On the contrary, after surgery both mDCs and pDCs diminished (p<0,001), without mDC/pDC ratio change(Table 1). At diagnosis, no difference in mDC was found between 16 septic survivors (SS) and 11 non survivors (SNS), while pDCs were significantly higher in SNS (p= 0,03). Moreover, with respect to HC, pDC were significantly higher only in SNS (p=0,002). In the final sample mDC were unchanged in SNS, but selectively increased in SS (p=0,001); no differences in pDC between the two samples were observed both in SS and in SNS. As a result, the ratio of mDCs to pDCs was unchanged in SNS whereas it significantly increased in survivors (p<0,001).

TABLE 1.

	Healthy (HC)	Sugical (SP)	Septic Pts
PBDC	36,5 (30,1-41,3)	10,7 (7,2-21,8)*	18 (9,4-36)**
mDC	26,5 (19,6-30,5)	9,9 (7,2-11,7)*	3,5 (1,5-7,7) * °°
pDC	11,1 (8,1-12,3)	2,7 (1,5-5,5) *	14,5 (9,3-29,2)** °°
mDC/pDC2	2,17 (1,9-2,3)	2,8 (1,4-3,3)	0,2 (0,16-0,34)*°

**p < 0,001 vs HC, ** p < 0,05 vs HC, ° p < 0,001 vs SP, °°p < 0,05 vs SP*

CONCLUSION. Our findings suggest that PBDC are affected by severe sepsis. Moreover the two subsets are differentially impaired. These alterations are sepsis specific and survival seems linked to recostitution of the normal mDC/pDC ratio.

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SEVERE SEPSIS. MORTALITY AND ASSOCIATED RISK FACTORS AT DIAGNOSIS. RESULTS OF A SPANISH MULTICENTER STUDY

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INTRODUCTION. There are no data available about the mortality of severe sepsis and its associated risk factors in the Spanish ICUs. OBJECTIVES. To know the hospital mortality rate of severe sepsis and the associated risk factors at diagnosis.

METHODS. Prospective, observational, multicenter, cohort study, carried in 14 ICUs of 13 hospitals in Spain during a six months period of 2002. All patients admitted for severe sepsis (1) or those who developed severe sepsis during the ICU stay were included. Age, sex, admission category and source of admission; co-morbidities, organs and systems failures at diagnosis, defined according to the PROWESS trial (2), the Logistic Organ Dysfunction (LOD) score (3) and the severity of the underlying disease, if any, according to McCabe´s classification; and the mode of acquisition and source of infection were recorded at diagnosis (day 0). The results are expressed in absolute numbers or as percentage. A logistic regression model was adjusted to define the mortality by variables existing at diagnosis, and their odds ratio (OR) estimated with 95 % C.I. were calculated.

RESULTS. 311 septic patients were included. Among those, 324 episodes of severe sepsis were diagnosed. The hospital mortality rate was 54.3 %. Risk factors significantly associated with death were: age (<45; 45-80; >80), OR 3.14 (1.51, 6.54); McCabe´s classification score (per point), OR 1.72 (1.25, 2.37); chronic alcoholism, OR 2.92 (1.01; 8.93); LOD score (day 0)(per point), 0R 1.37 (1.24, 1.51) and urinary source of sepsis (pulmonary source = 1), OR 0.09 (0.02, 0.52).

CONCLUSION. 1. Incrementing age according to the defined intervals was strongly associated with death risk. 2. Higher McCabe´s classification score was significantly associated with increased risk of death 3. Mortality risk in severe sepsis is almost three times higher in chronic alcoholics. 4. A higher LOD score at diagnosis was significantly associated with higher risk of death. 5. In patients with severe sepsis, urinary tract source conveys significantly lower mortality risk.

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QUALITY OF GENETIC ASSOCIATION STUDIES IN SEPSIS, A SYSTEMATIC REVIEW

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INTRODUCTION. Epidemiological studies demonstrate that genetics play a significant role in the development and prognosis of sepsis. However genetic association studies in sepsis have failed to provide compelling evidence of an effect from individual polymorphisms. Major methodological flaws have been reported in a number of non-sepsis genetic association studies, relating to problems with control group, case group, reliability of genetic assay technique, blinding, study size, statistical rigour and publication bias [1,2]. We therefore systematically appraised the quality of published genetic association studies in sepsis using a newly devised scoring system.

METHODS. A systematic review of all genetic association polymorphism studies in sepsis was performed using a combined primary electronic and secondary hand based search strategy. Selected papers were scored on methodological quality using a nine point scale [1,2] assessing the robustness of patient and control groups, whether control groups were in Hardy-Weinberg equilibrium, blinding, reproducibility and validity of polymorphism detection, study power and the presence and adequacy of statistical methods employed. Power calculations were performed for all case control studies.

RESULTS. 133 articles were identified; of these 62 studies assessing 98 polymorphisms were suitable for inclusion. Median score was 5 out of a possible score of 9. No study achieved a score greater than 7. Only 3 of 33 case control studies were adequately powered. Only 23% of total studies demonstrated Hardy-Weinberg equilibrium, 31% used an externally validated polymorphism assay and only 52% used appropriate statistical techniques in analysis.

CONCLUSION. The majority of genetic association studies were of sub-optimal quality and underpowered. This could explain the lack of consensus in the published literature, regarding the effects of genetic polymorphisms in sepsis.

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WHOLE GENOME EXPRESSION PROFILING IN MULTIPLE TRAUMA PATIENTS

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INTRODUCTION. Severe trauma patients are at high risk developing sepsis and MOF[1-3]. Serial gene expression analysis obtained from patients with multiple trauma should provide a molecular portrait of mechanisms leading to sepsis and finally MOF.

METHODS. We conducted a prospective study after obtaining institutional approval from the Ethics Committee of the University of Giessen. Whole blood samples were collected at admission to the ICU (TP 0) from 21 patients with multiple trauma. Total RNA was isolated from peripheral blood of each patient at TP 0 and subjected to microarray analysis using the CodeLink UniSet Human I Bioarray (Amersham) containing 9,877 human genes. Data analysis was done using ImaGene5(Amersham), dChip(www.dchip.org) and SAM(www-stat.stanford.edu).

RESULTS. 10 patients developed sepsis while 11 remained non-septic. Multiple testing with a FDR of 1.1 [4] revealed in total 692 significantly regulated genes in septic patients at TP 0, of which 480 genes had significantly higher and 212 genes significantly lower expression levels compared with non-septic patients at TP 0. The highly expressed genes were mainly involved in inflammatory- and stress- responses, apoptosis and development while the lower expressed genes could be assigned to defense responses, protein biosynthesis and lipid binding (Fig. 1). Hierarchical clustering of the samples clearly differentiated between time point of admission and sepsis (Fig. 2).

CONCLUSION. Statistical analysis of expression data enabled clear differentiation between non-septic and septic trauma patients at admission to the ICU (TP 0). Septic patients showed significant over expression of genes involved in immune responses and anti-apoptosis indicating a strong inflammatory interaction at time of admission as compared to non-septic patients. The early vigorous inflammatory response appears to activate a program, subsequently leading to SIRS and finally MOF.

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POLYMORPHISMS IN THE INTERLEUKIN 1 GENE CLUSTER IN CHILDREN WITH SYSTEMIC MENINGOCOCCAEMIA

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INTRODUCTION. Meningococcal disease can present as sepsis, meningitis or a combination of both. Upregulation of proinflammatory cytokines, especially Interleukin 1a (IL1a), 1b (IL1b) and the Interleukin 1 receptor antagonist (IL1RA), are crucial components in the initiation and regulation of the inflammatory cytokine cascade in meningococcal sepsis. Over-expression of IL1a and IL1b or suppression of their antagonist IL1RA has been shown to lead to the clinical characteristics of septic shock. Previously, an association between mortality and the functional polymorphisms in the Interleukin 1 cluster in children with meningococcal disease has been reported. We have carried out a prospective, multicenter study to confirm these observations in the Central European and UK population.

METHODS. Blood samples and clinical information of 281 previously healthy children with meningococcal infection were collected from 95 paediatric hospitals in Germany, Switzerland, Italy, the United Kingdom, and Austria between 2000 until 2002. Cord blood of 481 healthy newborns, all of Central European origin, served as population based healthy controls. The following 6 polymorphisms within the Interleukin 1 cluster were analysed by a newly developed multiplexed mutagenic separated PCR assay: IL 1a (-899)C/T, IL 1a(-4845)G/G, IL 1b (-511)C/T, IL 1b (-31)C/T, IL 1b (+3954) and IL1RA (2018)C/T).

RESULTS. Significant differences in genotype frequencies between patients and controls were only observed for the IL1RA (+2018)C/T polymorphism: The CC genotype was more frequent in patients (11%) compared to healthy controls (5%, p=0.008). The C allele was significantly more prevalent (67%) in non survivors than in survivors (42%, p=0.02).

CONCLUSION. In our study we provide evidence that the IL1RA (2018)C/T polymorphism is not only associated with outcome but also the risk for meningococcal disease. As the C allele is associated with decreased IL1RA levels, further studies evaluating IL1RA substitution in selected patients with meningococcal disease might be worth considering.

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GENETIC VARIATION OF TNF IS ASSOCIATED WITH SEPSIS AND DEATH IN MULTIPLE TRAUMA PATIENTS

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INTRODUCTION. Patients encountering severe trauma are at high risk of developing SIRS and MOF(1-4). By examining several candidate genes (TNF, PAI-1, IL-1, IL-6)(5;6), we now report that genetic variation in TNF and/or LTA is predictive for the development of sepsis in multiple trauma patients.

METHODS. 159 multiple trauma patients were included prospectively at admission to the ICU with an ISS of 12 pts or more. We genotyped all known SNPs including those in the 5´ region of the TNF gene, including LTA. Univariate analysis and multivariate logistic regression analysis were performed.

RESULTS. 72 patients (45.3%) fulfilled the criteria for sepsis after severe trauma and 32 (38.9%) patients died from a sepsis leading to MOF. Allele distributions were according to the Hardy-Weinberg-equilibrium. A significant association for the incidence of sepsis after multiple trauma was observed for the TNF -308A allele (OR 7.14; 95% CI, 3.1 to 16.45; p<0.0001), and the completely linked LTA +252G allele (OR 1.96; 95% CI, 1.02 to 3.78; p<0.042). Additionally, both alleles showed significant association with death after severe trauma (TNF -308A: OR 7.65; 95% CI, 13.27 to 17.93; p<0.0001; LTA +252G: OR 5.58; 95% CI, 2.02 to 15.44; p<0.0002).

Genotype TNF alpha -308	total n=159	sepsis n=72	death n=32	Genotype LTA +252	total n=159	sepsis n=72	death n=32
homozygous G/G	117	35	12	homozygous A/A	67	24	4
heterozygous G/A	41	36	20	heterozygous A/G	74	38	20
homozygous A/A	1	1	0	homozygous G/G	18	10	8

CONCLUSION. The presence of one or two copies of the TNF -308A, LTA +252G haplotype is strongly predictive for the incidence of sepsis and death in multiple trauma patients.

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ASSOCIATION BETWEEN MORTALITY AND TWO TNF POLYMORPHISMS IN ACUTE SEVERE PANCREATITIS

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INTRODUCTION. The objective of this study is to assess if there is any association between mortality and the presence of two TNF polymorphisms in patients admitted to the ICU due to acute severe pancreatitis

METHODS. Prospective cohort study, including patients admitted to the ICU due to acute severe pancreatitis.After obtaining informed consent, it was proceeded to extract DNA and determine two TNF polymorphisms from peripheral blood:-308 promoter region of TNF alpha (TNF1/TNF2)and NcoI (TNFB1/TNFB2) polymorphisms were determined with specific probes by means of RCP, enzymatic restriction and electrophoresis.Demographic variables, aetiology, underlying deseases, APACHE II, SOFA and Ramson scale were registered at admission.Hospital mortality was registered.The research team carrying out the polymorphism was blinded to the clinical evolution of the patients.The statistic analysis was performed using exact Fisher test and t-student (p<0.05 significance level).

RESULTS. Forty six patients suffering acute severe pancreatitis were included.There were no differences between mortality in TNF1 (35 GG;25.7 mortality) and TNF2 (11 GA and 1 AA; 18.1 mortality) groups.Twenty two patients had TNFB1 genotype (5 GG and 17 GA)and 24 patients had TNFB2 (AA).Hospital mortality was significantly higher in TNFB2 than in the rest of subjects (37.5% vs 9%, p<0.05).There were no differences in SOFA and Ramson scores between both groups. Billiary aetiology was the most frecuent one in TNFB1 group (16 episodes), whereas that in TNFB2 group was alcohol aetiology (11 episodes).

CONCLUSION. Homozygotic patients for TNFB2 admitted to the ICU due to acute severe pancreatitis exhibit higher mortality.

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4G/4G POLYMORPHISM OF THE PLASMINOGEN ACTIVATOR INHIBITOR-1 GENE ASSOCIATES WITH PLATELET COUNTS BUT NOT WITH FIBRINOGEN LEVELS IN CHILDREN WITH MENINGOCOCCAL DISEASE

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INTRODUCTION. Severe forms of meningococcal disease are invariable associated with derangement of plasmatic coagulation. We and others have shown that the 4G4G genotype of a common 4G/5G insertion/deletion polymorphism located within the promoter region of the PAI-1 gene, 675 base pairs upstream of the transcription start site, was significantly more frequent in non survivors than in survivors. In the present study we describe the influence of this polymorphism on plasmatic coagulation of the same patient group.

METHODS. We have designed a prospective, multicentre study in a Central European population to investigate the influence of selected genetic polymorphisms on susceptibility and outcome of meningococcal disease. Between January 2000 and October 2002 blood samples and clinical information of 240 previously healthy children with meningococcal infection were collected from 95 pediatric hospitals in Germany, Switzerland, Italy, and Austria. For the detection of the insertion/deletion polymorphism, an allele specific PCR was used. PAI-1 genotypes were correlated with platelet counts, serum fibrinogen levels, aPTT and INR on admission, and disseminated intravascular coagulation (DIC) during the course of disease. DIC was defined according to the 2001 International Sepsis Definition Conference guidelines.

RESULTS. On hospital admission, patients with the 4G4G genotype showed a significantly lower mean platelet count (173.0 G/L vs. 225.4 G/L, p=0.003), but no association with mean serum fibrinogen levels, aPTT, and INR was found. DIC showed a strong association with the 4G4G homozygotes (36.0% in DIC patients vs. 21.3% in non-DIC patients, p=0.013). The allele frequencies of 4G and 5G were similar between patients and controls.

CONCLUSION. Our data show that the 4G4G genotype of a common PAI-1 promoter polymorphism has a distinct influence on manifestation of coagulopathy in meningococcal disease. On hospital admission, the 4G4G allele causes lower platelet counts but has no influence on fibrinogen levels. During the course of the disease the 4G4G genotype is significantly associated with DIC.

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TISSUE FACTOR GENE POLYMORPHISMS AND MORTALITY IN SEPTIC SHOCK PATIENTS

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INTRODUCTION. The Tissue Factor (TF) is a powerful activator of the coagulation cascade and plays an important role in the pathogenesis of the septic shock. Four polymorphisms have been described that are in linkage disequilibrium. Two different haplotypes (D and I) are associated with different TF production. This study aims to evaluate if the presence these haplotypes in patients with septic shock is associated with an increased mortality.

METHODS. Prospective cohort study including patients admitted to the ICU for septic shock (ACCP/SCCM criteria). Alter obtaining written consent, DNA was extracted from peripheral blood cells to determine the polymorphism of TF (-1208 D/I). DNA was amplified with specific probe using PCR, enzymatic restriction and electrophoresis in agarose (band of 204 pb homozygous I, band of 186 pb homozygous D and two bands heterozygous H). The following variables were collected: age, gender, underlying comorbidities, clinical presentation, source of sepsis, APACHE II score at admission, SOFA score, adequate empirical antibioteraphy, and in-hospital mortality. The statistical analysis was performed using the chi-square, t-student, and ANOVA tests, with level of significance at p< 0.05.

RESULTS. Ninety-three consecutive Caucasian patients fulfilling septic shock criteria were enrolled: 46 H, 27 D and 20 I. The mortality was respectively of 43.5%, 37% and 20 % (p> 0.05). The groups were comparable in relation to the primary site of infection, and severity of illness at admission (APACHE II and SOFA score). If the patients with inadequate empirical antibiotherapy were excluded from the analysis (5 in H, 1 in D and 2 in I) mortality was not statistically different (41.5%, 34.6 % and 27.7%)

CONCLUSION. TF polymorphism (-1208 D/I) does not seem to influence the outcome of patients admitted to the UCI for septic shock.

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DIFFERENTIAL GENE EXPRESSION IN THE TH1/TH2 DIFFERENTIATION PATHWAY IN SIRS AND PRE-SEPTIC PATIENTS

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INTRODUCTION. To determine differences in gene expression related to Th1/Th2 cell differentiation between SIRS patients that remain uninfected and SIRS patients who subsequently develop clinical sepsis.

METHODS. SIRS patients admitted to critical care units of a major university trauma center (n=90)were evaluated daily from onset of SIRS until 72 hours after onset of sepsis or up to 14 days. 2 cohorts were studied: 1) Pre-septic SIRS (n=45) SIRS patients who subsequently developed clinical sepsis; 2) SIRS patients (n=45) who remained clinically uninfected. Pre-septic patients were compared to case and time matched SIRS patients. Blood collected in PAXgene tubes was analyzed by Affymetrix Hg_U1332.0+ microarrays. Data were analyzed for significant differences ($p < 0.05$) while controlling for multiple comparisons.

RESULTS. SIRS patients who subsequently developed sepsis had decreased gene expression for HLA-DR. Although IL12, IL18 and IL4 were not significantly different, preferential Th1 differentiation occured in Pre-Septic patients secondary to increased expression of IL18R1 and INFGR at 12 and 36 hours prior to clinical sepsis.

TABLE 1.

	Fold-Change (Sepsis:SIRS) -12 hrs / -36 hrs.	Relative Expression	Adjusted p-value -12 hrs / -36 hrs.
HLA-DRA	1.29 / 1.23	Down	0.003 / 0.019
HLA-DRB	1.25 / 1.27	Down	0.003 / 0.019
IFNGR1	1.39 / ns	Up	0.003 / ns
INFGR2	1.25 / ns	Up	0.003 / ns
IL18R	1 3.17 / 2.37	Up	0.003 / 0.019
IL4R	1.70 / 1.39	Up	0.003 / 0.019

ns=not significant

CONCLUSION. SIRS patients who subsequently developed sepsis preferentially expressed genes for increased Th1 differentiation, compared to uninfected SIRS patients. These differences occurred 36 hours prior to clinical onset of sepsis.

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HYPOXIA MARKERS IN MIXED VENOUS AND SUPRAHEPATIC VEIN BLOOD SAMPLES IN SEPTIC PATIENTS

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INTRODUCTION. We try to compare the behaviour of tissue hypoxia-ischemia markers in hepatosplachnic blood area and in pulmonary artery blood, in early phases of severe sepsis in patients admitted to ICU and to correlate these parameters with patients outcome.

METHODS. The study was performed in 13 patients with severe sepsis criteria (S) and a 10 patients control group (NS). All of them were admitted to ICU after abdomen surgery for different pathologies. All of them maintained mean blood pressure higher than 70 mmHg during the 12 first hours. Septic patients (S) were sedated, and under mechanical ventilation (arterial blood oxygen saturation > 96%). Three thermo-dilution catheters were placed in each patient. One in the pulmonary artery; a second one inserted through right femoral vein puncture with distal lumen in suprahepathic vein (HV); and the third one inserted during the surgery into the jejuna vein and positioned with the tip in the portal vein. Between 24 and 48 hours after ICU admission blood samples were obtained simultaneously through the three lines and O2 saturation (SO2), haemoglobin level, pH, pO2 and lactate concentration were determined.

RESULTS. SO2 in AP was higher in S than in NS (+2,03%). These differences changed in sign and magnitude when we compare SO2 from samples of HV, with a statistically significant difference (-13,12%; IC95% -25/-1,6). Comparing SO2 in S group between survivals (V) and non survivals (M), SO2 in PA was higher in M group (3,41%). This is more evident when comparing SO2 from HV circulation, with a difference of -17,95% (IC95% -32,5/-2,7). Simultaneously, partial pressure of oxygen changed in the same way that SO2 did. In S patients pH trended to acidosis, with a maximum difference of –0,07 (IC95% -0,13/-0,01) in HV samples. A similar drift was observed in lactate levels, with a maximum difference of 1,77 in favour of group S (IC95% 0,49/3,3).

CONCLUSION. It is possible to identify markers of early cellular hypoxic injury in septic patients at early stages of illness and this can be done at the bedside using simple and easy available sampling (HV catheters are very easy to place) and laboratory techniques. SO2 in mixed venous blood, and especially in the splanchnic region, is the indicator with the highest discriminative value and the one that provides more information.

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TOTAL AND FUNCTIONAL LIVER BLOOD FLOW: A DIFFICULT RELATIONSHIP.

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INTRODUCTION. Measuring liver circulation is difficult due to its anatomic particulars. We tested the correlation between Doppler flow of the total influx of the liver in a small animal model and compared this to the functional liver blood flow (FLBF) as determined by hepatic sorbitol clearance (HSC) (1).

METHODS. Blood flow through portal vein and hepatic artery were measured by ultrasound flow probes in male Wistar rats and compared to hepatic clearance of D-sorbitol and computed as the extrarenal clearance: HSC = (I-U)/SCss, where I is sorbitol infusion rate, U is the mean urinary sorbitol excretion and SCss the sorbitol plasma concentration at steady state (2).

RESULTS. TLBF correlated only weakly to HSC in the control group (r2=0.2657, p=0.0342). *Hemihepatectomy vs endotoxin, p<0,01, **controls vs hemihepatectomy, p<0,01, ***hemihepatectomy vs endotoxin, p<0,001, ****controls vs endotoxin, p<0,05.

TABLE 1.

Parameter	Controls	Hemihepatectomy	Endotoxin
TLBFss	21,6 ± 7,0	16,6 ± 3,8	25,8 ± 7,4*
Hepatic artery	4,3 ± 2,8	3,4 ± 1,6	4,5 ± 2,7
Portal vein	17,3 ± 4,8	13,2 ± 2,8	21,3 ± 6,8*
HSC (ml/min)	11,1 ± 2,0	7,6 ± 1,3**	15,0 ± 4,0***
USC (% of total)	9,9 ± 4,6****	20,5 ± 9,4**	1,6 ± 1,5***

CONCLUSION. 1. The difficult correlation of total blood inflow into the liver with functional liver blood flow in our experiment suggests caution in interpreting ultrasound portal and/or hepatic artery flow data in patients. 2. The increase in TLBF in the endotoxin group can be primarily ascribed to an increase in portal vein flow. 3. Renal sorbitol clearance is significantly altered under pathophysiologic conditions.

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EFFECTS OF PEEP ON LIVER FUNCTION AND SPLANCHNIC MICROCIRCULATION

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INTRODUCTION. Effects of PEEP on liver function and blood flow were found to be non-uniform [1,2]. We studied the effects of PEEP on hepatic blood flow (indocyanine green plasma disappearance rate, ICG-PDR) and gastric mucosal PCO2 (PRCO2) using air tonometry.

METHODS. With approval by our local ethics committee and written consent, we studied 14 patients after elective coronary bypass surgery (13 male, one female; age 48-74, mean 63±7 years). Central venous pressure (CVP), left atrial pressure (LAP) and cardiac index were measured. Furthermore, ICG-PDR and PRCO2 were assessed on ICU admission (PEEP 5 mbar), 2 hours after increasing PEEP to 10 mbar and again as control after 2 hours at PEEP 5 mbar. All patients were on pressure-controlled ventilation and inspiratory peak pressure was adjusted to maintain arterial PaCO2. Vasoactive drugs and sedatives were kept constant.

RESULTS. Cardiac index significantly increased following PEEP5_1. There was a trend for ICG-PDR to decrease with PEEP10 (p= 0.05). However, the difference between regional and arterial PCO2 (PRCO2-PaCO2) significantly increased following PEEP5_1 and remained higher at PEEP5_2 than at PEEP5_1.

TABLE 1.

	PEEP5_1	PEEP10	PEEP5_2
CVP [mmHg]	8 ± 4	9 ± 3	8 ± 3
LAP [mmHg]	7 ± 3	9 ± 3	8 ± 3
Cardiac index [l/min/m²]	2.7 ± 0.5	3.0 ± 0.6*	3.1 ± 0.4*
ICG-PDR [%/min]	24.0 ± 6.9	22.0 ± 7.9	25.3 ± 7.8
PRCO2-PaCO2 [kPa]	0.2 ± 0.9	1.1 ± 1.0*	0.9 ± 1.0*

*P< 0.05. * vs. PEEP5 (1) (ANOVA)*

CONCLUSION. Increasing PEEP from 5 to 10 mbar resulted in a trend of decrease in ICG-PDR. Although significant, the changes in PCO2-gap were within the physiological range and are of no clinical relevance. In patients after coronary bypass surgery, an increase in PEEP from 5 to 10 mbar can be applied without compromising flow-dependent liver function and splanchnic microcirculation.

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SPLANCHNIC MACRO AND MICROCIRCULATORY RESPONSE TO ARGININE VASOPRESSINE (AVP) IN ENDOTOXIC RABBITS

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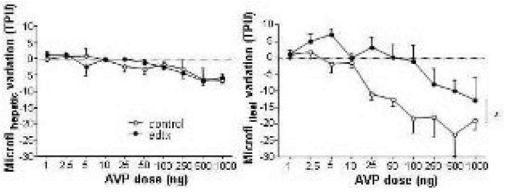
INTRODUCTION. AVP is a well-known mesenteric vasoconstrictor and splanchnic perfusion is particularly at risk during sepsis.

METHODS. 11 anesthetized New Zealand rabbits (2.6±0.3 kg) were studied after iv endotoxin (edtx) or saline (control). After 90min, incremental iv boluses of AVP (100ng = 0.04U) were injected. Mean blood pressure (MAP, mmHg), systolic (SVmes) and diastolic (DVmes) mesenteric artery blood flow velocity (20 MHz pulsed Doppler, cm/s), laser Doppler (TPU) ileal (microFlileal) and hepatic (microFlhepatic) microcirculatory flow were recorded. Results expressed as absolute difference from baseline related to a given AVP dose.

RESULTS. Baseline MAP was 71±11, SVmes 57±13, DVmes 13±7, microFlileal 57±19 and microFlhepatic 27±9 (mean±SD). Despite edtx-induced hypotension (-27%, p<.01), SVmes, DVmes and microFlhepatic were maintained with a decreased microFlileal (-29%, p<.05). Increasing doses of AVP increased MAP but decreased Vmes, especially DVmes, whether septic (p<.01) or control (p=.05). At the microcirculatory level (fig 1), microFlhepatic was constant after AVP in both groups. Although microFlileal was reduced with increasing doses of AVP in control (p<.001), it was preserved in edtx animals. Figure 1 in mean±SEM, * p<.05 control vs edtx.



CONCLUSION. MicroFlhepatic was remarkably stable after edtx, and after AVP both in control and edtx animals. As expected in control, AVP reduced macro and microcirculatory mesenteric flow. Edtx pretreatment modified the AVP response since microFlileal did not change until the higher AVP doses.

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80% REDUCTION OF MESENTERIC BLOOD FLOW INDUCES SIGNIFICANT RISES IN BLOOD IFABP CONCENTRATION

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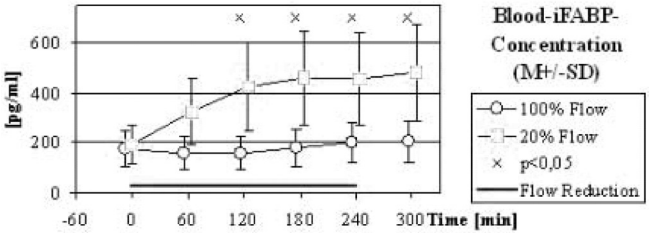
INTRODUCTION. Absence of diagnostic options presents a major problem for early treatment of non-occlusive mesenteric ischemia. We studied Intestinal Fatty Acid Binding Protein (iFABP)(1) in a model of controlled mesenteric hypoperfusion.

METHODS. With ethical board approval, 12 pigs of 75 kg were anesthetized and haemodynamically monitored. In 6 animals, sup. mesenteric artery blood flow was mechanically reduced to 20%, 6 others underwent no flow reduction. IFABP levels were analysed before and during ischemia and after 1 hour of reperfusion.

RESULTS. With hemodynamic and respiratory parameters identical between groups, iFABP showed significantly raised values in flow reduction.



CONCLUSION. Blood iFABP-concentrations rise as early as 120 minutes after onset of intestinal hypoperfusion.

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NOREPINEPHRINE IS SUPERIOR TO EPINEPHRINE IN INCREASING GASTRIC MUCOSAL OXYGENATION

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INTRODUCTION. Maintenance of adequate microcirculatory oxygenation is crucial for the integrity of the gastric mucosa [1]. In this context, the effects of the naturally occurring catecholamines epinephrine (EPI) and norepinphrine (NOR) are unclear. EPI could increase gastric mucosal oxygenation (μHbO2) by increasing oxygen delivery (DO2) while NOR is supposed to decrease μHbO2 by increasing vascular resistance.

METHODS. Six anaesthetized and mechanically ventilated dogs (sevoflurane 1.5 MAC, FiO2 0.3, etCO2 35 mmHg) received increasing doses (0, 0.05, 0.1 and 0.2 μg/kg/min) of either EPI or NOR. μHbO2 was measured by reflectance spectrophotometry [2] and the results were related to DO2 and oxygen consumption (VO2). Statistics: Means±SEM, ANOVA, p<0.05.

RESULTS. Despite a substantial increase in DO2 from 12.3±1 to 26.5±3 ml/kg/min, EPI did not increase μHbO2, jet μHbO2 was lowered at 0.05 μg/kg/min of EPI. In contrast, NOR only slightly changed DO2 from 12.3±1 to 19.9±2 ml/kg/min, whereas μHbO2 increased dose dependent from 57±1% to 67±1%. For EPI and NOR, vascular resistance always paralleled the course of μHbO2. Both catecholamines increased VO2 similarly by about 15%.

CONCLUSION. NOR is superior to EPI in increasing μHbO2 despite a higher DO2 during EPI-infusion. This phenomenon may be partly explained by a redistribution of blood flow to the gastric mucosa which could result from increased vascular resistance during NOR at extramucosal tissue. Thus for optimizing gastric mucosal oxygenation NOR should be preferred to EPI.

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C1- INH REDUCES LIVER DAMAGE AND MAINTAINS LUNG FUNCTION AFTER PARTIAL ISCHAEMIA OF THE LIVER

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INTRODUCTION. The protective effects of C1-estease inhibitor (C1-INH) on liver function after ischaemia and reperfusion of the liver have been demonstrated in several rat models.[1, 2] However, there is still lack of data about systemic effects of C1-INH after ischaemia in the liver [3]. This study investigated, how C1-INH after warm partial ischaemia of the liver affects systemic and splanchnic haemodynamic parameters and pulmonary function.

METHODS. Following approval by the local animal ethics committee 24 anaesthetised, ventilated and acutely instrumented pigs (catheter in pulmonary artery, portal vein, hepatic vein and femoral artery, and pO2-electrode onto the liver) were randomly assigned to 3 groups (gr. 1: 90 min occlusion of hepatic artery followed by 5 hours reperfusion without C1-INH; gr. 2: 90 min occlusion of hepatic artery followed by 5 hours of reperfusion with application of 20 IE/kg C1-INH before reperfusion; gr. 3: control group, no intervention). Measurements of haemodynamic and parameters of oxygenation were made at baseline, after 90 min of ischaemia and after 5 hours of reperfusion. Histological examination of the liver after 5 h reperfusion was graded after Calabrese [4].

RESULTS. Histological examination of the animal's liver revealed less damage in animals treated with C1-INH. Differences in systemic and regional splanchnic perfusion could not be detected between group 1 and 2. PaO2/FiO2 ratio after 5 hours reperfusion was significantly higher in animals treated with C1-INH.

CONCLUSION. C1-INH reduces hepatic injury after 90 min of partial warm ischaemia of the liver in pigs. There have been no effects of C1-INH on systemic or regional haemodynamic parameters and on splanchnic oxygenation. The PaO2/FiO2 ratio as a parameter of lung function was higher after treatment with C1-INH. Treatment with C1-INH after partial ischaemia of the liver does improve lung function without impairing systemic haemodynamic parameters in pigs.

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EFFECTS OF INTRALUMINAL FENOLDOPAM ADMINISTRATION ON MESENTERIC PERFUSION

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INTRODUCTION. The splanchnic circulation is particularly susceptible to ischemia during shock(1). This regional ischemia is thought to play an important role in the development of multiple-system organ failure by activation of a systemic inflammatory response. Fenoldopam is a DA1 selective agonist that seems to attenuate the vasoconstrictive response to gut ischemia(2). The aim of present study is to determine the effects of intraluminal Fenoldopam administration on intestinal mucosal perfusion (IMP).

METHODS. Anesthetized Sprague-Dawley rats were either subjected to intraluminal (duodenum) administration of Fenoldopam (1 gamma/kg/min) (n=5) or saline (control n=5). Laser Doppler flowmetry (LDF) method was used to evaluate mucosal blood perfusion and measurements were undertaken with a intraluminal probe inserted at Jejunum, before (baseline) and 30 min after drug administration (post-infusion). Perfusion was expressed in perfusion unit (media±s.d.) and percentage of change between baseline values and each measurements. T-Student Test was use to compare groups (p<0.01).

RESULTS. A significant increase in IMP compared to baseline conditions, detected by LDF, was observed in the group treated with Fenoldopam (Table 1).

TABLE 1.

Intestinal mucosal perfusion (P.U.)

	Baseline	Post-infusion %	of variation
Control	351±91.5	356±120	5
Fenoldopam	314±168	546±234*	94

**p<0.01*

CONCLUSION. Fenoldopam seems to improve IMP in animals according to previous studies(2). Intraluminal administration of investigated drug is effective in rats under stable conditions. Whether this increment in intestinal perfusion could prevent vasoconstrictive response during mesenteric ischemia must be investigated.

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DOES THE ADJUSTMENT OF THE POSITIVE END-EXPIRATORY PRESSURE (PEEP) INFLUENCE THE VALUE OF INTRA ABDOMINAL PRESSURE?

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INTRODUCTION. Intra abdominal hypertension (IAH) has been shown to produce multiple adverse effects, involving both intra abdominal (liver, bowel, kidney…) and extra abdominal organ systems (respiratory, cardiovascular, cerebral…). Clinical symptoms can occur when pressure exceeds 12 mmHg. Management of patients with abdominal compartment syndrom can lead to the decision of mechanical ventilation with PEEP, sometimes at high levels. From a certain threshold of IAP, the only effective treatment is surgical decompression, sometimes in emergency. Whereas methods used to measure IAP are now well codified, few studies have investigated the influence of the adjustment of respiratory parameters on IAP values. The aim of this observational study was to evaluate the impact of PEEP levels on IAP values.

METHODS. Thirty patients admitted in our intensive care unit with acute respiratory failure (PaO2/FiO2 < 300 mmHg) under mechanical ventilation were included. Hemodynamic, respiratory and IAP (via tranurethral bladder catheter) parameters were recorded during PEEP trial search, for three PEEP values (0, 6 and 12 mmHg). The values are expressed as means ± SD and assessed by ANOVA.

RESULTS. Increase in PEEP involved a significant rise in IAP. This increase was little marked when basic IAP (at ZEEP) was less than 12 mmHg whereas it was significantly high for higher levels of IAP (> 12 mmHg)(Table).

TABLE 1.

	PEEP= O (ZEEP)	PEEP= 6 cmH2O	PEEP= 12 cmH2O
IAP all (n= 30)	10±3	11±4	13±4*
- IAP < 12 mmHg (n= 15)	8±2	9±2	10±2
- IAP > 12 mmHg (n= 15)	15±3	17±4*	20±4*

p< 0.05 versus ZEEP

CONCLUSION. Our results suggest that the IAP can be over-estimated and its interpretation may sometimes lead wrongly to the decision of a hazardous surgical decompression for selected patients. It seems necessary to take into account the level of PEEP regulated in mechanical ventilation on the interpretation of IAP values.

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EFFECTS OF NITROPRUSSIDE AND ESMOLOL-INDUCED CONTROLLED HYPOTENSION ON GUT PERFUSION AND OXYGENATION

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INTRODUCTION. Sodium Nitroprusside (SNP) and Esmolol (ES) are used for Controlled Hypotension (CH) in aortal stent implantation. Actually, there are no data available on the effects of SNP and ES on gut oxygenation and perfusion in deep CH.

METHODS. (1): After ethical approval 17 anesthetized and ventilated pigs were studied. Blood flow was measured in the sup.mesenteric artery (SMABF). Catheters were inserted into the femoral and pulmonary art. and mesenteric vein. Intest. CO2 was determined by tonometry. CH was maintained at a level of 40 mmHg (MAP) via a closed-loop system (2). Animals were randomly assigned to two groups (ES, SNP). Measurements were obtained at baseline (t0), 15 (t1) and 30 (t2) min after starting CH. Statistics:data are median with 25-75% interquartile range, Wilcoxon´s signed rank test (§ = p<0,05 vs NP,# = vs t0)

RESULTS. see Table 1

TABLE 1.

Table 1

	t0	ES t1	(n=8) t2	t0	NP t1	(n=9)t2
Cardiac Index	139	51§#	50§#	119	111	114
ml*min-1*kg-1	(118-150)	(38-55)	(44-53)	(105-133)	(101-135)	(95-166)
SMABF	12,6	10§	10§	13,4	17,6	20,6#
ml*min-1*kg-1	(10,4-16)	(9-11,5)	(8-11,4)	(9,7-17)	(13-21)	(16-26)
small.int.DO2	56	38§#	40§#	58	69	80
ml*min-1	(46-72)	(34-40)	(33-48)	(47-73)	(49-83)	(59-96)
tPO2 Mucosa	29		2,6§#	26		12#
mmHg	(23-37)		(0,1-18)	(22-34)		(5-22)

CONCLUSION. ES leads to a significant decrease in small intestinal perfusion and oxygenation due to a reduction in cardiac index. In contrast SNP does not affect cardiac index but increases mesenteric perfusion and mesenteric oxygenation consecutively. In conclusion, SNP might be of beneficial effect with regard to intestinal perfusion and oxygenation.

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PROGNOSTIC RELEVANCE OF THE PRO-ATRIAL NATRIURETIC PEPTIDE IN SEPTIC PATIENTS

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INTRODUCTION. Pro-atrial natriuretic peptide,ProANP(1-98),is a well established prognostic marker in patients with myocardial infarction and chronic heart failure. However,its prognostic relevance among septic surgical patients is not clear.

METHODS. 40 surgical patients with the diagnosis of sepsis, severe sepsis and septic shock were included in the study.Blood samples from the proximal part of the pulmonary artery catheter, where ProANP(1-98)is predominantly secernated, were drawn on admittance to the ICU. ProANP(-98)was determined using a commercial assay (Biomedica gmbh, Wiena). ProANP(1-98)plasma level was correlated with all standard biochemical parameters,haemodynamic variables and clinical scoring systems, APACHE II and MODS.

RESULTS. ProANP(1-98) was significantely higher in nonsurvivors (6390±7688 fmol/L) than in survivors (2811±1926 fmol/L,p=0.03). It is also correlated with APACHE II (r=0.46, p=0.003) and MODS (r=0.57, p=0.001). The results of logistic regression show the highest prognostic value for ProANP(1-98)(ln)(p=0.03), MODS(p=0.03), platlets (p=0.03)and calculated creatinine clearence (p=0.05). ROC analysis shows that the cut-off value of 4700 fmol/L of ProANP(1-98) has sensitivity of 85 % and specificity of 45 %.The AUC in the model of the logistic regression which includes all four variables is 0,89 which implies that the combination of the three standard prognostic markers and ProANP(1-98) has a high prognostic value.

CONCLUSION. The results of the study show that ProANP(1-98)is correlated with the standard clinical scoring systems APACHE II and MODS in septic patients on admittance to the ICU.It joins the biochemical parameters which are well established prognostic markers, platlets and calculated creatinine clearence in the global logistic regression model with a high predictive value. The study imply that ProANP(1-98) could be a novel prognostic marker and an important mediator in sepsis,possibly through its haemodynamic effects or interaction with cytokine system (1).

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QT DISPERSION (QT-D) AS AN EARLY MARKER OF MODS IN SEPTIC PATIENTS

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INTRODUCTION. QT-d(QT-dispersion)indicates cardiac autonomic function and reflects regional repolarization differences in the heart. QT-dispersion is a marker of cardiac repolarization instability and is seen in conditions of high risk of sudden death.When combined with low HR variability is a risk factor for cardiac mortality in various patient populations.Sepsis and septic shock are characterized by an impaired sympathetic modulation of the heart,suggesting that a central autonomic regulatory impairment contributes to the circulatory failure that is seen.The purpose of this study was to evaluate QT-d in septic patients and determine whether measuring QT-d in this group of septic patients without MODS can be used as an early indicator of MODS.

METHODS. Prospective study on a six bed ICU of a University Hospital and a five bed medical ICU of a teriary care Hospital.Data was collected prospectively over a period of one year.We studied thirty eight septic patients.All patients that were included in the study met the ACCP/SCCM consensus criteria for sepsis and septic shock During the first day of their septic episode, measurements of the patients QT intervals on a 12 lead ECG were made.The QT interval was corrected (QTc) using the HR according to Bazett's formula.The QT-d was defined as the difference between the max and the min value of the QTc in different leads.QT-d was also measured on days 3 and 5 from the initiation of the septic episode. APACHE II scores were also calculated for days 1,3and 5.

RESULTS. The patients were divided into 2 groups.One group included patients with sepsis that developed(MODS) and the second group included patients with sepsis but without MODS.The APACHE II scores were similar for both groups especially for days 1 and 3.The overall mortality rate was approx.45% but the MODS group showed a mortality rate of 70%.Twelve patients went on and developed MODS during their sepsis while twenty six did not.The QT-d measured from the ECG on days 1 and 3 were significantly increased in patients that went on to developed MODS (49± 20ms vs 34±11ms) than in patients that had only sepsis without MODS.QT-d values of day 5 were similar to day 3 on either groups.

CONCLUSION. Increase of QT-d in septic patients in ICU may be useful in identifying septic patients at risk of developing MODS.This predictive tool could be used to direct interventions aimed at preventing development of multi-organ dysfunction.

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INVESTIGATION OF THE ACTIN CYTOSKELETON IN AN ORGAN CULTURE SEPSIS MODEL

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INTRODUCTION. We have shown that activation of the ATP-sensitive potassium (K_{ATP}) channel contributes to LPS-induced vascular hyporeactivity[1]. Disruption of the alpha actin cytoskeleton is a possible mechanism for activation of the K_{ATP} channels[2]. Moreover, dynamic changes in actin structure actin are involved in regulation of vascular tone. Therefore changes in the actin cytoskeleton may be an important mechanism of contractile dysfunction in septc shock.

METHODS. Lipopolysaccharide (LPS, S. typhosa) was used to create an organ culture model of sepsis (DMEM ± LPS, 0.1 mug ml-1). This was validated by measuring contractile responses to phenylephrine (10^{-9}-10^{-5}), in rat aorta at 0, 24 and 48 hr timepoints. Sectioned rings (10 mum) of LPS-treated aorta or were imaged using confocal microscopy. Alpha actin was stained with either phalloidin-rhodamine or DNaseI-Texas Red (which bind F and G actin, respectively). Quantitative comparisons were obtained by collecting images in three Z stacks (5 x 1 mum) per slide, with the pixel intensity analysed for each image (LaserPix). Centrifugation of rat aorta homogenate at 260,000g (4 °C) for 1hr achieved isolation of F (pellet) and G (supernatant) actin, detected by SDS PAGE using anti-alpha actin antibody (1:50,000).

RESULTS. Hyporeactivity to PE was observed at 24 hr (100% hyporeactive) and 48 hr (60% reduction in maximum contraction). Total alpha actin, F actin and G actin levels are unchanged at 24 hr, as indicated by confocal microscopy (n = 4) and Western blotting (n = 3). However, a 30% decrease in F actin was seen at 48 hr by confocal microscopy (n = 3), but not by Western blotting (n = 3).

CONCLUSION. The actin cytoskeleton is unchanged in vascular smooth muscle in a model of septic shock. There are inconsistencies in results at the 48 hr timepoint. A straightforward correlation between the structure and function of the cytoskeleton was not observed.

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EFFECTS OF RECOMBINANT HUMAN ACTIVATED PROTEIN C ON ENDOTHELIAL FUNCTION DURING SEPSIS

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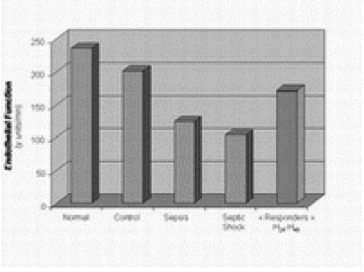
INTRODUCTION. Endothelial function is depressed during sepsis, which in turn interacts with the proinflammatory response. If the rhAPC anticoagulatory effects have been extensively characterized, there are few studies analyzing its microcirculatory actions. Our aims were to evaluate endothelial function variations during sepsis and to investigate the microcirculatory effects of rhAPC.

METHODS. Endothelial function was assessed using near-infrared spectrophotometry (InSpectraTM, Hutchinson). Measurements were performed during the early management (H0) and during the subsequent 48 hours (H8-H24 and H24-H48). The study was approved by our local ethics committee.

RESULTS. 38 patients were monitored (age 57±18; $SAPS_{II}$ 60±23), of which 10 without sepsis (control), 28 severe sepsis, and 22 septic shock. They were compared to 6 healthy volunteers (normal). Endothelial function was depressed during sepsis but septic shock was associated to more severe alteration ($p<0.05$). From the septic shock patients who received rhAPC (n=10), a „normal" endothelial function was restored in 50% cases (see figure). These improvements were not observed within septic patients without rhAPC.



CONCLUSION. These results confirm that endothelial dysfunction occurs during severe sepsis and that during septic shock, rhAPC infusion had microcirculatory effects within the first 48hrs of infusion.

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EXPERIMENTAL MODELS OF ACUTE LUNG INJURY: HAEMODYNAMICS AND GAS EXCHANGE COMPARISON

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INTRODUCTION. Experimental models of acute lung injury (ALI) are used to investigate the effects of different therapies and/or mechanical ventilation strategies to treat respiratory failure. We present the haemodynamics and pulmonary gas exchange comparison effects of three different ALI experimental models.

METHODS. We studied eighteen anesthetized and mechanically ventilated animals with ALI induced by three different injuries: 1) endotoxin or lipopolysaccharide infusion (LPS), 2) ventilator (VILI) and cardiopulmonary by-pass (CPB). The LPS model was induced in 6 sheep by an infusion of 2mg.kg plus 0.5mg.kg.min- of E. coli endotoxin for 4 hours. The VILI model was induced in 6 sheep after 6 hours of mechanical ventilation with a transpulmonary pressure of 35 mmHg plus 1x108 UFC/ml of Klebsiella pneumoniae lung instillation. The CPB model was induced in six pigs after 2 hours on cardiopulmonary bypass. Measurements of systemic and pulmonary haemodynamics and arterial blood gases were obtained at baseline and after ALI was induced.

RESULTS. The effects on haemodynamics and gas exchange of the three ALI models are shown in table 1.

TABLE 1.

Haemodynamics and gas exchange

	LPS model baseline	4 h LPS	VILI model baseline	6h VILI	CPB model baseline	2h CPB
MeanPAP mmHg	13±1	25±4*	14±1	24±4*	18±2	23±2*
CO L/min	4.6±1	2.1±0.5*	3.0±0.4	2.6±0.7	3.8±0.5	3.3±0.4
PaO2/FiO2	448±44	120±13*	422±10	214±60*#	428±23	188±11*#

*Mean±SD, ANOVA * p< 0.05 versus baseline, # p< 0.05 versus LPS model*

CONCLUSION. All three experimental models mimic the main features of ALI which are hypoxemia and pulmonary hypertension. Hypoxemia was more severe in the LPS model in which CO was significantly decreased. All three models can be used for ALI therapies research.

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INFLAMMATORY RESPONSE OF TRACHEOBRONCHIAL EPITHELIAL CELLS TO ENDOTOXIN

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INTRODUCTION. Lipopolysaccharide (LPS)-induced lung injury is a very useful experimental model to investigate and characterize immunopathogenic changes and mechanisms in the process of inflammation in ALI and ARDS. Alveolar epithelial cells play a major role in the regulation of the immune and inflammatory responses in the lung, while scarce information is available about TBEC and their participation in the inflammatory process (1, 2).

METHODS. mRNA and proteins of TNF-alpha, MCP-1, CINC-1, MIP-2 , ICAM-1, and VCAM-1 were assessed in control and LPS-stimulated rat TBEC in vitro. Functional assays such as chemotaxis, neutrophil adherence, and cytotoxicity assays were performed, as well as Caspase-3 activity and TUNEL. Analysis of variance (ANOVA) was used to assess the statistical significance of differences.

RESULTS. Increased production of proinflammatory cytokines and chemokines in primary culture of rat TBEC in response to LPS was found to increase chemotactic activity for neutrophils (370% increase, $p<0.0001$). Enhanced expression of TBEC ICAM-1 and VCAM-1 led to a 95% increased adherence of neutrophils ($p<0.05$), inducing epithelial cell necrosis. Effector cell-induced cytoxicity was increased by 19% in LPS-stimulated TBEC ($p<0.01$). Blocking ICAM-1 led to 52% less TBEC necrosis, while VCAM-1 blocking reduced necrosis by 34% (both $p<0.05$). After LPS exposure caspase-3 activity in TBEC increased by 36% ($p<0.01$). TUNEL test further confirmed increased apoptosis rate upon LPS stimulation.

CONCLUSION. TBEC seem to participate in the pulmonary inflammatory response to LPS by production of inflammatory mediators. Increased expression of cytokines/chemokines might lead to enhanced recruitment of neutrophils, which become adherent to TBEC and induce epithelial cell necrosis.

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CASE REPORT: INHALED VIP IMPROVED PULMONARY GAS EXCHANGE IN ACUTE RESPIRATORY DISTRESS SYNDROME

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INTRODUCTION. Acute respiratory distress syndrome (ARDS) is characterized by massive intraalveolar inflammation, impaired pulmonary gas exchange and high mortality. So far, only low-tidal-volume ventilation has been demonstrated to reduce the mortality in this entity. Vasoactive intestinal peptide (VIP), an endogenous human neuropeptide, has been shown to exert positive effects on the pathophysiology of ARDS via its anti-inflammatory and anti-apoptotic properties. Furthermore, VIP is a potent bronchodilator and vasodilator and has beneficial effects in experimental ARDS and sepsis. VIP can be safely inhaled by healthy humans. Three patients with ARDS were treated with inhaled VIP in order to confirm safety and to determine potential effects on the gas exchange and hemodynamics.

METHODS. Three ventilated patients with parapneumonic ARDS and an indwelling Swan-Ganz catheter were studied. Pulmonary gas exchange and hemodynamics were measured at baseline. A cumulative dose of 2400 \mug VIP was administered via ultrasound inhalation over 24 hours. Pulmonary gas exchange and hemodynamics were recorded at 12 and at 24 hours after start of treatment. Vital signs were monitored continuously during the study period. Apart from FiO2, ventilator setting remained unchanged during inhalation of VIP.

RESULTS. At baseline P/F ratio was 97, 94 and 120, respectively. AaDO2 was 431,388 and 292 mmHg, respectively. mABP (mean arterial blood pressure) was 56, 74 and 65 mmHg, respectively. mPAP (mean pulmonary artery pressure was 26, 21 and 31 mmHg, respectively. VIP inhalation was well tolerated by the three patients. Changes in pulmonary gas exchange and hemodynamics are shown in the table. All patients survived and left the hospital in good condition.

TABLE 1.

Gas exchange and hemodynamics in three patients with ARDS treated with inhaled VIP

	Patient I	Patient II	Patient III
\DeltaP/F ratio	+ 50	+ 57	+ 61
\DeltaAaDO2 mmHg	– 165	– 153	– 85
\DeltamABP mmHg	+ 16	+ 6	+ 40
\DeltamPAP mmHg	+ 7	± 0	-1

CONCLUSION. Inhaled VIP was safely applied to three patients with ARDS. Inhalation of VIP might have positive effects on pulmonary gas exchange in this entity.

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IS THE EFFECT OF INJECTION OF CONTRAST MATERIAL IN HEALTHY AND IN ALI/ARDS PATIENTS DIFFERENT?

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INTRODUCTION. The injection of contrast material in ALI patients was found to increase the lung volume probably due to an increase in lung density caused by intrapulmonary diffusion of contrast material (1).
Aim of this study was to quantitatively evaluate the effect of contrast material in healthy subjects and in ALI/ARDS patients on CT number.

METHODS. A spiral CT scan (140 kV, 270 mA) was performed at end expiration before and after injection (1, 2, and 3 minutes) of contrast material (2 ml/Kg of Iopomidolo, Bioindustria, Italy). The CT number was measured using a dedicated software after manually delineating each lung image. 8 ALI / ARDS sedated and mechanically ventilated patients (age 68±13 ys, weight 72±9 Kg, PaO2\FIO2 190±60 mmHg) and 10 healthy subjects (thoracic CT was performed independently from the study as a follow-up for previous lung diseases)(age 71±9 ys, weight 66±5 Kg) were enrolled.

RESULTS. Either in ALI/ARDS patients and in healthy subjects the CT number significantly increased from -591±105 to -572±111, to -575±100, to -578±108 and from -774± 58 to-747± 56, to -761± 47, to -746± 63 respectively without any difference between the two groups.

CONCLUSION. Altough we can not discriminate if the increase of CT number was due to only an effect of intravascular contrast material or an increase in lung edema (effect of contrast material), healthy subjects and ALI/ARDS presented a similar behaviour.

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INCREASE OF PLASMA IL-13 IN RATS WITH ACUTE LUNG INJURY INDUCED BY "TWO-HIT"

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INTRODUCTION. To mensurate the interleukin-13(IL-13) content in plasma in rats with acute lung injury (ALI) induced by „two-hit" with olic acid (OA) and lipopolysaccharide (LPS).

METHODS. Wistar rats were received infusion of OA (0.2ml/kg) first and LPS (O111 B4 2mg/kg) second to set up the ALI model. The indexes of respiratory rate(PaO2), wet weight/dry weight(W/D) of lung lobar pathological observation, and enzyme-linked immunosorbent assay (ELISA) were employed.

RESULTS. ALI was stimulated in rats with OA-LPS and OA-LPS might cause the significant increase the IL-13 content in plasma in rats (39.64±4.93 ng/L at 1h; 58.28±5.06 ng/L at 4h; 50.92±5.61 ng/L at 12h; 38.13±6.23 ng/L at 24h), especially in OA-LPS/4h group. During the following 24hs, the levels of plasma IL-13 were significantly higher than in Saline control group (12.13±5.02 ng/L), LPS control group (27.35±5.90 ng/L) and OA control groups (34.42±4.69 ng/L at 1h; 52.55±4.90 ng/L at 4h; 44.47±5.13 ng/L at 12h; 25.99±4.98 ng/L at 24h) respectively ($P<0.01$).

CONCLUSION. The OA-LPS might cause the ALI in rats. Meanwhile, the formation and development of ALI might be related to the obvious increase of the IL-13 content in plasma.

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PLATELET-ACTIVATING FACTOR ACETYLHYDROLASE IS INCREASED IN EARLY ACUTE LUNG INJURY

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INTRODUCTION. Platelet-activating factor(PAF)is a key mediator in the pathogenesis of acute lung injury(ALI).PAF-acetylhydrolases(PAF-AHs)are enzymes that terminate PAF signals, thus regulating inflammatory response.In this study,we describe the kinetics of plasma and bronchoaleveolar lavage(BAL)PAF-AH in early ALI.

METHODS. Six piglets were ventilated for 6 hours after ALI was induced by oleic acid infusion.A recruitment maneuver was applied and PEEP levels titrated.Respiratory mechanics were recorded.Blood and BAL samples were collected every 2 hours (times 0,2,4,6h and "injury",defined as the time when ALI was achieved).PAF-AH activity was measured using a colorimetric enzymatic assay.PAF-AH immunoperoxidase was performed in lung tissues from ALI and controls with anti-hPAF-AH(Cayman Chemicals).IL-6 and IL-8 were measured using ELISA (R&D systems).Kruskal-Wallis and Mann-Whitney tests were used.p<0.05 was considered statistically significant. Data are expressed as mean±SEM.

RESULTS. Decrease in PaO2/FiO2 was observed(t0=435±61mmHg vs injury =100±21mmHg,p=0.007)and,there was increase in pulmonary elastance(t0= 33 ± 4 vs injury=62.8±8.6,p=0.015).Elevation in BAL protein count (t0= 193.2 ± 119.1 µg/mL vs t6h= 1038 ± 268.3 µg/mL, p= 0.008)was present. There were increases of IL-8 levels in BAL fluid (t0=0.15±1.06 vs t6h=5.06±1.24 pg/ml,p=0.02) but not in plasma samples.IL-6 levels were negligible.PAF-AH activity was corrected by total protein content in plasma and BAL.After normalized per protein,PAF-AH in BAL was significantly increased at t6h(PAF-AH T0=0.001±0.001 vs 0.031±0.018 nmol/ml/min/g,p=0.04).We also observed increased PAF-AH expression by immunoperoxidase in the lung of ALI compared to controls,mostly in macrophages.Plasma PAF-AH was not significantly increased (p=0.81)

CONCLUSION. During the early stages of experimental ALI there is significant elevation of PAF-AH levels in BAL.We hypothesize that the increase in PAF-AH levels are due to local production of PAF-AH instead of leakage from plasma and it represents a way to offset the pro-inflammatory stimuli in the alveolar milieu

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HSP-70 EXPRESSION IN THE LUNG ATTENUATES ARDS BY DISRUPTING

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INTRODUCTION. Sepsis secondary to cecal ligation and double puncture (2CLP) in rats causes acute respiratory distress syndrome (ARDS). Previous studies have shown that use of an adenoviral vector that expresses HSP-70 (AdHSP) increases HSP-70 and protects against ARDS. The mechanism is unknown, but HSP-70 has been reported to inhibit activation of the intracellular signaling molecule NF-kB. IKK beta has been demonstrated as the important subunit for IkB alpha phosphorylation during stress. Its activity depends on regulatory subunits which form the large active heterodimer of IKK. We hypothesized that the inhibition of the NF-kB pathway by HSP-70 is, in part, due to disruption of the IKK complex.

METHODS. 48 hours following 2CLP and treatment with AdHSP or the vehicle solution (PBS) lung tissue was harvested. Nuclear and cytosolic protein was isolated. Gel filtration was used to separate cytoplasmic protein complexes by molecular weight. This was followed by an ex-vivo GST-IkB kinase assays to evaluate the fluctuations in IKK beta function.

RESULTS. In cytoplasnic extracts from PBS treated 2CLP animals IKK containing complexes eluted in the higher (600-1500 kDa) molecular weights. Treatment with AdHSP dramatically altered the elution of the complexes: IKK complexes preferentially detected in smaller (67-440 kDa) molecular weight fractions. The GST-IkB kinase assay demonstrated that AdHSP treatment shifted IKK activity from the 600-1000 kDa fractions in the PBS group to the 100-200 kDa fractions in the AdHSP treated group. Further, using our ex vivo GST-IkB kinase assay, we examined IkB alpha phosphorylation by immunoprecipitated IKK beta as a function of the time at which the reaction was terminated. The results revealed that, relative to PBS treatment, AdHSP slowed the ability to IKK beta to phosphorylate IkB alpha.

CONCLUSION. HSP-70 expression induced by AdHSP suppresses NF-kB activation. This appears, in part, to result from inhibition of IkB alpha phosphorylation by IKK beta. As a result, IkB alpha cannot be ubiquitinated or degraded. The key finding is that enhanced HSP-70 expression alters the composition of the IKK complex.

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GENETIC MUTATIONS IN PATIENTS WITH PULMONARY EMBOLISM IN NORTHWESTERN GREECE

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INTRODUCTION. To investigate genetic mutations that predispose for Pulmonary Embolism (P.E).

METHODS. Spiral CT Pulmonary Angiography was performed in 76 patients presenting with symptoms of P.E. Finding consistent with acute pulmonary embolism (PE)were observed in 43 patients (group A. The other 33 patients were without P.E (group B). We investigated the prevalence of the following thrombogenic mutations :
1) the G1691 factor V Leiden mutation, 2)the G20210A mutation in the prothrombin gene, and 3) C677T mutation in the methylenetetrahydrofolate reductase (MTHFR). Statistical analysis was done using the Fisher exact test (p=0.05).

RESULTS. Heterozygous mutation of factor V Leiden and MTHFR are not statistically different between the 2 groups. The same for homozygous mutation of MTHFR. Heterozygous mutation of factor G20210 in the prothrombin gene is significantly more frequent in patients with PE (p<0.05). None without P.E did not release this mutation.

CONCLUSION. The prevalence of Heterozygous mutation of factor II (G20210) in our region is high (16.3%). We stress that no one without P.E. did not appear this mutation. We continue our study with more patients in order to establish more reliable conclusions.

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INCREASE OF LEVEL OF GRANULE MEMBRANE PROTEIN-140 ARE ASSOCIATED WITH ACUTE LUNG INJURY IN RABBITS

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INTRODUCTION. To explore the significance of changes of level of the Granule membrane protein-140(GMP-140) in Rabbits with acute lung injury(ALI).

METHODS. Thirty one rabbits were randomized into the control(n=10) and the BME(n=21 Bone marrow extract ,BME0.35ml/kg 2ml/h) groups. The measurement of granule membrane protein-140(GMP-140), endothelin-1(ET-1), angiotensin converting enzyme(ACE) and circulating endothelial cell(CEC) was carried respectively at multiple time points.

RESULTS. All the parameters of GMP-140, ET-1,ACE and CEC were increased in a early phase(0.5h) and lasted for 6hrs.The dramatically elevated level of plasma GMP-140 in early phase was negatively related to PaO2,but positively to other coresponding parameters.The GMP-140 revealed by immunohistochemistry(IHC)-staining on the surface of pulmonary vescular endothelial cell(PVEC) became weak.

CONCLUSION. GMP-140 might be a satisfactory criterium for the early surveillance and for the evaluation of prognosis of ALI in the clinical practice.

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PROGNOSTIC FACTORS IN HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS' REQUIRING MECHANICAL VENTILATION

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INTRODUCTION. Hematopoietic stem cell transplant (HSCT) patients have a poor outcome when acute respiratory failure requiring mechanical ventilation develops. Several studies have identified prognostic factors that correlate with mortality in this population, such as longer ventilation time (> 72 hours) and acute liver and kidney failure.

METHODS. Between Jan/99 and Dec/04 at our oncological hospital were performed 517 HSCT. We evaluated 49 patients admitted to the ICU that needed mechanical ventilation: 30 males and 19 females, mean age 42 years-old (min 9, max 66), 29 had acute leukaemia, 7 had lymphoma, 7 had multiple myeloma and 6 had other hematological diseases. Forty-one did allogenic HSCT and 8 did autologous HSCT.

RESULTS. We analysed these 49 patients. In 3 patients non invasive ventilation was effective and 46 HSCT patients needed invasive ventilation. Twenty-eight patients had clinical graft versus host disease. In 3 there wasn't engraftment. Twenty-seven patients needed vasopressors. Severity scores were: APACHE II 27±9, SAPS II 60±4, SOFA 12±1. The 19 patients that developed both acute liver and renal failure died. All the 14 patients that needed hemofiltration died. Twelve patients were discharged from the ICU: the 3 patients that needed non-invasive ventilation and 9 that were weaned from mechanical ventilation.

CONCLUSION. In our HSCT patients isolated acute respiratory failure needing invasive ventilation is not always predictive of death. But as in other studies, acute respiratory failure needing mechanical ventilation added to hepatic and renal failure is always fatal. We feel that this last group of patients do not benefit from ICU admission and intensive treatment.

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EFFECTS OF BODY POSITIONING IN VENTILATED OBESE PATIENTS

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INTRODUCTION. The effects of 45 degrees body position on the peripheral oxygen saturation (SpO2), end-tidal CO2 (ETCO2) and the rapid shallow breathing index (RSBI) were observed in relation to the body mass index (BMI) especially in ventilated obese patients

METHODS. Twenty patients were studied for effects of < 10 degrees (supine) position and 45 degrees body position. We investigated one group with a BMI lower then 30 and one group with a BMI higher than 30 (obese group). Body position was changed with a Total Care® bed (Hill-Rom). The results of the 45 degrees position were compared using Kruskal-Wallis-H nonparametric test of significance. The results of body positioning change in the individual patients were analysed with paired samples T test

RESULTS. The SpO2, ETCO2 and RSBI were improving after patients had been placed in the 45 degrees position in all patients. Only the ETCO2 improved significantly for the 45 degrees position compared to < 10 degrees position in the obese group compared with patients with a normal BMI

TABLE 1.

All patients analysed

	SpO2	ETCO2	RSBI
Supine	95.95±1.96	4.88±1.19	34.79±17.64
45 degrees	96.90±1.97	4.56±1.17	28.49±13.44
Significance	p < 0.001	p = 0.001	p = 0.001

TABLE 2.

Obese group vs normal weight group

	SpO2 45-10 degrees	ETCO2 45-10 degrees	RSBI 45-10 degrees
BMI < 30	1.00±0.94	- 0.90±0.23	- 5.20±7.33
BMI > 30	0.90±0.99	- 0.55±0.31	- 7.40±6.53
Significance	p = not significant	p = 0,003	p = not significant

CONCLUSION. Placing ventilated patients in the 45 degees position should be done more frequently, because it improves the SpO2, ETCO2 and the RSBI. Obese patients have additional benefits compared with patients with a normal BMI. Body position is very important on an ICU; the 45 degrees position is an easy, effective and lower cost application

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REGIONAL PULMONARY PERFUSION IS REGULATED BY NITRIC OXIDE

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INTRODUCTION. Improved oxygenation has previously been shown in patients with acute lung injury when ventilated in prone position. V/Qs were more uniform in prone position leading to a more efficient gas exchange compared with supine. We hypothesized that this was due to higher regional production of nitric oxide (NO) in dorsal lung regions. We previously showed higher mRNA expression of nitric oxide synthase (NOS) and NOS activity in dorsal compared with ventral human lung tissue. Lung perfusion was shifted towards ventral regions during NOS inhibition. To expand our investigation we examined NOS activity and reactivity of arteries in porcine lung tissue in vitro.

METHODS. We measured NOS mRNA expression and NO production by citrulline assay in ventral and dorsal lung tissue from patients operated for cancer and pigs. In vitro responses of arteries from dorsal and and ventral porcine lung regions to different endothelium-dependent vasodilators were investigated. In human volunteers, regional lung perfusion in prone and supine postures was assessed by Single Photon Emission Computed Tomography using ^{99m}Tc macroaggregated albumin before and after inhibition of NOS by N^G-monomethyl-L-arginine infusion.

RESULTS. NOS mRNA expression was significantly higher in dorsal compared with ventral human lung regions. NO synthesis was higher in dorsal lung tissue from both humans and pigs. Acetylcholine, bradykinin and calcium ionophore A23187 induced endothelium-dependent relaxations of porcine pulmonary arterial rings precontracted with norepinephrine. Acetylcholine and bradykinin were more potent in dorsal compared with ventral vessels. In volunteers in supine position, lung perfusion was shifted to ventral parts during NOS inhibition, whereas in the prone posture lung perfusion remained unchanged.

CONCLUSION. Our results suggest a role for endogenous nitric oxide in regulation of regional pulmonary perfusion.

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N-TERMINAL-PROBRAIN NATRIURETIC PEPTIDE AS A MARKER OF WEANING-INDUCED ACUTE CARDIAC IMPAIRMENT

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INTRODUCTION. Discerning between respiratory and cardiac causes of weaning failure in patients with both COPD and cardiac disease is a clinical problem. B-type natriuretic peptide (BNP) and its N-terminal propeptide (NT-proBNP), biomarkers of acute cardiac overload, have been validated to discriminate between cardiac and respiratory causes of acute dyspnea. We set up the hypothesis that an acute increase NT-proBNP could identify weaning-induced acute cardiac impairment.

METHODS. Serum NT-proBNP level (Roche Diagnostic method), central venous oxygen saturation (ScvO2), left ventricular end diastolic volume and ejection fraction (LVEDV, LVEF-transthoracic echocardiography) were obtained immediately before and after an unsuccessful weaning trial. Measurements of NT-proBNP, SaO2 and ScVO2 were repeated after 24 hours of resumption of mechanical ventilation.

RESULTS. In 6 patients NT-proBNP increased more than 30% after weaning failure, whereas in 8 patients it remained stable.

TABLE 1.

	Before	*Increase* After	24 h	before	*Stability* After	24 h
NT-proBNP (pg/ml)	4812±3388	12800±6441*	5326±4187#	2513±2096	2386±2106	1683±1203
SaO2 (%)	99 ± 1	93 ± 6*	99 ± 1 #	99 ± 1	94 ± 5 *	98 ± 2
ScvO2 (%)	72 ±	14 60 ± 19*	69 ± 14 #	70 ± 6	68 ± 12	70 ± 12
LVED V (mm3)	134 ± 28	150 ± 34*	-	117 ± 45	133 ± 39*	-
LVEF (%)	40 ± 6	33 ± 11*	-	36 ± 9	39.2 ± 9*	-

**) p < 0.05 after versus before; #;); p < 0.05 24 h versus after*

CONCLUSION. In patients with weaning-induced increase in NT-proBNP, we found evidence of acute left ventricular dysfunction and mismatch in tissutal oxygen supply/demand.

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IMPACT OF ORGAN FAILURE ON MORTALITY PREDICTION IN A TURKISH SURGICAL INTENSIVE CARE UNIT

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INTRODUCTION. To compare, and externally validate commonly used prognostic scoring and multiple organ failure scoring systems, and determine the epidemiology of organ failure, and impact of organ failure on mortality in a single Turkish surgical intensive care unit.

METHODS. Between February-June 2004, 197 patients who stayed more than 24 hours have been included in the study. Prospectively collected data is used for related calculations, performed by investigators blinded to the outcome of the patient. Scores and predicted mortalities for APACHE II, SAPS II, MPM II at admission and 24 hours and scores for APACHE III have been calculated. Additionally daily calculations of MODS, SOFA and LODS scores have been performed, and compared in the assesment of multiple organ failure.

RESULTS. Area under receiver operating curves were more then 0.8 for all of the evaluated scoring systems, MPM II at admission being the best performing among prognostic scoring systems. On the other hand the Hosmer-Lemeshow Goodness of Fit statistics are not as satisfactory. There was a statistically significant difference in ROC areas between maximum organ failure scores and MPM II-0 predicted mortalities. Most commonly failing organ systems were pulmonary and renal systems, neurologic organ failure although rare having the most signifiant impact on mortality.

TABLE 1.

	ROC	HL Chi²	HL p
Maks LODS	0.9973	0.31	0.9975
Maks SOFA	0.9928	3.08	0.79
Maks MODS	0.9832	1.79	0.9379
MPM II-0	0.9331	8.86	0.3541
MPM II-24	0.9234	10.01	0.2642
SAPS II	0.8995	16.94	0.0307
LODS	0.8743	12.51	0.0284
APACHE II	0.8196	7.72	0.4612

Calibration and discrimination statistics of scoring systems.

CONCLUSION. Conventional prognostic scoring systems have good calibration but less then optimal discrimination in our unit. Development of organ failure has a significant impact on mortality which may reduce the reliability of admission scores.

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OUTCOME AND PROGNOSTIC FACTORS IN PATIENTS WITH HEMATOLOGICAL MALIGNANCY ADMITED TO ICU

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INTRODUCTION. When patients with hematological malignancies develop a life-threatening complication may be admited to the ICU with a cetain reluctance. However, new chemotherapeutic regimens have greatly improved their outcome. The aim of this study was to evaluate prognostic factors,long-term survival and mortality.

METHODS. Retrospective study of 58 ICU patients with hematological diseases (january/00-may/04). Mean age 55(15-75). Men/Women(38/20). Hematological desease: No Hodgkin's lymphoma (18 patients), acute myeloblastic leukemia (10), acute lymphoblastic leukemia (9), multiple myeloma (6), chronic lymphoproliferative disorder(5), chronic myeloproliferative disorder(4), myelodisplastic syndrome (3), aplatic anemia (2) and Hodgkin's lymphoma (1). Hematopoietic stem cell transplant (7). The acute illness precipitating the ICU transfer were: septic shock 26(45%), respiratory failure 21 (36%), non-septic shock 5 (9%), neurological event 2 (3%), post-surgery 2(3%),cardiac infarction 1 (2%) and polytrauma 1 (2%)

RESULTS. Mean Apache II at admission: 23(+/-6.8).Twenty-one patients (36%) could be discharged alive from the ICU. The median overall survival for ICU patients was 23(0-54)months, with a median follow-up of 8 months. From them, the probability of being alive at 6 months was 56%(CI 95%:31-75), and at 12 months was 48%(CI 95%: 13-70). Univariate analysis: We associated with a higher mortality rate the APACHE II at admission (p=0.01), neutropenia (p<0.05), maximum FiO2 requirements at 24 hours from admission (p<0.01), renal impairment (p<0.05), liver damage (p<0.05), septic shock (p<0.01), multiple organ failure (>2) (p<0.05), demonstrated fungal infection (p<0.05). APACHE II at 48 and 72 hours of ICU and the type of hematological malignancy did not predict outcome in our series. Multivariate logistical regression model, only cardiovascular failure requiring vasoactive drugs (p<0.01) and the need of mechanical ventilation (p<0.05) predicted bad autcome

CONCLUSION. The mortality of patients affected of hematological malignancy admited to the ICU was 63.8%. The cardiovascular failure and the need of mechanical ventilation were the main surviving prognostic factors. Although the mortality rate immediately after ICU discharge was high, those patients that survived the first week outside ICU had an expected surivival only conditioned by their hematological malignancy.

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RISK FACTOR FOR CRITICAL ILLNESS POLYNEUROPATHY (CIP) : A CASE CONTROL STUDY

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INTRODUCTION. A growing interest regarding for CIP has emerged. We performed a retrospective study to analyse our CIP population.

METHODS. Since January 2003 all patients in our ICU exhibiting a marked weakness after recovering from initial disease have undergone an electrophysiological evaluation. In order to determine risk factors of CIP after sepsis, patients who developed CIP (n=12) were compared to a group of control patients without CIP (n= 24) blindly selected in the whole population of sepsis patients who required mechanical ventilation and a length of at least 7 days in ICU.

RESULTS. Results are summarized in the two following tables:

TABLE 1.

	CIP (n = 12)	Controls (n = 24)	p
Age	59 ± 9	61 ± 1	NS
SAPS II	66 ± 23	52 ± 9	NS
Length of ICU stay (d)	100 ± 82	20 ± 8	< 0.001
Length of MV (d)	77 ± 72	13 ± 2	< 0.001

TABLE 2.

	CIP (n = 12)	Controls (n = 24)	p
Average of glycaemia (mmol.L-1)	10.5 ± 2.1	9 ± 0.1	< 0.05
Procalcitonin (ng.mL-1)	75 ± 80	108 ± 136	NS
Ramsay	5 ± 1	4 ± 1	< 0.001
Duration of steroids (d)	4.4 ± 3.4	3 ± 2.8	NS
Duration of muscle relaxant (d)	1.3 ± 1.8	1 ± 2.8	NS
Renal failure (d)	4.3 ±3.1	2 ± 4.2	< 0.05

CONCLUSION. As previously reported, CIP in our study led to higher MV and ICU duration. The results also showed that hyperglycaemia, renal failure and the average sedation level was associated with CIP occurrence.

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PHYSIOLOGICAL DERANGEMENT IDENTIFIES PATIENTS AT HIGHER RISK OF HOSPITAL DEATH & PROLONGED ADMISSION

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INTRODUCTION. Physiological measurements are frequently recorded within an acute hospital. There is a growing trend to use derangements in physiological variables as calling criteria for critical care emergency teams. We collected physiological measurements on all inpatients in a district general hospital to determine whether they accurately identified those patients at risk of death or prolonged hosptial admission.

METHODS. On a single day (9th November 2004), all Stirling Royal Infirmary inpatients (n=206) were surveyed for Medical Emergency Team (MET) calling criteria 1. All adult medical and surgical inpatients were included in this 'snap-shot' study, regardless of why or when they were admitted to Stirling Royal Infirmary. Outcome was assessed by recording time to discharge from acute care, and one-month mortality.

RESULTS. One or more positive MET criteria were associated with a higher risk of death (Odds Ratio: 3.5), and greater length of hospital admission (p<0.01). A greater proportion of medical patients fulfilled one or more calling criteria compared with surgical patients (23% vs 11%). 'Triggering' was associated with a 24% mortality in medical patients compared with a 9% mortality in surgical patients.

TABLE 1.

Table 1: MORTALITY

	Number of patients (%)	One month mortality (%)	Odds Ratio (OR)	OR 95% confidence intervals
No M.E.T. criteria	170 (82)	6.5		
One or more M.E.T. criteria	36 (17)	19.4	3.5	1.25 - 9.7

CONCLUSION. Physiological derangement can be used to identify patients at higher risk of hospital death and prolonged hospital admission. The use of these, or similar, calling criteria could be used to prioritise acute care. A rapid and effective approach to these patients may reduce the length of hospital stay and overall mortality rate.

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SCORING SYSTEMS FOR IN-ICU MORTALITY IN BLUNT CHEST TRAUMA

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INTRODUCTION. There is no generally accepted standard for early judgment of the severity of injuries in regard to related complications in patients with chest blunt trauma. We investigated the impact of the existing scoring systems on predicting intra-ICU mortality and assessed which parameters evaluated at admission could have a prognostic role for mortality.

METHODS. Sixty-three patients with blunt chest trauma – mean age 41 ± 19 yrs, F 13 - consecutive admitted to our ICU from 1st January to 31th December 2004 were included in the study. The length of stay was calculated as well as ISS, RTS and SAPS. Plasma levels of cardiac troponin I was measured at admission.

RESULTS. The reasons for trauma were motor vehicle accident in 44 (70%), accidental fall in 11 (18 %) and other in 8 (12%). The length of stay was 13 ± 12 days and intra ICU mortality 20.6 % (13/63). Sternal fractures in 7 pts (11%), rib fractures in 35 (56%). Hemothorax was detectable in 14 pts (23%), pneumothorax in 29 (47%) and pulmonary contusion in 50 (79%). ISS was 33 ± 15, RTS 6 ± 2, SAPS 41 ± 18. Mean values of troponin I at admission were 2.4 ± 7.8 ng/ml (range 0.0 – 60.7). Logistic regression identified 4 variables able to correctly recognize the 89.6 % of survived patients and the 58.3 of dead patients with an accuracy of 83.3% (chi-square 20.042 p = 0.003). This logistic model was compared with values of ISS, RTS and SAPS by means of ROC curve analysis as depicted in table 1 (confidential limits of under curve area 95%).

TABLE 1.

		Std. error	95% confidence inter	95% confidence inter
Test result variable			Lower bound	Upper Bound
ISS	0.874	0.079	0.719	1.030
RTS	0.245	0.085	7.812E-02	0.412
SAPS	0.688	0.093	0.505	0.871
Predict Probability	0.866	0.052	0.763	0.969

CONCLUSION. in the present investigation we elaborated a logistic model composed by four parameters evaluated at admission able to provide a scoring system of severity in patients with blunt chest trauma. Among the existing scoring systems, the ISS appears to be the most capable in predicting intra-ICU mortality.

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PATTERNS OF ORGAN FAILURE PRECEDING DEATH IN THE ICU: RESULTS OF THE SOAP STUDY

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INTRODUCTION. We investigated the patterns of organ failure preceding death in the ICU.

METHODS. In this multicenter, observational study, all adult patients admitted to the participating centers between May 1 and May 15, 2002 were included. Of 3147 patients, the 583 (18.5%) who died in the ICU represent the focus of this study. Organ failure was defined as a corresponding organ SOFA score >2, and multiorgan failure (MOF) as >1 failing organ. The total daily SOFA score was used to assess the evolution of organ failure over the 3 days preceding death.

RESULTS. The 583 patients [57% males, mean age 64 years] died after a median of 3 [IQ: 1-10] days. During the 24 hours preceding ICU death, 57% had central nervous system (CNS) failure, 53% cardiovascular (CVS) failure, 42% renal failure, 37% respiratory failure, 17% hematological failure, and 9% had hepatic failure; 46 patients (8%) had no evidence of organ failure. The number of organ failures were: 1 in 23% of cases, 2 in 33 %, 3 in 24 %, and > 4 in 13% of cases. Single organ failure was mostly CNS (52%), less commonly renal (21%), CVS (15%), respiratory (8%), hematological (4%), and rarely hepatic (1%) failure. In the 402 patients (69%) with MOF, CVS failure occurred in 71% of cases, followed by CNS (65%), renal (53%), respiratory (51%), hematological (24%), and hepatic (13%) failure. In patients with CVS failure (n=307), it was mostly (94%) associated with another organ failure, commonly, CNS (55%), respiratory (50%), and renal (45%) failure, while those without CVS failure (n=230) mostly had CNS (70%) and renal (45%) failures, and commonly a single organ failure (50%). The Total SOFA scores increased moderately over the 3 days preceding death (mean ± SD: 8.5±4.5, 9.3±4.4, and 9.9±4.4, p<0.001), excluding patients who died within 48 hours of admission.

CONCLUSION. In this observational study, only 8% of patients dying in the ICU had no evidence of organ failure preceding death. Single organ failure was mostly CNS, while MOF was commonly associated with CVS failure. Hematological and hepatic failures usually occur in the context of MOF, mostly in combination with CVS.

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PATIENTS AGED 80 AND OLDER IN INTENSIVE CARE UNITS

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INTRODUCTION. Severely ill elderly patients are increasingly being admitted to hospital emergency departments and are frequently considered for treatment in intensive care unit (ICU). Objectives: To determine factors influencing ICU outcome and intra-hospital clinical evolution of critically ill elderly patients (aged ≥ 80), in order to evaluate their ICU admission benefits.

METHODS. In a retrospective research design, among the 376 critically ill elderly patients consecutively admitted to an ICU from the 1st January to the 31st December 2004, we examined data from the 56 (15%; 43% male, 57% female) oldest-old patients (aged ≥ 80). Days of ICU hospitalisation and of mechanical ventilation, hospital length of stay, severity of illness [simplified acute physiology score (SAPS II), admission sequential organ failure assessment (SOFA)] and ICU / hospital mortality were analysed.

RESULTS. Six patients died within the first 24 hours. Comparison of survivors and nonsurvivors revealed no statistically significant differences in age, or length of mechanical ventilation or of ICU stay. Higher admission SOFA scores were predictors of a higher ICU mortality. ICU mortality was 37.5% and total hospital mortality was 51.8%, being the expected SAPS II mortality 60.2%.

CONCLUSION. The findings of this study indicate that severity of illness was the only predictor of ICU outcome; age as well as other patient characteristics were not. This supports the recommendation that "very old age" should not be used as a criterion for ICU exclusion.

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LACTATE AS A PROGNOSTIC INDICATOR IN SEPSIS SYNDROME

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INTRODUCTION. The purpose of this study was to evaluate the prognostic value of 3 categories of initial lactate [high (HL) (>/= 4.0), medium (ML) (2.0–3.9) and low (LL) (<2.0)] on outcome.

METHODS. We performed an observational study of Emergency Department admissions to the hospital(Jan 2002-Dec 2004). Inclusion criteria: > 18yrs, diagnosis of septicemia, infection or(+)non-viral culture, antibiotics, and serum lactate measured. Patients were grouped by initial lactate values: HL (>/= 4.0), ML (2.0 – 3.9) and LL (<2.0). Subdivision was done by ICU admission, ICU transfer from the floor, and floor admission only.

RESULTS. We enrolled 764 patients (17% mortality). After controlling for age and comorbidity (Charlson-Deyo Score) mortality increased with increasing initial lactate. Lactate independently predicted mortality in the HL or ML group, whereas comorbidity and age independently predicted mortality in the LL group. Mortality of normotensive (NT) floor patients with HL was 36.8% with 44% transferred to the ICU

TABLE 1.

Lactate Level (mmol/L) vs Total Mortality and Admission Unit Mortality

	n	Charlson-Deyo Comorbidity	ICU %M	Floor to ICU % M	Floor Only % M	Total Chohort % M	p - value
High(>=4) % M	212	L: 35% H:42%*	39/89 (43.8%)	11/25 (44%)	10/32 (31%)	60/146 (41%)	<=0.001
Medium (2.0-3.9) % M	212	L:7.7% H20%*	26/85 (30.6%)	6/27 (22.2%)	7/100 (7%)	39/12 (18.4%)	<= 0.001
Low (<2.0)	406	L:0% H:9%**	17/111 (15.3%)	8/47 (17%)	6/248 (2.4%)	31/406 (7.6%)	<= 0.001

p>=0.22;p<= 0.02; Charlson-Deyo: Low risk(L) 0-2, High risk(H)=3, %M: mortality*

CONCLUSION. Lactate >/= 2 mmol/L is an independent predictor of mortality. In NT patients, initial lactate was associated with ICU admission, floor transfer to the ICU, and increased in-hospital mortality.

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SERIAL EVALUATION OF THE SOFA SCORE IN NON-CORONARY MEDICAL PATIENTS

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INTRODUCTION. To determine the usefulness of daily Sequential Organ Failure Assessment (1, SOFA) score for prediction of mortality in non-coronary medical intensive care unit (ICU) patients.

METHODS. A prospective, observational study was conducted from May 1997 to April 2001. Nine hundred nineteen consecutive adult patients admitted to the ICU for more than 24 hours were included (10164 patient days). The SOFA score was calculated on admission and every 24 hours until discharge.

RESULTS. Study patients had a mean age of 59 ±17 (±SD) years; 70% were male, mean ICU length of stay was 11 ±15 days, mean APACHE II score after 24 hrs was 19 ±10. Initial, maximum and mean (sum of daily SOFA scores divided through days of ICU stay) SOFA scores correlated well with mortality in the ICU (25.7%). The ability of the SOFA to discriminate between ICU survivors and non-survivors was assessed using the area under the receiver operating characteristic curve (AUC). AUC was largest for the mean SOFA score (0.90, 95% CI: 0.88-0.93) and the maximum SOFA score (0.88, 95% CI: 0.86-0.91). A mean SOFA score of more than 7 corresponded to a mortality of more than 83% vs 10% for a mean score of 7 or less. When analyzing trends in the first 48 hours, regardless of the initial score, the mortality was 56% when the score increased, 24% when it remained unchanged, and less than 20% when it decreased.

CONCLUSION. Sequential assessment of organ dysfunction during the first few days of ICU admission is a good indicator of prognosis. Both the mean and the maximum SOFA scores are particularly useful predictors of ICU outcome. Independent of the initial score, an increase in SOFA score during the first 48 hours predicted in our sample a mortality rate of 56%.

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SEVERE SEPSIS IN THE EMERGENCY DEPARTMENT: THE HIDDEN PATIENT

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INTRODUCTION. The success of the tratment of patients with severe sepsis and septic shock is directly related to the quality of assistance during the "golden hours"(1). Thus, it is a key factor that the emergency department (ED) team, who is the responsible for the initial care, has the right skills to deal with this disease. The aim of this study is to present the epidemiologic features of patients with severe sepsis in the ED and the capability of the ED team to identify those patients.

METHODS. Contemporary cohort study involving adult patients with severe sepsis attended at the emergency department (ED) in a tertiary hospital, using the criteria of SCCM/ACCP consensus conference to standardize the diagnosis of severe sepsis.

RESULTS. During six months period of the study, 5532 patients were admitted to the ED, of whom 342 fulfill the severe sepsis criteria. The median age was 73.7±13.5 years and 52.6% were male. The mean APACHE II and SOFA score were 20.4±7.1 and 5.3±2.8, respectively. There were a mean of 2.1+1.1 organic disfunctions per patient at the time of enrollment. The mean lenght of stay in the hospital was 12.9+11.9 days and the hospital mortality was 64.0%. About 90% of the patients had antibiotics prescribed by yhe ED physician. However, only 31% of the patients were diagnosed as having sepsis in the ED. Amongst the 342 patients with severe sepsis in the ED, only 115 (33.5%) were referred to an Intensive Care Unit (ICU) in the hospital. The mean time between the admission in the ED and arrival at the ICU was 1.7+2.7 days. The hospital mortality rate of the patients admitted to the ICUs was 75.7%.

CONCLUSION. The incidence of severe sepsis in the ED was 6.2%. ED team made the diagnosis of sepsis in less than a third of the patients and the majority of the patients with severe sepsis admitted in the ED did no arrived at the ICUs. Strategies to fight sepsis must include the training of the ED teams in the diagnosis and adequate interventions during the "golden hours".

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THE PREDICTIVE VALUE OF TIME SPENT IN INTENSIVE CARE ON THE PROBABILITY OF HOSPITAL SURVIVAL

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INTRODUCTION. When a patient is treated in the ICU, patient, family and staff wonder about the patients chances for survival, especially if he has been critically ill for several days. To get a feel for these chances we studied hospital survival in relation to APACHE II score at admission and the number of days spent in the ICU.

METHODS. The unit is a 10 bed general closed format ICU. All patients admitted between Jan 1st, 2004 and October 31st, 2004 were analysed and were considered in the analysis as a single cohort starting ICU treatment on day 1. For each day the number of patients remaining in the cohort and the proportion of patients surviving to hospital discharge were calculated.

RESULTS. Discharge status and APACHE II score were complete on 526 patients, mean age 65,7 yrs, accounting for 536 hospital admissions and 2149 ICU treatment days. If a patient was admitted to the ICU more than once during a single hospital admission, total ICU admission time was counted. Out of 536 admissions 41 died in the ICU and 15 died in hospital after ICU discharge. In a multivariate model including APACHE II, age and length of stay in the ICU, only length of stay in the ICU was not a predictor of hospital survival. What happened to the cohort is shown in Table 1.

TABLE 1.

Number of patients still in ICU / percentage to leave hospital alive

	Day 1	Day 3	Day 5	Day 10	Day 15	Day 20
All patients	536/90%	225/88%	121/84%	40/77%	20/75%	11/64%
A <10	179/97%	40/82%	13/85%	2/100%	3/100%	1/100%
A 10-14	148/98%	61/98%	27/96%	10/90%	3/100%	3/100%
A 15-19	107/91%	65/89%	42/86%	15/80%	7/86%	2/50%
A 20-29	74/73%	47/74%	29/74%	9/67%	5/60%	3/33%
A 30-44	28/39%	12/67%	12/67%	4/50%	3/33%	2/50%

A = APACHE II score at first ICU admission

CONCLUSION. Chances of hospital survival decrease with time spent in the ICU in the first weeks of ICU treatment, only because less ill patients leave the ICU earlier. In other words: patients with similar APACHE scores but different ICU length of stay have similar chances of hospital survival.

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PROGNOSTIC ROLE OF CARDIAC TROPONIN LEVELS AT ADMISSION IN BLUNT CHEST TRAUMA

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INTRODUCTION. Serum cardiac troponin (Tn I) is known to be highly specific of myocardial injury . This study was aimed at: a) assessing whether TnI levels at admission are able to affect intra ICU mortality; b) evaluating the relation(s) between Tn I levels and ECG changes and abnormalities at echocardiography.

METHODS. In 62 patients with blunt chest trauma– mean age 41 ± 19 yrs, M 50- consecutive admitted to our ICU during 2004 we evaluated: a) Tn I levels at admission; b) ECG indexes; c) abnormalities at TTE/TEE; d) intra ICU mortality.

RESULTS. The reasons for trauma were motor vehicle accident in 43 (69%), accidental fall in 11 (18 %) and others in 8 (13%). ISS was 33 ± 15. The length of stay was 13 ± 12 days and intra ICU mortality 19.4 % (12/62). At TTE/TEE pericardial effusion was observed in 16 pts (26%), wall motion abnormalities in 5 (8%) and cardiac hematoma in 1 (2%).

TABLE 1.

	Tn I < 0.1	> 0.1< 1 ng/ml	> 1 ng/ml	p
Dead	1	1	10	
Survived	20	17	13	0.044
ST elevation	56.5%	17.4%	26.1%	
No ST elevation	20%	35%	45%	0.013
Asynergia	0%	60%	40%	
No asynergia	36.2%	25.9%	27.9%	0.39

CONCLUSION. a) high levels of Tn I at admission are associated with a high intra ICU mortality, thus indicating a prognostic role for Tn I; b) Tn I is not related with ST elevation. Tn I concentration at admission appears to hold a prognostic role for intra-ICU mortality.

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EVOLUTIONARY PROGNOSTIC FACTORS IN ACUTE LUNG INJURY

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INTRODUCTION. Our aim is to value severity scores, focusing on ALI evolution patient's diagnosed acute lung injury (ALI), and to find prognostic factors.

METHODS. Prospective descriptive study from January 2004 to March 2005. Selected patients were diagnosed the ALI, in 2 ICUs. We analyzed epidemiology factors and evolution severity scores at the first five days ALI period, documenting PaO2/FIO2, LIS, oxygenation index (OI), APACHE II, APACHE III, SAPS II, SOFA, MODS y ventilation characteristics. Statistical tests: Chi-square, Fisher test, Student's t, U Mann-Whitney, Friedman and logistic regression analysis. Data expressed as mean (SD).

RESULTS. 51 patients, 35 men (68.6%), mean aged 56.06 (14.71) yr, APACHE II 21.09 (9.37). Patients showed intrapulmonary ALI 32 (62.8%) and sepsis 23 (45.1%). In the diagnostic time, 48 (94.1%) patients satisfied respiratory distress criteria, presenting PaO2/FIO2 127 (55.19), OI 28.5 (14.21), LIS 2.99 (1.15), APACHE II 18.9 (6.71), APACHE III 55.31 (18.49), SAPS II 56.02 (21.39), SOFA 9.37 (3.33), MODS 7.82 (3.04) and number failed organs 3.04(1.2). Initial respiratory parameters: plateau pressure 30.7 (6.04) cmH2O, peak pressure 34 (5.97) cmH2O and PEEP 10.25 (3) cmH2O. ICU length of stay (LOS) was 24.26(19) d, mechanical ventilation (MV) 21.26(16) d and MV length of pre-ALI 3.86 (5.25) d. Total mortality rate was 49% (25 patients.Patients with worse prognosis were older 61.92 (12.03) vs. 50.42(15.04) yr (p<0.01) and shorter ICU LOS 17.42 (14.6) vs. 30.58(18.75). From third day, we find out significant differences about mortality in PaO2/FIO2 133 (72.25) vs. 185.6 (67.16) (p<0.05), OI 35.53 (22.03) vs. 23.35 (25.45)(p 0.01)and from fourth day in LIS 2.88 (1.74) vs. 2.47(1.74)(p 0.001). Independent associated factors a higher mortality were ICU LOS (OR 0.62 (0.47-0.84); p=0.0018)and MV LOS (OR 1.53 (1.14-2.07); p=0.004. We observe evolution improvement in (p<0.0001), IO (p<0.0001), LIS (p<0.0001), APACHE II (p=0.04), SOFA (p<0.001), MODS (p<0.0001)and number failed organs (p<0.01) in the alive group.

CONCLUSION. The rise mortality in our study is due to a higher rate of patients with respiratory distress criteria. From the third day, PaO2/FIO2 and OI indicate us the evolutionary tendency and outcome prediction in patients with ALI at ICU.

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DIFFERENTIAL CHARACTERISTICS OF STENOTROPHOMONAS MALTOPHILIA (SMA) INFECTIONS IN AN ICU

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INTRODUCTION. The importance of Stenotrophomonas maltophilia (SMA) as an etiologic frequently polyresistant pathogen in severe nosocomial infections has increased. However there is a few data about its role in intensive care units. The aims of this study were to know the epidemiology, clinical features and outcome of SMA infections in ICU and to analyse the possible differences with SMA infections in other hospitalization areas.

METHODS. During a five and a half-year period (1999 - 2004) we have retrospectively evaluated all of SMA infections in a teaching hospital and especially those occurred in ICU. Epidemiological clinical and microbiological features were recorded from clinical charts. Univariate analysis was performed to determine the possible differences between ICU and hospitalization wards infections.(p values < 0.05 were considered significant)

RESULTS. Forty-two SMA infections were reviewed. Fifteen episodes were ICU-SMA infections. The mean age of these patients was 66.6 SD 17.7 years. Masculine sex, prior vascular surgical procedure, mechanical ventilation, presence of abdominal drainage, APACHE II and SOFA score at onset of infection, and the incidence of septic shock were significantly higher in SMA infections. The main foci of ICU-SMA infections was respiratory in 53%, unknown in 26% and abdominal 13% without any differences between two groups. Episodes of Bacteriemia were not either more frequent in ICU-SMA infections. Although there were no differences in the patterns of resistance and the incidence of inadequate empirical antibiotic treatment global mortality (73,3% vs 22,2 %; p= 0.001) and related mortality to infection (20% vs 0%; p= 0.01) were statistically higher in ICU-SMA infections

CONCLUSION. ICU-SMA infections showed different clinical features and higher mortality rates than SMA infections in hospital wards although there were no differences in the pattern of resistances, the incidence of inadequate empirical antimicrobial treatment or foci of infection between two groups.

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A PREDICTIVE MODEL FOR PROLONGED MECHANICAL VENTILATION (MV) IN 5015 CARDIAC SURGICAL PATIENTS

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INTRODUCTION. Cardiac surgical patients (pts) need prolonged (>72 hrs) MV in 3-9.9% and tracheostomy (T)in (1.6-4.5%)of cases(1). This prospective audit was set up to assess a predictive model (PM) for MV in our cohort of such pts.

METHODS. On all admitted pts, since Jan 1997 to June 2004, we collected (i) demographics, surgical operation type, gravity score and risk factors (ii)cardiopulmonary by-pass (CPB) and aortic cross clamp (ACC)times (iii) ICU supportive techniques (MV, CVC)and presence of T. SPSS was used for statistical analyses. A binary Logistic Regression Model (b-LRM) was used to estimate the effect of each independent variable [age,operation type, gravity scores, hypertension, diabetes, chronic renal failure (CRF), COPD, CPB and ACC times, emergency operation] on a T (yes/no) outcome. P values less than 0.05 were considered significant.

RESULTS. Out of 5015 pts [M:F = 2.5 : 1, median (IQR) age 67 (59-73) yrs; 72.3% with coronary artery disease and 23.3% with valvular heart disease], 112 underwent a percutaneous T. The overall recorded mortality was significantly higher in T pts than in others (36.6% vs 3.2%, p = 0.0000). The b-LRM allowed us to identify the following independent variables i) age > 65 yrs [O.R. (95% IC) 2.1 (1.4-3,2), p 0.0387] ii) combined (valve + CABG) surgical operation [O.R. (95% IC) 2.2 (1.3-3.8), p 0,0018] or re-do [O.R. (95% IC) 3.2 (1.6 – 6.4), p 0.0223] iii) CCS [O.R. (95% IC) 1.9 (1.1-3.2), p 0.0453] or NYHA > 2 [O.R. (95% IC) 4.8 (2.5 - 9.5), p 0.0000] iv) CRS > 8 [O.R. (95% IC) 7.2 (4.8 – 10.7), p 0.0000] v) presence of CRF [O.R. (95% IC) 4 (2.7 – 6.1), p 0.0000] or COPD [O.R. (95% IC) 2.7 (1.8 – 4), p 0.0088] or arteriopathy [O.R. (95% IC) 2.2 (1.5 – 3.2), p 0.0000] vi) CPB > 90' [O.R. (95% IC) 3 (1.5 – 5.9), p 0.0008] or ACC time > 60'[O.R. (95% IC) 1.7 (1.1 – 2.6), p 0.0015] as independent predictive factors of prolonged MV and T.

CONCLUSION. The bedside set up PM may help us to identify "a priori" pts that are more likely to need a prolonged MV. Further studies are needed to corroborate our RESULTS.

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THE "SANDWICH" MEDICATION: A NEW METHOD TO PREVENT CVC INFECTIONS. A RANDOMIZED TRIAL

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INTRODUCTION. Eighty percent of central venous catheter (CVC) infections are caused by skin pathogens. Excessive CVC manipulation increases risk to develop catheter-related bloodstream infections (CRBSIs). We evaluated if a new type of medication, which reduces CVC manipulation, may reduce the occurrence of catheter-related infection.

METHODS. All patients admitted from March 2001 to June 2004 receiving a CVC in the subclavian or internal jugular vein were randomized to two groups: in one group, the catheter was kept apart from skin by including it between two transparent sheets, so that the insertion site remained the only point of contact of CVC with the skin; the sandwich remained always closed for the entire catheter life ("Sandwich" medication). In the other group, the CVC remained on the skin surface covered by a single transparent sheet, with medication opened and the insertion site disinfected every 48 hours ("Flat" medication). Exclusion criteria were: patients under 18 years of age; CVCs placed in femoral vein; lack of sterile techniques; forecast of catheterization under of 3 days. Primary outcome was the number of infected catheters/1000 days of catheterization. Secondary outcomes were: CRBSIs/1000 days of catheterization, skin colonization around the insertion site, number of CVC used, number of medications, length of CV catheterization, duration of antibiotic therapy, length of ICU hospitalization, mortality at 14 and 28 days.

RESULTS. 152 patients were randomized, 81 in the "Sandwich" group and 71 in the "Flat" group. There were no differences in all considered outcomes between the two groups, except for the number of medications: 1.65 medications/catheter in the "Sandwich" group versus 4.38 in the "Flat" group (p<0.0001).

CONCLUSION. "Sandwich" medication is a safe and efficient method of CVC management. It may consent a reduction of nursing time and costs.

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THE EFFECT OF STERILE AND NON-STERILE TOWELS ON SKIN BACTERIAL FLORA FOLLOWING IODINE SHOWER

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INTRODUCTION. Postoperative infection is still a serious consequence of surgical procedures. Reducing normal skin flora by showers containing desinfectant may help preventing this complication. In this study we examined the effect of sterile and non sterile towels on the desinfecting effect of preoperative showers.

METHODS. Forty male patients, age 61 ± 8 years, scheduled for cardiac surgery were included in the study.Twenty used his own towel, twenty used sterile towels following each showers with povidone-iodine.
The first sample was obtained before the first shower, the second following it.The third sample was taken before the second shower and the fourth following it.Povidone-iodine containing 7.5 mg free iodine , Egis, Hungary) was used as the skin mL-1 (Betadine samples were taken with contact Rodac"disinfectant.Bacterial Petri plate (Neomed, Italy). Samples were taken from the same part of the chest. The plates were incubated for 24 hours at 37 oC and the colony forming units (cfu) were counted.Statistical method: Wilcoxon rank-sum test.

RESULTS. The bacterial count increased after the second shower when patients used their own towels. It reduced after the second shower using sterile towels for drying.The effect of povidone-iodine shower and drying on skin flora. Using own towel: before first shower 6.7 (2-12.9) cfu/cm2, after first shower 7.4 (5-13.8) cfu/cm2, before second shower 3.3 (2-7.5) cfu/cm2, after second shower 15.9 (11-44)* cfu/cm2. Using steril towel: before first shower 26,9 (8-51) cfu/cm2, after first shower 10,75 (4-11,6)* cfu/cm2, before second shower 6,3 (1,9-15,4) cfu/cm2, after second shower 2,1 (0,8-4,1)* cfu/cm2. Median of colony forming units (cfu) (min-max). *P<0.05.

CONCLUSION. Our results suggest that drying with non-sterile towel affect adversely the beneficial effect of preoperative showering with povidone-iodine.

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BACTEREMIA IN THE ELDERLY ICU PATIENTS: ANALYSIS OF 53 CASES

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INTRODUCTION. The purpose of this trial is to study the clinical features of bacteremia in the elderly ICU patients (pts), the pathogenic microorganisms and their resistance and the factors affecting mortality.

METHODS. We studied retrospectively 232 ICU pts, 196 men (84.5%) -36 women (15.5%) who developed bacteremia. Mean age: 48.1±20.7 years (16-88), mean stay: 19.2±9.4 days. All pts underwent mechanical ventilation and were divided in 2 groups according to their age: Group A 179 (77.2%) ≤65 and group B 53 (22.8%) > 65 years. In groups A and B respectively: mean age 40.1±15.6 and 75.2±4.8 years. Mean stay 20.3±6.7 and 15.5±6.2 days. Underlying diseases: Multiple trauma 112 (62.6%) and 20 (37.7), complicated surgery 48 (26.8%) and 28 (52.8%), other 19(10.6%) and 5 (9.4%), Malignancies were present in 5 (2.8%) and 5 (9.4%), diabetes mellitus in 16 (8.9%), and 10 (18.9%), cardiac failure in 8 (4.5%) and 8 (15.1%) and COPD in 5 (2.8%) and 6 (11.3%). Several parameters of bacteremia occurred by a single strain were analyzed.

RESULTS. The invading microorganisms in groups A and B were: Ps. aeruginosa 78 (43.6%) and 30 (56.6%), Ac. baumannii 64 (35.8%) and 1 (1.9%), St. aureus 26 (14.5%) and 10 (18.9%), St. epidermidis 4 (2.2%) and 2 (3.8%), Kl. pneumoniae 4 (2.2%) and 2 (3.8%), other 3 (1.7%) and 8 (15.1%). Site of infection: Pneumonia 118 (65.9%) and 23 (43.4), intra-abdominal infection 28 (15.6%) and 10 (18.9%), central venous catheter-related infection (CVC-RI) 29 (16.2%) and 19 (35.8%), meningitis 4 (2.2%) and 1 (1.9%). Multiple organ dysfunction syndrome (MODS) occurred in 18 (10.1) and 24 (45.3%). Mortality rates 24/179 (13.4%) and 22/53 (41.5%). Global mortality rates: 46/232 (19.8%).

CONCLUSION. 1) Invading organisms were similar in both groups except A. baumannii, which was much more frequently isolated in younger pts and almost never in the elderly (p<0.001). 2) Elderly developed more frequently CVC-RI (p<0.01) than younger pts. All other sites of infection were similar. 3) Elderly developed more frequently MODS (p<0.001) and had higher mortality rates (p<0.01). 4) The resistance of the organisms was similar in both groups. 5) The outcome of the infection was independent of the type of invading organism and its resistance.

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COLONIZATION AND INFECTION BY MRSA IN CRITICALLY ILL PATIENTS

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INTRODUCTION. To determine the incidence of colonization and infection by MRSA in critically ill patients.

METHODS. It is a prospective study during 30 months of the patients admitted in ICU during 24 hours o more. Were taken throat swab, tracheal aspirate and urine on admission and twice weekly. Were registered the colonization and infection by MRSA. The infections were diagnosed according to CDC criteria. The infections were classified bassed on thorat flora as: Primary endogenous (PE) when they were caused by germs that were already colonizing the throat on the ICU admission; Secondary endogenous (SE) when they were caused by germs that were not colonizing the throat on the ICU admission but were acquired during the stay in ICU; Exogenous (EX) when they were caused by germs which were not colonizing the throat. The infections were classified bassed on the onset moment as: Early onset (EO) were those developed during the first 4 days of ICU-stay; Late onset (LO) were those developed 5 days after ICU-admission.

RESULTS. Were admitted 1582 patients, 953 males (60.24%). The mean age was 57.91±18.83 years. The mean APACHE-II score was 13.95±8.93. Admission diagnoses were: 737 (46.59%) heart surgery, 189 cardiological (11.95%), 196 neurologic (12.29%), 185 trauma (11.69%), 120 respiratory (7.59%), 104 digestive (6.57%) and 51 intoxication (3.22%). Mortality 14.79% (234 patients). A total of 36 patients had colonization by MRSA, 2 patients at ICU-admission and 34 patients during the ICU-stay. Were documented 24 infections caused by MRSA (4 EO and 20 LO; 0 PE, 21 SE and 3 EX): 18 pneumonias (3 EO and 15 LO; 0 PE, 15 SE and 3 EX), 3 primary bacteremias (1 EO and 2 LO; 3 SE), 2 surgical wound infections (2 LO and SE) and 1 pressure sore infections (1 LO and SE). Death 7/24 patients (29.17%) with infection caused by MRSA: 6/18 (33.33%) pneumonias, 1/3 (33.33%) primary bacteremias and 0/3 other infections.

CONCLUSION. In our serie, the most of infections caused by MRSA were pneumonias, had a late onset and were secundary endogenous.

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REPEATED PREVALENCE: AN ALTERNATIVE TO THE CONTINUOUS MONITORING OF INCIDENCE

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INTRODUCTION. The surveillance for nosocomial infections (NI) in intensive care units (ICU) is one of the major parts of the NI control programme. This surveillance is generally carried out through daily report of new cases of NI, which provides rate and incidence density. In daily practice, this method is time consuming and needs medical involvement, which is not always compatible with the amount of work in an ICU. This is why, in our ICU we chose to implement a surveillance system based on half-monthly repeated one-day prevalence surveys.

METHODS. We conducted a six-month double survey including continuous incidence and repeated prevalence.

RESULTS. The results of this study are resumed in the table below :

TABLE 1.

	Incidence	Repeated prevalence
Number of patients	184	128
Rate of infected patients (95% confidence interval)	25% (19-32%)	27,3% (20-36%)
Incidence density	37 NI / 1000 days	-
Respiratory tract	48,3% (38-59%)	57,5% (41-73%)
Urinary tract	21,8% (14-32%)	22,5% (11-38%)
Bacteremia	14,9% (8-24%)	10,0% (3-24%)
Time spent to collect data	about 10 hours / month	about 2 hours / month

CONCLUSION. There is a little difference between incidence and repeated prevalence. The main interest of the continuous monitoring of incidence liesis to provide a density of incidence. This advantage must be compared to less workload and better compliance from the medical staff for the repeated prevalence survey. However a surveillance system based on repeated prevalence surveys should not encourage a lack of interest for NI prevention. For this reason, it is essential that the ICU medical staff takes an active part in the data collection. On this condition, repeated prevalence surveys should be an acceptable alternative to the continuous monitoring of NI incidence.

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MORBIMORTALITY ASSOCIATED WITH PRIMARY BACTEREMIA AND INTRAVASCULAR CATHETER

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INTRODUCTION. To analyze the morbimortality associated to bacteremia

METHODS. A cases-controls study, patients were admitted in intensive care unit(ICU) from March 2003-December 2004. Each was matched with two controls compared by: sex, APACHEII, GCS,age and MV. We analized ICU stay and mortality. Cuantitative variables were compared by t-test and categorical by x2 test. Logistic regression analysis was used for variables no uniform distribution. A p < 0,05 was considered statiscally significant.

RESULTS. Of the 1592 patients were admitted in the ICU during study period,66 bloodstream infection that means 7.8/1000 days of catheterization, wich compared 132 controls. There were no differences between the two groups in: age(56.7casesvs56.8 controls, sex (male: 77% vs 80%),GCS (11vs11.3), APACHEII (16.3vs16.4) and MV (91.6vs91.7). The most common organisms were: St. coagulase negative 28%, St. aureus 24%, Klebsiella 10%. Mortality was no statiscally significant (20% vs 24%). ICU stay was statistically higher in cases 28.7vs18.2 in controls (Dif 10.5;CI 95%:5-16.1). Categorical variable were similar: comorbilities, diagnostics, NEMS, SOFA, need of MV, tracheostomy, need of reintubation, IPC, urinary catheter, nasogastrical tube and parenteral nutrition. There were significant differences in:number arterial catheter (67%vs80%), Swan-Ganz catheter (0%vs10%), need of non MV (21%vs10%), digestive dysfuntion (21%vs10%), ARDS (41%vs29%) and haematology disfuncion(14%vs5%). No bacteremia nosocomial infection different was no statistically different (35%vs23%). Multivariant analysis was performed and bacteremia was only associated with morbidity (table)

TABLE 1.

	OR	CI: 95%
Bacteremia	6.6	(1.12-12.03)
Arterial catheter	8.6	(2.62-14.53)
Non invasive MV	8.6	(1.26-15.86)
Digestive dysfuncion	14	(0.54-27.40)
Nosocomial infection	11.3	(5.64-16.88)

CONCLUSION. This investigation observed that the primary nosocomial bacteremia and intravascular catheter bacteremia is associated with higher ICU stay , whithout changing mortality

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PERFORMANCE OF THE MENINGOCOCCAL SEPTIC SHOCK SCORE

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INTRODUCTION. As strict selection criteria are needed to identify severe cases of meningococcal septic shock candidate to new therapies, we evaluated the performance of the recently proposed Meningococcal Septic Shock Score (MSSS)Ref in children admitted to a Portuguese intensive care unit (ICU).

METHODS. We reviewed the medical charts of 168 meningococcal disease patients <18 yrs, admitted from 1988-2002 to the ICU and 65 cases (31 girls/34 boys, median age 2 yrs.) met the criteria for septic shock. Patient's MSSS was obtained using the worst clinical and laboratorial results recorded during the initial 2 admission hours. MSSS ranges from 0 to 10 points: cyanosis (2 points), Glasgow coma scale <8 (2 points), refractory hypotension (2 points), oliguria (1 point), leukocytes <4000/mm3 (1 point), partial thromboplastin time >150% of control value (1 point) and base deficit >10 mmol/l (1 point). The outcome variable was ICU death. Individual probability of death was calculated using the original alpha and eta valuesRef. Standardised mortality ratios (SMR) and 95% confidence intervals (95%CI) were calculated. The score sensitivity, specificity, positive and negative predictive values (PV), and accuracy were estimated and a receiver-operating characteristic (ROC) curve constructed.

RESULTS. The sample case-fatality was similar to the MSSS predicted value (32.3% vs. 35.1%), the SMR being 0.92 (95%CI:0.53-1.32). In the low (score <4), intermediate (score 4-5) and high (score >5) risk groups, the actual/MSSS predicted mortality ratios (%) were 3.2/3.3; 38.5/34.5 and 71.4/82.3, respectively. The best accuracy corresponded to a score >5 (81.5%) with sensitivity=71.4%, specificity=86.4%, positive PV=71.4%, and negative PV=86.4%. The area under the ROC curve for the MSSS score was 0.89 (95%CI:0.81-0.97).

CONCLUSION. The MSSS showed a good ability to discriminate patients prognosis. In children with presumed meningococcal septic shock at ICU admission the score seems an appropriate tool to assess the severity of illness, making it useful in clinical practice and research.

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TREND OF NOSOCOMIAL BACTEREMIA IN A POLYVALENT ICU (2000-2004)

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INTRODUCTION. The aim of this clinical trial is to study nosocomial bacteremia (NB) in our polyvalent ICU (10 beds in a tertiary - 880 beds hospital).

METHODS. We studied retrospectively the cases of NB occurred in the ICU from 1/1/2000 until 30/11/2004. We enrolled 1123 pts, 801 men (71.3%) – 322 women (28.7%). Mean age 52.4±19.6 years (15-88). Underlying diseases: Multiple trauma 620 (55.2%), complicated surgery 412 (36.7%), vascular cerebral accident 19(1.7%), neuromuscular disease 18 (1.6%), myocardial infarction and cardiac arrhythmias 16 (1.4%), other 38 (3.3%). Types of microorganisms were recorded and sources of NB were determined. The trend of NB was analyzed over the last 5 years. On June 2003 a restriction antibiotic policy was introduced in our ICU.

RESULTS. Table's abbreviations: Rate: NB/1000 patient-days, VAP: Ventilator-associated pneumonia, CVC-RI: Central venous catheter-related infection, MRSA: Methicillin resistant St. aureus, VRE: Vancomycin resistant enterococcus.

TABLE 1.

	2000	2001	2002	2003	2004
PD	3510	3488	3522	3459	3252
NB	98	108	131	168	170
Rate	27.9	30.9	37.2	48.6	52.3
CVC-RI (%)	8.4	10.9	14.3	17.6	21.1
St. aureus (%)	12.6	13.4	14.3	16.1	17.1
MRSA (%)	8.9	12.1	15.4	19.3	23.4
VRE (%)	0	5.1	10.2	10.8	9.4
VAP (%)	31.4	33.6	32.4	35.1	30.4

CONCLUSION. 1) The overall NB rate increased significantly passing the years (p<0.05). 2) All types of infections causing NB remained stable except CVC-RI which increased significantly every year passing (p<0.05). 3) We noticed a slight increase of the frequency of isolation of St. aureus (p<0.1); among these, the percentage of MRSA increased significantly (p<0.05). 4) St. epidermidis and enterococcus remained stable, but we experienced the emergence of VRE since 2001. 5) Candida sp., Ps. aeruginosa, Ac. baumannii, Kl. pneumoniae and other Gram (-) organisms remained stable.

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USEFULNESS OF MEDS SCORE FOR PATIENTS ADMITTED IN INTENSIVE CARE UNIT (ICU)

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INTRODUCTION. Mortality in Emergency Department Sepsis Score (Shapiro et al.Crit.Care Med.2003;31:670) is a clinical prediction rule (9 items) for patients (pts) undergoing blood cultures in the Emergency Department (ED).Objectives:to study the accuracy of MEDS and SAPS II scores;to define a helpful cut-off value for the clinicians in the ED triage.

METHODS. Monocentric study.Pts:All septic adults admitted from the ED into the ICU during 39 months.Measurements:Demographic data,clinical informations (source of infection),hospital outcome were obtained.Lenght of stay (LOS),MEDS and SAPS II scores were calculated.To risk stratify patients and to compare demographic data,outcome,MEDS and SAPS II scores performances,pts were stratified in the 5 risk groups previously validated.

RESULTS. 213 pts (62.3±10.8 yr) with proven sepsis (respiratory:112, urinary tract: 22, abdominal: 29, neurologic: 22,other sources:28) were included.Mean MEDS and SAPS II scores were respectively (10±4,54±24),median ICU LOS:4d (1-114),hospital LOS:13d (1-155).Hospital mortality rate was 31.4 %.MEDS variables:26 pts had a terminal illness (<30 d) (6 points),177 a tachypnea or hypoxia (3 points),106 a septic shock (3 points),84 had platelets<150 000/mm3 (3 points),1/48 bands>5 % (3 points),111 were >65 yr (3 points),111 had a lower respiratory infection (2 points),20 were nursing home residents (2 points) and 115 had altered mental status (2 points).Demographic characteristics and mortality rate according to MEDS groups are reported in table.A MEDS score ≥ 10 points is performant to predict a high risk of mortality (48 %):OR:5.91 (95 % CI 3.006–11.625), Se:0.482, Sp:0.864, PPV:0.791, NPV:0.610.

TABLE 1.

MEDS Score	Patients	Age (yr)	SAPS II	Mortality %
a (0-4)	19	44.6±16	31.8±16.7	5.2
b (5-7)	35	48.4±15.5	38.3±16.6	8.5
c (8-11)	96	63.6±18.7	52.2±20.4	27.1
d (12-15)	38	74.1±11.6	67.1±22.5	47.4
e > 15	25	72.7±11.5	78.1±23.2	76

CONCLUSION. For ICU patients with proven infection,MEDS score allows stratification according to mortality risk;a value of 10 or greater could be helpful for ED triage and ICU decision.

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LEPTOSPIROSIS IN ICU. THE FRENCH POLYNESIAN EXPERIENCE

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INTRODUCTION. Leptospirosis remains a public health issue in tropical areas. The natural course of Leptospirosis in intensive care (ICU) is poorly documented.

METHODS. We conducted a retrospectiv study, that included all patients (pts) admitted to ICU with serologically confirmed Leptospirosis, between February 2001 and March 2004

RESULTS. 42 patients were included in the study, 35 m/7f. The ICU mortality was 12%. 4 /5 pts died because of refractory shock. Time between first clinical symptoms and admission to ICU was 5 ± 2.5 days (d). 29 pts were shocked (69%), septic shock in 25 pts (64%), hemorrhagic shock in 3pts (7%), and cardiogenic shock in 7 pts (12%). 27 pts required vasopressors (58%). The mean vasopressor administration duration was 9 ± 8 d. Neurological complications were reported in 5 pts (12%). One patient died in uncontrolled status epilepticus. 21 pts were mechanically ventilated (50%), among them 7 required proning (17%). Mean ventilation duration was 10 ± 8 d. 18 pts received blood products (43%), 16 pts received Desmopressin (DDAVP) (38%). 36 pts were in renal failure (85%), among them 10 required hemodiafiltration (24%). The mean hemodiafiltration duration was 7 ± 6 d.

TABLE 1.

Age [yrs]	7 ± 6
SAPS II	44 ± 22
Duration in ICU [d]	7 ± 6
Seizures	3 (7%)
CVA	2 (4.8%)
ARDS	15 (35%)
Hemoptysia	22 (52%)
Intra alv hemorrhage	18 (40%)

CONCLUSION. The morbidity and mortality of patients suffering Leptospirosis remains significant despite intensive care. Further clinical studies are required to improve our knowledge about disease process, outcome, and optimal management

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ICU ACQUIRED INFECTIONS AND THEIR RISK FACTORS IN THE PREZIES SURVEILLANCE SYSTEM

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INTRODUCTION. ICU patients are at increased risk of nosocomial infections due to their frequently impaired immunity and dependence on invasive devices. Knowledge of the ICU acquired infection rate and its risk factors can give insight in possibilities for infection prevention.

METHODS. During 1997-2000 19 Dutch hospitals prospectively collected demographic data, type of admission and APACHE II score for patients, admitted without infection, who stayed at the ICU > 48 hours. The use of SDD, intravenous antibiotics (AB), mechanical ventilation, central venous catheters and urinary tract catheters (CAD) was registered daily. The occurrence of (device-associated) pneumonia, sepsis and urinary tract infection (UTI) was monitored. Relative risks were calculated using Cox regression (infection) and logistic regression (time at risk, mortality).

RESULTS. Data were collected on 2,644 patients with 25,432 ICU days. Of all patients 26% developed one or more nosocomial infections: pneumonia occurred in 15%, sepsis in 7% and UTI in 8% of the patients. Pneumonia cases: 84% associated with mechanical ventilation. Sepsis cases: 21% primary sepsis, 30% CVC-related and 49% secondary to another infection. UTI cases: 95% CAD-associated. The mean incidence of VAP was 32, of CVC-related sepsis 4 and of CAD-associated UTI 11 per 1000 device days. Ventilation increased the risk of all three types of infection. CAD use increased the risk of both pneumonia and UTI whereas CVC use increased the sepsis risk only. The risk of pneumonia was also affected by an increased APACHE II score, admission for internal medicine or cardiology/-surgery and SDD. The latter two risks decreased with longer time at risk. The risk of sepsis was affected by an increased APACHE II score. UTI risk was increased for women, admission for internal medicine and impaired immunity. Intravenously given antibiotics at admittance were associated with a lower risk. A longer device use increased the risk of CVC-related sepsis (5-14 and ≥ 15 days) and the CAD-associated UTI risk (≥ 15 days). Mortality was 25% and median ICU stay 14 days for patients with and 13% and 5 days for those without infection. Mortality was associated with ICU acquired infection, age, APACHE II score, specialty, acute admittance, length of stay.

CONCLUSION. Device use, time at risk, APACHE II score, specialty, intravenous AB at admittance, immunity, SDD use, sex and acute admittance are of importance when stratifying ICU acquired infection risks for interhospital comparison. As of 2000 Dutch hospitals can use specific surveillance protocols for CVC-related sepsis and ventilator-associated pneumonia, which take more treatment risk factors into account and may better support infection prevention policy in the ICU.

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RELATIONSHIP BETWEEN PLASMA GLUCOSE LEVELS AT THE ONSET OF BACTEREMIA IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Some infections occur with increased severity and are associated with an increased risk of complications in patients with diabetes. However, the influence of the level of glucose in plasma on the prognosis of severe infections is a debated subject. The aim of this study was to know the impact of the level of plasma glucose at the onset of bacteremia on the prognosis of bacteremia in critically ill patients, with and without diabetes mellitus.

METHODS. From 1996 to 2004, 308 patients admitted to an intensive care unit of an university hospital, with clinically significant bacteremia were evaluated. The glucose in plasma at the moment of the extraction of blood culture was determined, and its relation with the prognosis of bacteremia, in diabetic and non diabetic patients, was analysed using the statistical programme SPPS.

RESULTS. Seventy six patients had diabetes mellitus (24,6%), with a mean level of plasma glucose at the onset of bacteremia of 246.4 ± 111.5 mg/dL, and 232 (75.4%) did not have diabetes mellitus, with a mean level of plasma glucose at the onset of bacteremia of 160.86 ± 88.9 mg/dL. The level of plasma glucose at the onset of bacteremia was not different between patients with related mortality to bacteremia (187.2 ± 117.2 mg/dL) and without related mortality to bacteremia (179.9 ± 95.5), p = 0.578. The related mortality to bacteremia according with different levels of plasma glucose at the onset of bacteremia were: glucose < 80 mg/dL, mortality 44.4%; glucose 80-110 mg/dL, mortality 22.2%; glucose 111-140 mg/dL, mortality 27.1%; glucose 141-180 mg/dL, mortality 25%; glucose >180 mg/dL, mortality 27.8% (p = 0.489).

CONCLUSION. In our study there was not a relationship between plasma glucose levels at the onset of bacteremia and inhospital related mortality to bacteremia, neither in diabetic nor non-diabetic patients.

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ICU-ACQUIRED BLOODSTREAM INFECTIONS (BSI) FROM 8 EUROPEAN COUNTRIES (HELICS-ICU)

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INTRODUCTION. The establishment of a large reference database for Nosocomial Infections in European ICUs was an objective of the HELICS protocol. Data concerning BSI were obtained from the pilot database.

METHODS. Data were obtained from national networks representing 659 ICUs in 8 countries (437,081 ICU patient): Austria, Belgium, Germany, Spain, France, Luxemburg, The Netherlands and Portugal. Inclusion criteria in the surveillance and definitions are given in the HELICS-ICU protocol (http://helics.univ-lyon1.fr/). In all the countries except Germany, patients-based data were obtained with patients staying 48 hrs or less excluded.

RESULTS. Incidence. ICU-acquired BSI incidence is 3.1% of patients staying > 2 d in the ICU (Germany excluded), depending of the country (2 to 6.9 %). Incidence density (per 1000 patient-days) was 2.2 (Germany excluded), varying from 2.2 to 6.7.

Origin of BSI. BSIs were catheter-related : 39.5%, secondary to another infection : 29.4% and of unknown origin : 31.1%. **Micro-organisms reported in ICU-acquired BSI.** The most frequently isolated micro-organisms were coagulase-negative staphylococci (CNS), at the first rank in all countries except one and count for 24.7 % (mean of all countries). S aureus represents only 13.2 %, enterobacteriaceae (EB)21.2 % and Gram negative (GN)non EB 11.6 % (8.7 % for Pseudomonas). **Distribution of micro-organisms by BSI origin (6 countries).** While GP cocci represent the majority of micro-organisms in catheter-related (69%) and of unknown origin (62.7 %) bloodstream infections, secondary micro-organisms are more frequently caused by BN bacteria : 63.4 % of pulmonary infections and 60 % of UTI. **Distribution of isolated micro-organisms according to the time of onset of the infection.** While the relative frequency of S. aureus remains rather constant, the % MRSA increases. The relative frequency of P. aeruginosa increases in late-onset infections, as well does the combined resistance to ceftazidim and ticarcillin.

CONCLUSION. Despite a important variability among participating countries, secular trends are obvious in microbiological epidemiology.

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THE CHANGING PATTERN OF RENAL REPLACEMENT THERAPY: RESULTS OF TWO SURVEYS IN 1998 AND 2004

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INTRODUCTION. A questionnaire on various renal replacement therapy (RRT) aspects was submitted to attending participants during the 1st and 3rd International Course on Critical Care Nephrology held in Vicenza Italy in 1998 and 2004, respectively. Responders were nephrologists and intensivists coming from five continents.

METHODS. 345 questionnaires in 1998 and 560 in 2004 were correctly completed. Two sets of fulfilled questionnaires were collected into an access database and results examined. Percentage values are reported.

RESULTS. Continuous Arterio-venous hemofiltration (CAVH), representing one of available options for more than 70% of candidates in 1998, was abandoned in 2004. Continuous veno-venous RRTs were also considered by more than 90% candidates in both surveys. In 2004 intermittent techniques, available in only 20% centers in 1998, were routinely available in more than 80% institutions, administered as intermittent hemodialysis (two-thirds) or as slow extended daily dialysis (one third). Peritoneal dialysis was present in 20% intensive care units (ICU) in both 1998 and 2004. Hemofiltration (HF) was and remained the preferred RRT modality. ICU physicians, independently prescribing RRTs, increased from 15 to 30%. Anticoagulation management did not change significantly, and patient bleeding remained one of the most selected complains during both meetings, together with circuit clotting. Responders notably modify their RRT prescriptions from 1998 to 2004: urea clearance increased from 1-1,5 L/h (range 0,5-2 L/h) to 2-3 L/h (range 1-10 L/h). Similarly, more than 50% of available equipment in 1998 consisted with CAVH kits, or adapted machines from chronic therapies, whereas in 2004 100% of participants declared to use dedicated integrated monitors. About 90% responders answered to agree with extra renal RRT indications (congestive heart failure, severe sepsis, septic shock, anasarcha) in both questionnaires: two thirds in 1998 and only a half in 2004 declared to prescribe RRT for extended indications even in absence of acute renal failure. Lack of scientific evidence supporting extra renal indications was reported by 320 participants over 560 in 2004.

CONCLUSION. In a relatively short lapse of time (6 years) most centers were provided with new dedicated platforms and RRT dose prescription and delivery significantly increased, with potentially enormous clinical benefits.

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COMPARISON OF USE TIME FOR POLYSULPHONE FILTERS WITH DIFFERENT GEOMETRY IN CVVHF

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INTRODUCTION. Continuous renal replacement therapy (CRRT) is an expensive and complicated method of treatment requiring training and competence. The filter use time may be maximised by the choice of filter, vascular access, anticoagulation and treatment options. When compared to other published studies our filter use time appeared significantly lower. As the first step in an initiative to improve use time, we looked at the two filters available for use in our ICU. While both have high-flux, polysulphone membranes, they differ in geometry. (Fresenius HDF100S: fibre diameter 185microns, priming volume 138ml. Fresenius HF80S: fibre diameter 200 microns, priming volume 110ml).

METHODS. 185 filters were studied. All were used for veno venous haemofiltration (CVVHF) in pre dilution mode with substitution infusion rates of 35mls/kg/hr. The data collected included the filter type, filter use time, reason for disconnection and the recording of potentially confounding factors (anticoagulation used, coagulation status, diagnosis, patients weight). For the filters that clotted, a multiple regression (SPSS) was used to assess the effect of filter type on use time, after adjusting for the confounding factors.

RESULTS. Clotting was the most frequent reason for disconnection (70%), followed by access problems (9%). After adjustment for diagnosis of sepsis and use of heparin (rather than epoprostenol or no anticoagulation at all), there was no significant difference in use time for the HDF100S and HF80S filters (HDF100S median 9.3hours, mean 14.0 hours, maximum 101 hours: HF80S median 9.0 hours, mean 13.2 hours, maximum 78 hours). A diagnosis of sepsis was associated with a reduction in filter use time by 29% (95%CI 5 to 47%, p=0.021). Use of heparin (rather than epoprostenol or no anticoagulant) was associated with an increase in filter use time of 36% (95% CI 1 to 83%, p=0.045).

CONCLUSION. The main conclusion of this audit is that there is no difference in filter use time for HDF100S and HF80S filters. This suggests that the potential increase in clotting due to reduced fibre diameter in the HDF100S is offset by the larger volume of this filter. It is possible that use time would improve if both fibre diameter and volume were increased. The effect of a diagnosis of sepsis and the suitability of the patient for treatment with heparin were strong predictors of filter use time.

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STRONG ION DIFFERENCE DURING CVVH; DIFFERENT RESPONSE DURING NADROPARIN AND CITRATE ANTICOAGULATION

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INTRODUCTION. One of the goals of hemofiltration in multi-organ failure is the correction of acid-base disturbances. We studied the changes in electrolytes and acid-base balance, using the Stewart equations, during continuous veno-venous hemofiltration (CVVH) in multi-organ failure. We compared the results of different CVVH anticoagulation strategies, nadroparin and citrate. Because citrate is a weak acid we studied whether this would affect strong ion difference (SID).

METHODS. Ten patients were included in the nadroparin group (age 64±19, APACHE 24 ± 5) and nine in the citrate group (age 67±13, APACHE 24 ± 7). Before start and after 24 hours of the first hemofiltration session, the SID was calculated using the following equations; SIDa = Na+ + K+ + Mg++ + Ca++ - Cl- - Lactate (normal 40-42 mmol/l), SIDe = HCO3- + 0.2 *Alb + 1.5* P and the strong ion gap (SIG) = SIDa - SIDe.

RESULTS. All patients completed the study.

TABLE 1.

	nadroparin t = 0	t=24	Citrate t = 0	t = 24
SIDa	36.1 ± 7.5	36.9 ± 5.4	35.7 ± 4.5	37.7 ± 2.6
SIDe	24.7 ± 4.5	32.9 ± 3.9	26.3 ± 5.8	29.6 ± 1.6
SIG	11.4 ± 4.2	4.0 ± 3.1	9.3 ± 1.9	8.1 ± 2.4
pH	7.30 ± 0.08	7.42 ± 0.07	7.37 ± 0.08	7.43 ± 0.07
HCO3- (mmol/l)	19.2 ± 3.4	28.0 ± 3.6	21.0 ± 4.5	24.7 ± 1.2
Citrate (mmol/l)		0.07 ± 0.09	0.57 ± 0.33	

CONCLUSION. The SIDe (effective) did not change after 24 hr CVVH during citrate anticoagulation in comparison with nadroparin. Because the SIDa did not change in either of the groups this resulted in a near normalisation of the SIG in the nadroparin group but in the citrate group the SIG remained elevated. An explanation could be that a small part of the used citrate is found in the systemic circulation. Citrate is a weak acid and therefore, it will influence the acid-base balance. The contribution of citrate to the SID remains invisible because it is not a part of the equation. Further study is needed to adjust the Stewart equation when citrate is used as regional anticoagulant to correct for citrate and its metabolites.

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THE FREE CORTISOL INDEX IN PATIENTS UNDERGOING ABDOMINAL SURGERY

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INTRODUCTION. Serum total cortisol is 80% bound to cortisol-binding globulin (CBG), and 10% bound to albumin. CBG levels may fall during severe illness of any type. The free cortisol index (FCI), defined as the serum total cortisol/CBG ratio, has been found to correlate with free cortisol, the biologically active component.

METHODS. To evaluate the hypothalamic-pituitary-adrenal axis following major elective abdominal surgery 27 patients (17 women) having a mean age of 70 years were studied. Blood was taken pre- and postoperatively to measure total cortisol, corticotropin (ACTH), and CBG levels. The FCI was calculated.

RESULTS. ACTH increased from 13 (median) pg/ml to 44 pg/ml (p<0.001). Serum total cortisol increased by 33% from 15±5 (mean±SD) mcg/dl to 20±11 mcg/dl (p=0.03). CBG levels decreased by 32% from 43±16 mcg/ml to 29±11 mcg/ml (p<0.001), whereas the FCI increased by 67% from 0.43±0.4 to 0.72±0.4 (p=0.004). In the entire patient population there was a significant correlation between postoperative serum total cortisol and CBG (r=0.54, p=0.003).

CONCLUSION. Our data suggest that in severely ill patients serum total cortisol levels should be interpreted with reference to CBG concentrations.

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RENAL REPLACEMENT THERAPY IN SEPSIS-RELATED ACUTE RENAL FAILURE: WHEN TO INITIATE THERAPY?

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INTRODUCTION. Despite renal replacement therapy (RRT) mortality of septic patients with acute renal failure is still high. Recent studies clearly showed dose dependent beneficial effects of RRT but there is still no evidence-based criteria when RRT has to be initiated.

METHODS. To characterize the ability of common clinical parameter to guide initiation of RRT we retrospectively analyzed a subset of septic patients that required RRT in our ICU. The records of 79 septic patients that underwent RRT for acute renal failure from late 1999 to the end of 2004 were reviewed. Primary end-point was death in the ICU.

RESULTS. 46 of 79 (58%) patients died in the ICU. Pre-existing risk factors were neoplasm, relative risk (RR, 0.95 confidence interval) 1.72 (1.17-2.5) and chronic renal disease RR 0.49 (0.33–0.72). At RRT initiation all ICU-scores correlate with mortality: APACHE II: 30.6 vs. 35.6 p = 0.003, SAPS II: 57.2 vs. 67.4 p = 0.001, SOFA: 9.73 vs. 13.8 p <0.001. Using bivariate analysis, no significant difference between survivors and non-survivors for serum-creatinine (4.61 mg/dl vs. 3.88 mg/dl, p = 0.228), BUN (89.8 mg/dl vs. 82.6 mg/dl, p = 0.436) and urine output (median: 32.9 ml/h vs. 14.6 ml/h, p = 0.056) could be found. If the renal contribution to the SOFA-score is omitted there is a significantly higher risk for patients with BUN > 60mg/dl at RRT initiation when a binary logistic regression model is applied, odds ratio 4.16 (1.07-16.07).

CONCLUSION. To the best of our knowledge, this is the first study that specifically analyzes the impact of timing of RRT initiation in patients with sepsis-related acute renal failure on a medical ICU. As renal parameters are the independent variables of this study, it seems reasonable to neglect their contribution to an otherwise validated score used to control for severity of underlying disease. This way the study shows that early initiation of RRT (BUN < 60mg/dl) is crucial in patients with sepsis-related acute renal failure. A reliable and early marker of severe kidney injury is not jet available to confirm the finding in a prospective study.

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THE ACCURACY OF SUBCUTANEOUS INTERSTITIAL FLUID GLUCOSE MONITORING DURING INDUCED HYPOTHERMIA

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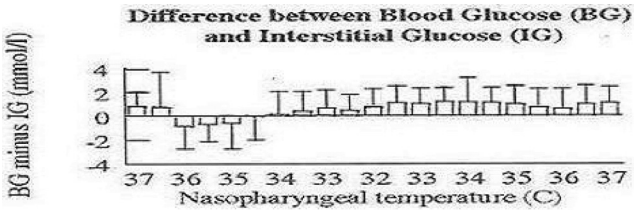
INTRODUCTION. During CPB, blood glucose (BG) levels are monitored at hourly intervals. A device to continuously measure interstitial glucose (IG) levels has been developed, the Minimed CGMS, which correlates with BG levels [1]. No study confirms its accuracy during hypothermia, and therefore its usefulness as a monitor of tight glycaemic control during cardiac surgery.

METHODS. 9 patients scheduled for CABG surgery were studied. The subcutaneous electrode was inserted in the upper arm. Nasopharyngeal (NP) temperature was measured. BG samples were taken every 0.5°C as the NP cooled and rewarmed during CPB. The corresponding IG value was later retrieved from downloaded data.

RESULTS. IG readings tended to be lower with a mean difference between BG and IG of 0.56 mmol/l. There was no significant difference between the accuracy of the IG as a guide to the BG level at any temperature between 36°C and 32°C measured during CPB.



CONCLUSION. We have demonstrated that IG measurements are a reliable guide to BG measurements during hypothermia in patients undergoing CPB. A new device that has a real time display and alarms may be a useful addition to the safety of intensive insulin therapy in patients having cardiac surgery.

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PROLONGED EXPOSURE TO INHALED NITRIC OXIDE TRANSIENTLY MODIFIES TUBULAR FUNCTION IN HEALTHY PIGLETS

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INTRODUCTION. Inhaled nitric oxide (iNO) is believed to be a selective pulmonary vasodilator. However some extrapulmonary, even renal effects of iNO has been reported.

METHODS. We have studied if prolonged exposure to 40 ppm iNO (30 hours) alters kidney function in healthy, intubated, spontaneously breathing piglets (pressure support ventilation, PEEP 5cm of water), weight 18kg in a blinded, placebo controlled study. Animals (n=20) were randomized to receive 40 ppm iNO or placebo. Blood and urine samples were taken for 3 separate renal profiles of 12, 12 and 6h. Samplings included: urine volume, both plasma and urine electrolytes (UNa, UCl), creatinine,urea and creatinine- (Ccr), osmolality-, free water clearances, fractional excretions (FeNa, FeK), urinary excretions (UENa, UECl); non-saline loss, renal failure index (RFI). Urine cystatine C was assesed before and at the end of observation. Haemodynamic data included hourly measurements of MAP, HR, CVP. Statistcs: U-Test p<0.05 (*).

RESULTS. For the first 12h profile, the following mean values (SD) were increased in the iNO vs. control group: UNa - 87,7* (35,0) vs. 39,3 (22,9), UCl - 80,4* (32,8) vs. 48,0 (26,7), FeNa - 2,1* (0,8) vs. 0,7 (0,5), FeK - 31,7* (7,0) vs. 20,7 (12,3), UENa - 61,0* (21,1) vs. 27,6 (17,9), UECl - 57,3* (24,5) vs. 37,6 (29,0), RFI - 3,0* (1,1) vs. 1,0 (0,7), without urine volume or serum creatinine changes. These modifications in renal profile were absent in period II-III. All haemodynamics remained stable with no differences between groups. Urine cystatine C did not reach the detection limit.

CONCLUSION. Prolonged exposure to 40 ppm iNO in healthy piglets modifies kidney tubular function for the first 12h. The effect is transient and not detectable in the next 18h period. Mechanisms of this extrapulmonary effect of iNO and it's reversal remains to be elucidated and are not associated with concomitant alterations in systemic haemodynamics.

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RENAL DYSFUNCTION IN THE ICU USING RIFLE: INCIDENCE, OUTCOME AND RESOURCE USE

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INTRODUCTION. Acute renal dysfunction (ARD) is common in ICU.The RIFLE classification of ARD defines three grades; Risk, Injury and Failure(2) based on urinary output (UOP) or acute rise in creatinine (CR).This pilot study evaluates RIFLE and associated outcomes and length of stay in a general ICU.

METHODS. Prospective data collection in patients admitted to an 8 bed med/surg ICU Nov 2004 through Feb 2005.Data included baseline weight and CR (from medical records in all but 6 cases where the MDRD equation (3) was used), daily CR, calculated GFR(Cockcroft-Gault) and UOP.ICU/hospital length of stay (LOS), outcome, need for RRT and APACHE II/III, MOFS, SAPS II scores were recorded.Patients with LOS < 24 hours were excluded.

RESULTS. Data were available for 35 female and 33 male patients, mean age 64 years, mean APACHE II score 20.6. 20 patients (29.4%) were classed as Risk, 10 (14.7%) as Injury, and 7 (10.3%) as Failure.31 patients (45.6%) had no RIFLE ARD.Higher RIFLE class was related to severity of illness using MOFS (p<0.05) but not other ICU scores.Higher RIFLE class was associated with longer ICU (p<0.05) and hospital (NS) LOS.There was no significant outcome difference between groups.5 patients received CRRT, 3 in Failure group for ARD, 2 in Risk group for non-renal reasons.

TABLE 1.

	rifle-none	rifle-risk	rifle-injury	rifle-failure
Hosp survival n (%)	22 (71%)	15 (75%)	6 (60%)	4 (57.1%)
MOFS (Mean)	2.64	3.1	3.66	4.57
ICU LOS (Mean)	6.24	7.36	9.91	17.5

CONCLUSION. Patients with Risk/Injury are common and at risk of further renal insult. They may not be identified using traditional scoring systems.Patients with higher RIFLE class have longer ICU stay and large impact on ICU resources.By drawing attention to ARD, RIFLE may facilitate prevention of ARD progression and we propose that all patients with RIFLE-identified ARD should be monitored after discharge for deteriorating renal function.

REFERENCE(S). (1)Acute Dialysis Quality Initiative, http://www.ADQI.net, 2002 (2)National Kidney Foundation. K/DQI Clinical Practice Guidelines for Chronic Kidney Disease. Am J Kidney Dis 2002; 39: S76-92 (3)The Renal Association. Treatment of Adults and Children with Renal Failure, London, Lavenham Press (2002)

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HIGH MOLECULAR WEIGHT HYDROXY-ETHYL STARCH INDUCES PROXIMAL TUBULAR DAMAGE

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INTRODUCTION. Controversy exists about the role of plasma expanders in inducing renal failure. Aim of the present study was to assess the ability of hydroxy-ethyl starch (HES) plasma expanders in inducing tubular injury in healthy subjects. Glutathione S-transferase(GST) A1 and P1 are cytosolic enzymes, present in the proximal and distal renal tubular cells respectively. They are sensitive and early markers of tubular damage(1).

METHODS. 7 female healthy volunteers received two separate infusions of 8 ml/kg plasma volume expander. HES 130/04 (Voluven 6%) and HES 200/06 (eloHAES 6%) were administrated in a randomized double blind cross-over fashion. Urinary GST A1 and P1/creatinine ratios were measured using an ELISA method (2). All data is expressed as mean+/-SEM.

RESULTS. GST A1 excretion was significantly higher during the first 3 hours after infusion of HES 200/06 compared to HES 130/04 (p=0.02). There was a trend towards higher excretion during the following three hours (p=0.06) (Table 1).

TABLE 1.

	GST A1 (mug/mmol) HES 130/04	GST A1 (mug/mmol) HES 200/06	GST P1 (mug/mmol) HES 130/04	GST P1 (mug/mmol) HES 200/06
0-3 hrs	0.38+/-0.18	0.59+/-0.20 (p=0.02)	0.52+/-0.10	0.71+/-0.12 (ns)
3-6 hrs	0.41+/0.16	0.58+/-0.12 (p=0.06)	0.56+/-0.20	0.84+/-0.14 (ns)
6-12 hrs	0.17+/-0.09	0.24+/-0.09 (ns)	1.01+/-0.47	0.56+/-0.11 (ns)
12-24 hrs	0.25+/-0.12	0.38+/-0.15 (ns)	0.50+/-0.11	0.51+/-0.09 (ns)

CONCLUSION. Our results demonstrate that a higher molecular weight HES plasma expander increases early GST A1 excretion as compared to a lower molecular weight HES plasma expander. Higher molecular weight HES plasma expanders are likely to cause increased proximal tubular injury.

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EARLY ONSET ACUTE RENAL FAILURE IS ASSOCIATED WITH WORSE CLINICAL OUTCOMES COMPARED TO LATE ONSET

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INTRODUCTION. Increasing severity of acute kidney dysfunction (AKD), classified according to the Risk, Injury, Failure, Loss, and End stage kidney disease classification (RIFLE) is associated with worse outcome in ICU patients. RIFLE defines 3 grades of severity of dysfunction based on either urine output (UO) or an acute increase in serum creatinine (Cr): R = Cr x1.5 or UO <0.5ml/kg/hr x6hr; I = Cr x2 or UO <0.5ml/kg/hr x12hr; and F = Cr x3, Cr ≥4 mg/dL, UO <0.3ml/kg/hr x 24 hrs, or anuria x12 hrs. It is uncertain whether patients who develop F criteria during ICU stay (late onset) have a different outcome compared to patients who are admitted already with F criteria (early onset). Thus, we determined whether deterioration to F was associated with different outcomes compared to patients who already had F on ICU admission.

METHODS. We analyzed data which was prospectively collected from all patients admitted to an ICU from July 1, 2000 to June 30, 2001 at the University of Pittsburgh Medical Center, a tertiary hospital with >120 ICU beds. We classified patients according to their worst RIFLE class on the day of ICU admission (RIFadm) and during ICU stay (RIFmax).

RESULTS. In our cohort of 5184 patients, 2247 (43.3%) had AKD (R, I or F) on ICU admission, and about half progressed to a more severe grade of AKD; RIFadm = No AKD, 47.5% progressed, RIFadm = R, 50.3% progressed, and RIFadm = I, 33.6% progressed. In total 3643 patients (70.3%) had AKD (R, I or F) during ICU stay. There was no difference in mortality for patients who had RIFmax=R or I on the day of ICU admission compared to patients who developed RIFmax=R or I later during ICU stay. However, mortality for patients with RIFmax=F was lower for those patients who developed F criteria during ICU stay (18.9%) compared to patients who already had RIFmax= F on ICU admission (31.7%). Late onset development of F was associated with lower mortality, even after adjustment for age, gender, race, non-renal SOFA score, surgical or medical type of admission, and length of ICU stay until RIFmax (Hazard ratio (95%CI) : 0.73(0.56-0.95), p=0.018) (proportional hazard analysis).

CONCLUSION. Nearly 50% of patients who had AKD on the day of ICU admission, already had a maximum severity of AKD. Patients with AKD RIFmax F criteria at ICU admission had a significant worse survival compared to patients who developed F criteria later.

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THE CHLORIDE/SODIUM RATIO FAILS TO PREDICT PRESENCE OF LACTIC ACIDOSIS IN CRITICALLY ILL ADULTS

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INTRODUCTION. Chloride was reported to decrease in metabolic acidosis due to elevated tissue anions, which among others include lactate. Since lactate measurements are not immediately and easily available in many ICUs, reliable and quick diagnostic tests for predicting its presence or absence are potentially useful. Thus, the chloride/sodium ratio was identified as a predictor for the presence and absence of elevated tissue anions in critically ill children. However, neither the actual behaviour of chloride secondary to changes of lactate nor the ability of the chloride/sodium ratio to predict the presence and absence of lactic acidosis has been investigated in critically ill adults. The aim of this study was to determine, whether chloride decreases as a consequence of increasing lactate and whether the chloride/sodium ratio can predict presence or absence of lactic acidosis in critically ill adults.

METHODS. Serial blood gases including sodium, chloride and lactate were retrospectively analysed in two patient collectives with 78805 blood samples from all together 2512 adult critically ill patients. The chloride/sodium ratio was calculated in order to study changes of chloride independent of sodium and the volume effect. The chloride/sodium ratio was correlated with lactate by the method of Bland and Altman.

RESULTS. The chloride/sodium ratio did not correlate with lactate (r = 0.01354, r2 = 0.00018, p = 0.0653). The area under the receiver operating characteristic curve of the chloride/sodium ratio for prediction of presence of lactic acidosis in samples with metabolic acidosis was 0.70 (95% confidence interval, 0.68-0.71). The positive predictive value of a chloride/sodium ratio < 0.75 for prediction of presence of lactic acidosis in samples with metabolic acidosis was 0.53.

CONCLUSION. Increasing lactate is not associated with decreasing chloride in critically ill adults. Consistently, the chloride/sodium ratio fails in predicting presence or absence of lactic acidosis in samples with metabolic acidosis.

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20S PROTEASOME PLASMA LEVELS IN KIDNEY TRANSPLANT PATIENTS: AN EARLY MARKER OF RENAL RECOVERY

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INTRODUCTION. The 20S proteasome plays an important role in the non-lysosomal pathway of intracellular protein degradation and apoptosis, thus being a possible marker for ischemic and reperfusion injuries. The aim of this study was to monitor the proteasome levels in kidney transplant patients to detect a relationship with the return of renal function.

METHODS. We examined 12 patients with end stage renal disease, receiving kidney transplants: Blood samples were collected intraoperatively and postoperatively on 5 consecutive days and 20S proteasome levels were measured for each sample with a sandwich ELISA as described by Dutaud et al. Anesthesia and immunosuppressive medications were standardized, creatinine clearance and urine output were assessed daily.

RESULTS. Patients who had no adequate urine output (430±300ml, 4 pts) on the 4th postoperative day had significantly higher proteasome levels intraoperatively than patients with sufficient output (4032±1076ml, 8 pts; 1000 ml cutoff). In both groups proteasome levels increased over time and the difference leveled out during the followup period. No significant relationship could be detected between creatinine clearance and proteasome levels.

TABLE 1.

Proteasome plasma levels (µg/ml)

	intraop	day 1	day 3	day 5
Proteasome µg/ml < 1000 ml urine	1.79 ± 1.56*	1.51 ± 1.45	2.23 ± 1.3	1.28 ± 0.43
Proteasome µg/ml > 1000 ml urine	0.5 ± 0.43	0.99 ± 0.86	1.36 ± 0.59	1.38 ± 0.61

** p < 0.05 (unpaired Student's T-test)*

CONCLUSION. 1) Patients with impaired renal function after kidney transplant had significantly higher proteasome levels intraoperatively. 2) A higher plasma level of proteasomes intraoperatively may therefore be a negative prognostic marker for postoperative recovery of renal function of the transplanted kidney.

REFERENCE(S). Dutaud D., Development and evaluation of a sandwich ELISA for quantification of the 20S proteasome in human plasma. JIM 2002; 260: 183-193.

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ELEVATION OF URINARY FREE CORTISOL LEVELS OBSERVED WITH VENTILATORY WEANING MANEUVERS

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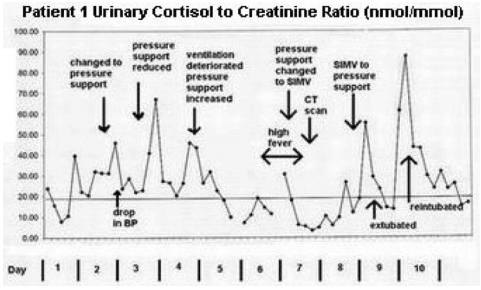
INTRODUCTION. Cortisol pathophysiology in critical illness remains poorly understood. Urinary free cortisol (UFC)measurements have not been reported in these patients. We investigated the use of UFC measurements in critically ill patients.

METHODS. 4-hourly UFC was measured using high performance liquid chromatography in 5 patients expected to stay more than 3 days in the Intensive Care Unit (ICU). Patients with oliguria were excluded. Urinary creatinine was measured by routine assay.

RESULTS. Marked day to day variation in UFC levels without diurnal variation was seen, as demonstrated in the figure. Some of the variation appeared to be associated with changes in mechanical ventilation, with a median increase in UFC to creatinine ratio of 33.72 nmol/mmol (Range 0 - 289.84; 13 events recorded).



CONCLUSION. UFC levels fluctuated markedly from day to day, without normal diurnal variation. Elevations in UFC were observed with ventilatory weaning maneuvers, even those considered relatively trivial, such as weaning of pressure support. This suggests a substantial stress response to the ventilatory weaning process.

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COMPARISON OF TWO APPROACHES TO METABOLIC ACID-BASE DISTURBANCES

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INTRODUCTION. Stewart's approach states that pH is primarily determined by three independent variables: PCO2, strong ion difference (SID) and non-volatile weak acids. Using this approach, Fencl et al (AJRCCM 2000) have shown that the traditional analysis based on HCO3-, base excess (BE) and anion gap (AG), frequently failed to identify severe metabolic disturbances, such as metabolic acidosis. Our hypothesis was that the Stewart's approach would show a better diagnostic and prognostic performance than the traditional analysis, in a large cohort of critically ill patients.

METHODS. We prospectively studied all patients admitted to the ICU from 01/03/04 to 28/02/05. On admission, arterial blood samples were analyzed for gases, Na+, K+, Ca++, Mg++, Cl-, albumin, Pi- and lactate. We also estimated HCO3-, BE, AG adjusted to albumin, SID, strong ion gap (SIG) and APACHE II. Diagnostic categories defined by Fencl et al were used. Normal ranges were established as mean ± 3 SD of 7 normal volunteers. Linear regression, Bland & Altman analysis and ROC curves were performed.

RESULTS. 647 patients were included for analysis. Hypoalbuminemia was present in 80% of the patients. In 57 patients (9%), Stewart's approach allowed the detection of a metabolic acid-base alteration in patients with normal HCO3- and BE. Of these, 49 (84%) had metabolic acidosis. However, 39 (80%) of them had increased AG. Consequently, the use of Stewart's approach permitted the diagnosis of metabolic acidosis in only 10 patients (2%) with normal HCO3-, BE and AG. On the other hand, Stewart's approach failed to identify 18 patients (3%) with metabolic alterations diagnosed with the traditional approach (11 acidosis and 6 alkalosis). In addition, the metabolic response to a respiratory disturbance was misinterpreted as a primary metabolic process in 98 patients (15%; 90 alkalosis and 8 acidosis). SID and BE, and SIG and AG were strongly correlated ($R2 = 0.85$ and 0.97, $p < 0.0001$ for both) and showed narrow 95% limits of agreement (7.9 and 3.3 mmol/l, respectively). Areas under ROC curves for mortality were 0.89, 0.66, 0.64, 0.61, 0.61, and 0.59, for APACHE II, lactate, SIG, AG, SID and BE, respectively (APACHE II vs. the rest, $p < 0.00001$).

CONCLUSION. In this large group of critically ill patients, Stewart's approach does not show significant diagnostic or prognostic advantages over the conventional approach.

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THE DETECTION OF SEIZURES IN ADULT ICU PATIENTS BASED ON CHANGES IN EEG SYNCHRONIZATION LIKELIHOOD

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INTRODUCTION. Seizures are probably common in ICU patients, and may increase injury. Recognition is hampered because of the large proportion of non-convulsive seizures. Automatic detection with the synchronization likelihood (SL) approach was feasible in neonates. The value of this method in adult ICU patients is unclear. The aim of this study was to explore the value of SL on seizure detection.

METHODS. Included patients (n=18) were admitted with a variety of diagnoses to the ICU of the VUMC Amsterdam or the UMC Utrecht. EEGs were recorded using 21 electrodes. The golden standard for further analyses was the consensus judgment of three clinical neurophysiologists who classified 150 EEG epochs as 'definitely epileptiform' (i.e. containing an electrographic seizure, score 2), 'definitely non-epileptiform' (score 0) or 'uncertain' (score 1). SL estimates the statistical interdependencies between two time series, such as two EEG channels. We computed the average synchronization by calculating the SL between one channel and every other channel, and taking the mean of these values. As a first evaluation, we studied episodes with maximum contrast, and compared the mean synchronization in epochs with the student-t test. Secondly, the Pearson correlation coefficient was computed between the summed visual score and the mean SL for every epoch of two complete EEG recordings.

RESULTS. The mean SL in the 38 'definitely epileptiform' epochs ranged from 0.095 to 0.386 (mean 0.189; SD 0.066). In the 34 'definitely non-epileptiform' epochs the mean SL ranged from 0.087 to 0.158 (mean 0.115; SD 0.016; $P<0.0005$). The area under the ROC curve was 0.894 (95% CI 0.815 to 0.973). Based on two complete EEG recordings, the correlation coefficient between the summed visual score and the SL of all epochs was 0.692 and 0.772 ($P<0.0005$).

CONCLUSION. Our findings suggest that in patients with a variety of diagnoses the mean synchronization can be used to adequately distinguish beween seizure and non-seizure epochs. The SL can be computed online during longterm EEG recording. Future research should investigate its false detection rate and should evaluate whether patient outcome improves with automatic detection and treatment of epileptic seizures in the ICU.

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ANACONDA: TEST ON BENCH AND IN PATIENTS

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INTRODUCTION. Until now, one had to use an anesthesia machine to deliver halogenate in ICU. Recently, the AnacondaTM (HudsonR) used on a conventional ICU ventilator, allows to vaporize halogenate and to perform like a closed circuit (CS). This device aimms at delivering short inhaled sedation in ICU, without using CS machine. We tested this device on bench and also in anesthetized patients ventilated during surgery, with an CS ventilator.

METHODS. The bench comprised a Servo 900C Ventilator (Siemens), a calibrated capnograph (Bruel & Kjaer), a syringe pump (Fresenius Viale). We used Isoflurane (I). We measured, at steady state, expired I concentrations (FeI) with I infused at 4 ml/h and with a range of VT, RR, VE, PEEP, I/E ratio. We also tested safety issues of the system. In 8 anesthetized patients (propofol-remifentanil), we recorded during surgery, expired I at an I infusion rate of 5 ml/h. Ventilation was provided by a conventional anesthesia machine (Advance, Datex-Ohmeda) with a VT adjusted to achieve an ETCO2 around 35 mm Hg, (RR = 12 b/min). Fresh gas flow (FGF) was first set at 12 l/min, until a plateau of expired I was achieved and then FGF was set at 1 l/min.

RESULTS. On bench, when ventilation was kept constant, we observed a linear proportional change in FeI in response to the change in I infusion. At constant I infusion rate, FeI rose linearly with RR. Rising V_T with constant I/E and RR led to a linear decrease of FeI. PEP induced a small proportional decrease in FeI whereas rising I/E ratio linearly increased FeI. Infusion rate of I required to achieve an FeI of 0.5% could be modelized: I rate=0.12xVE+0.13 ($r^2 = 0.99$). We observed that during the change of the I syringe, pumping phenomena could occur with 5 min long two-fold rise in FeI. On anesthetized patients using a conventional AM, we observed that reducing FGF from 12 l/min (open circuit configuration) to 1 l/min (closed circuit configuration) led to a 43% rise of FeI at constant I infusion rate. Of note, the I syringe connects via a Luer Lock, thus, it may be inadvertently connected to an i.v. line.

CONCLUSION. Anaconda has vaporizing properties which allow to confidently reach a preset FeI. Using an anesthesia machine with low FGF, one can generate an important reduction of I consumption. However, several safety issues should be fixed.

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HEMODYNAMIC MEASUREMENTS AFTER CORONARY BYPASS OPERATION AND INTRA-AORTIC BALLOON PUMP IMPLANTATION

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INTRODUCTION. We had compared two hemodynamic monitoring methods (PiCCO plus – transthoracic electrical bioimpedance TEB) after coronary artery bypass operation last year. We had a good correlation with the invasive methods, but there is only a very few data about hemodynamic monitoring in patients with intra-aortic balloon pump. Our aim was to measure hemodynamic changes in early postoperative period simultaneously either invasive both non invasive.

METHODS. To evaluate the reliability of transthoracic electrical bioimpedance (TEB) in comparison with termodilution method, the gold standard Swan-Ganz catheter. Arriving at the postoperative care unit the narcotised and ventillated patients were measured simultaneously every 15 minutes for 2 hours. We measured hemodynamic parameters in 14 patients (9 males, 5 females) by TEB and Swan-Ganz catheter simultaneously. Average age was 61±7 years. The anaesthesia was induced and maintained with sevoflurane. These patients were inplanted intra-aortic balloon pump (IABP) because of left main stenosis, instable angina pectoris, low ejection fraction (EF), stenosis of internal carotis artery. Preoperative EF was 41±5%. All the patients were operated by coronary artery bypass grafting (CABGx1-4). The average extracorporal bypass time was 69±27 minutes. We compared cardiac output (CO), stroke volume index (SVI) and systemic vascular resistance index (SVRI).

RESULTS. Results of measurements by Swan-Ganz catheter vs. TEB: CO: 3,76±0,73 vs 3,41±0,6 l/min, SVI: 31,7±5 vs 28,9±6 ml/m2, SVRI: 2017±496 vs 2650±541 dynsec-5/m2. Linear regression was CO:0,73, SVI:0,78, SVRI:0,86.

CONCLUSION. The noninvasiv hemodynamic measurement (TEB) has a good correlation with the invasive methods after the coronary bypass surgery. Therefore the transthoracic electrical bioimpedance is a reliable and noninvasive hemodynamic tool for the cardiovascular monitoring for the patients after cardiac surgery even the patients IABP had inserted.

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THE PULMONARY PERMEABILITY INDEX (PICCOSYSTEM) DIAGNOSES HYDROSTATIC VS PERMEABILITY PULMONARY EDEMA

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INTRODUCTION. The PiCCO technology provides clinicians with extra-vascular lung water index (EVLWi) and pulmonary permeability index (PPI) a parameter that increases in case of increased permeability of the alveolar-capillary barrier. However, the ability of this parameter to discriminate between hemodynamic pulmonary edema and increased permeability pulmonary edema has never been evaluated. The goal of this study was to test whether PPI enables a reliable diagnosis of increased permeability pulmonary edema.

METHODS. We measured PPI in 24 critically ill patients ventilated for acute respiratory failure with bilateral alveolar or interstitial infiltrates on chest X-ray, a PaO2/FiO2 ratio <300 and an EVLWi <= 12 mL/kg. The etiology of pulmonary edema determined a posteriori by 4 independents experts was based on medical history, clinical features, chest radiograph, biological parameters (including BNP) and the evolution with therapy. The experts were blind for the PPI value and the global end-diastolic volume provided by PiCCO.

RESULTS. For the whole population, EVLWi was 18±6 mL/kg and the PaO2/FiO2 ratio was 125±69. Increased permeability pulmonary edema was diagnosed by the experts in 17/24 cases. The best diagnosing cut-off value of PPI for increased pulmonary edema was 2.7. A PPI greater than 2.7 provided a correct diagnosis of increased pulmonary edema with a sensitivity of 84% and a specificity of 100%.

CONCLUSION. The pulmonary permeability index automatically provided by the PiCCO device is a reliable parameter for diagnosing the mechanism of pulmonary edema formation.

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INTRATHORACIC BLOOD VOLUME OR STROKE VOLUME VARIATION DO NOT PREDICT FLUID RESPONSIVENESS IN SEPSIS

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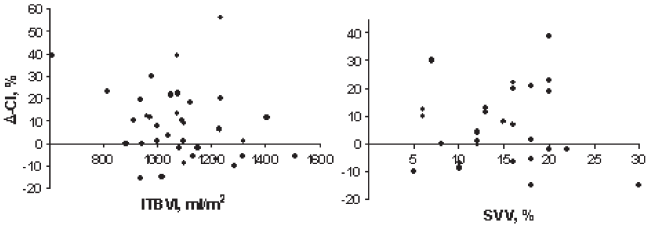
INTRODUCTION. Guidance of fluid treatment remains a challenge in patients with septic shock. The pulse contour cardiac output (PiCCO®) system measures intrathoracic blood volume index (ITBVI) and stroke volume variation (SVV), which may predict the cardiac response to fluid challenge in patients on controlled ventilation.

METHODS. 37 consecutive, mechanically ventilated patients with established septic shock (>12 h) were subjected to fluid challenge using 500 ml of colloid. Patients were ventilated with *assisted spontaneous breathing with or without BiPAP.*

RESULTS. 46 % of the patients were fluid responders defined as an observed increased in thermodilution cardiac index of more than 10%. ITBVI and SVV prior to fluid administration were similar in responders and non-responders (mean ± SD 1036 ± 178 vs. 1117 ± 157 ml/m2, p=0.15 (t-test) and 15 ± 5 vs. 15 ± 6 %, p=0.76, respectively). Moreover, there was no relationship between ITBVI or SVV prior to fluid challenge and the subsequent change in cardiac index (see figure).



CONCLUSION. ITBVI or SVV did not predict the cardiac response to fluid challenge in patients with established septic shock, who were on varying degrees of assisted ventilation.

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IMPLEMENTATION OF A COMPUTER ASSISTED, NURSE-DRIVEN GLUCOSE CONTROL PROTOCOL AT A SURGICAL ICU

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INTRODUCTION. Glucose control has become an integral part of intensive care medicine. Insulin is administered more often, the risk of hypoglycaemia has increased, and glucose is sampled more regularly. Current nurse-driven protocols are paper-based and, therefore, rely on simple rules. We hypothesized that a computer program applying more complex logic can improve both effectiveness and safety of control while reducing the needed human effort.

METHODS. We developed a standalone Java computer program that queries the central laboratory database for glucose and other data. Additional information including feeding and use of inotropic drugs and steroids is asked from the user. Directly after a glucose measurement, taken by a point-of-care analyser, the program advises a new insulin pump rate and glucose sampling interval. The program uses a configurable glucose target value, which was set to 6.5 mmol/L in this study. We used two months of observation and gradual implementation before treating patients at our 12-bed surgical ICU. Control was quantified by calculating the fraction of time that the glucose level was less than 1 mmol/L over the target (i.e., between 4.0 and 7.5 mmol/L).

RESULTS. From January 1st, to April 1st, 2005, 123 patients (for a total of 780 patient-days) were treated using the advice given by the program. Table 1 shows patient characteristics with glucose and insulin parameters. Sampling frequency ranged from 1 to 11 samples a day. Control was acceptable. Severe hypoglycaemia did not occur.

TABLE 1.

Age (years)	62 (53-73)	Insulin rate (IU/h)	0.9 (0.4-1.6)
Length of stay(days)	1.8 (0.9-6.2)	Sampling frequency	5.1 (4.3-6.4)
APACHE-II	14 (11-19)	% in target range	71 (55-83)
Body mass index	25 (23-28)	N with G<2.2 mmol/L	0 (0%)
N requiring insulin	105 (85%)	N with G<3.5 mmol/L	12 (10%)

Patient demographics and glucose and insulin parameters. Data are median(IQR).

CONCLUSION. A computer assisted, nurse driven protocol can be a safe and effective way of glucose control. Future algorithms with arbitrary complex rules may further improve control.

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SALINE VOLUME IN TRANSVESICAL INTRAABDOMINAL PRESSURE MEASUREMENT: ENOUGH IS ENOUGH

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INTRODUCTION. Transvesical measurement of the intraabdominal pressure (IAP) is widely used, but when a urinary catheter is in place, the bladder may become less compliant, leading to falsely increased IAP. The goal of this study was to measure bladder compliance in critically ill patients, and to determine the minimal instillation volume at which an IAP curve can be observed.

METHODS. IAP was measured transvesically in 20 critically ill sedated patients at risk for intraabdominal hypertension (IAHT). Measurements were performed after a median of 5 days of bladder drainage. IAP was measured starting with instillation of 10mL saline, and continued with 10mL increments up to 100mL, after a 1 minute equilibration period after each instillation. An oscillation test was performed, to determine the minimal volume at which the IAP could be measured. The relative increase of IAP between the minimal volume at which an IAP could be measured (IAPmin) and the conventionally used volumes (50 and 100 mL) was calculated by dividing the difference between IAP50 or IAP100 and IAPmin by the IAPmin value. Additionally, in patients with IAHT, we analyzed the correlation between the duration of bladder drainage before the measurement and the calculated difference in IAP between IAPmin and IAP 100.

RESULTS. The minimal volume at which the oscillation test was positive was 10mL in all patients. Mean IAPmin was 12.8mmHg (±4.9), mean IAP50 15mmHg (±4.5) and mean IAP100 17.1mmHg (±4.7). The mean relative increase between IAPmin and IAP50 was 21%(±17%), and 40%(±29%) between IAPmin and IAP100. Twelve patients were categorized as suffering from IAHT when 10mL saline was used for IAP measurement, increasing to 15 and 17 patients respectively when using 50 and 100mL was used. In patients with IAHT, there was a significant correlation between the duration of bladder drainage and mean relative increase between IAPmin and IAP100 (Pearson correlation coefficient 0.60, p=0.03)

CONCLUSION. In this sample of ICU patients at risk for IAHT, bladder compliance was compromised in all patients. This resulted in a considerable overestimation of the IAP when instillation volumes of 50 to 100 mL were used. In these patients, an instillation volume of 10 mL was sufficient for reliable IAP measurement.

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FLUID RESPONSIVENESS IS DETECTED BY ESOPHAGEAL DOPPLER: RESPONSE TO LEG RAISING AND AORTIC FLOW TIME

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INTRODUCTION. The goal of this study was to compare two methods provided by esophageal Doppler and potentially able to detect volume responsiveness: (1) the time of the aortic blood flow (ABF) signal corrected for heart rate (FTc), a static preload parameter previously proposed to guide fluid infusion, and (2) the changes in ABF induced by passive leg raising (PLR) that acts like a "self-volume challenge".

METHODS. We examined 38 mechanically ventilated patients monitored by esophageal Doppler (Hemosonic100Ò, ArrowÒ) for whom volume expansion (VE) was planned. We measured FTc and the changes in ABF induced by PLR (1 min at 45°). Patients were defined as responders if VE increased ABF by ≥15%.

RESULTS. In responders (n=19), ABF increased by 32±22 % during PLR ($p<0.05$) and by 43±21 % after VE ($p<0.05$). In these patients, FTc increased from 278±37 to 307±55 ms after VE ($p<0.05$). In non-responders (n=19), ABF was not altered by PLR, but FTc increased from 314±30ms to 350±60ms after VE, confirming its ability to correctly track the changes in cardiac preload. However, before VE, FTc was not different between responders and non-responders. Considering all patients, a PLR-induced increase in ABF ≥ 10% predicted fluid responsiveness with a sensitivity of 94% and a specificity of 94% while a FTc < 277ms predicted fluid responsiveness with a sensitivity of 57% and a specificity of 94%. The area under the ROC curve for the PLR-induced changes in ABF (0.95±0.04) was greater than that for FTc (0.76±0.08) ($p<0.05$).

CONCLUSION. By measuring the changes in ABF induced by PLR, esophageal Doppler provides a reliable tool to detect volume responsiveness in mechanically ventilated patients. Conversely, FTc, a static marker of cardiac preload, is of poorer predictive value.

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VALIDATION OF A NEW TECHNIQUE FOR CONTINUOUS INTRAABDOMINAL PRESSURE MEASUREMENT

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INTRODUCTION. Intraabdominal pressure (IAP) is increasingly monitored in critically ill patients. Several techniques have been described to measure IAP, of which the transvesical technique remains the most popular. The use of an intragastric balloon catheter may be an interesting alternative for continuous IAP measurement. Previously, we found in a laboratory experiment that the pressure in a balloon-tipped catheter (Compliance catheter, International Medical Systems, Zutphen, The Netherlands) filled with 1 to 3 mL of air accurately measures static pressures (1).

METHODS. The study was performed in patients undergoing elective laparoscopic cholecystectomy. After induction of anaesthesia, a Compliance catheter was introduced under direct vision in the esophagus and into the stomach. The catheter was connected to a pressure transducer, the balloon was filled with 3mL of air, and the transducer was plugged into the patient monitor. The reference pressure (IAPref) was measured directly in the peritoneal space through the working channels of the surgeon. Both pressures were recorded at 1 minute intervals. The mean difference and 95% confidence interval between the IAPgastric and IAPref was calculated by means of the Bland-Altman statistics.

RESULTS. A total of 156 paired measurements were recorded, in 7 patients (4 male, mean age 46 years). For each patient, between 16 and 27 paired measurements were recorded. The IAP ranged from 6 to 18 mmHg. Mean difference between IAPgastric and IAPref was 0.12mm Hg (95% CI 0.01-0.23 and standard deviation 0.70mmHg).

CONCLUSION. IAP measured using an intragastric Compliance catheter accurately reflects the reference IAP in patients with induced , moderate intraabdominal hypertension.

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MONITORING PROPOFOL CONCENTRATION IN BREATHING GAS - A COMPARISON TO PLASMA PROPOFOL CONCENTRATION

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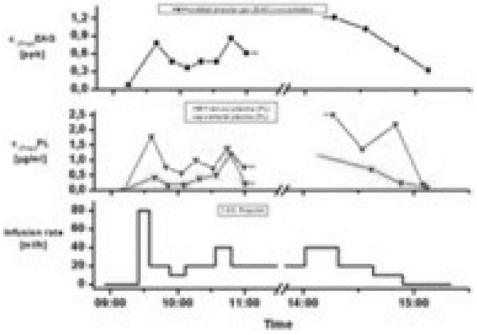
INTRODUCTION. A non-invasive alternative for the determination of propofol concentration (Cprop)in plasma might be the measuring of propofol in respiratory gas (RG). There is still no procedure for monitoring propofol in RG and the role of propofol metabolism in the lung is unclear. The presented study should answer these questions: can propofol be detected in RG, how is the dosage of a continous propofol infusion related to the Cprop in RG and can the relationship between the Cprop in RG and in blood before and after lung passage be described ?

METHODS. After official approval 7 goats were premedicated, intubated and normocapnic ventilated. Propofol was applied using standardized procedure. Mixed venous and arterial blood samples were drawn in parallel with the RG samples and further processed to reversed phase high pressure liquid chromatography with fluorescence detection. For RG analysis samples of exhaled breath were collected into sampling tubes filled with Tenax and transferred to a gas chromatography mass spectrometry unit.

RESULTS. As shown in figure 1 the measured concentration of propofol in RG tended to follow Cprop and the infusion dosage.



CONCLUSION. Propofol can be detected in RG with analytical methods. Cprops in RG follow the dosage profile. The relationship between Cprops in RG and in blood before and after lung passage can be described.

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DIARRHEA CONTROL DEVICE IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Prolonged diarrhea is a common incident in critically ill patients, that leads to severe irritations of the perineal skin, produces unpleasant odor, requires additional care by the nursing personnel and often embarrasses the patient, causing a feeling of weakness and limited self confidence. Intra rectal insertion of a tube connected to a collector is usually a practical way of dealing with the problem, but it cannot effectively control the situation.

METHODS. As a prospective study in our six bed mixed ICU we compared two different modifications of the plain rectal tube in order to evaluate the usefulness of such a device. In the first device we attached an inflatable balloon to the tube analogue to Foley catheter in order to keep it in place and to ensure leakage limitation. In the second device we used an analog to the bezzer type tube that was inserted through a rectoscope. All of the devices were connected to collectors. In all cases we performed rectoscopy to estimate the situation of the rectal mucosa prior to insertion and after removal of the devices. We registered the condition of the perineal skin, the presence of leakage, the presence of odor. Dislocation of the devices was also registered.
The devices were used for five days in 15 patients with prolonged diarrhea, divided in three groups of five patients for each device.

RESULTS. CRITERIA for : Plain tube - Analogue to Foley - Analogue to bezzer(Tube retention 2 - 4 - 5, Skin irritation 3- 2 - 1, Leakage 4- 1 - none, Odor presence 4 -2 -1
Rectal mucosa: No injury - No injury - No injury, Sphincter weakness 0- 0 -1,Nurses opinion :Good - Better - Best

CONCLUSION. Both modifications of the plain tube were well accepted by the patients and the personnel,no injuries or additional risk factors for the patients were registered.Irritation of the skin was minimal mainly due to leakage but not totally eliminated.Unpleasant odor was significantly less and the rectal mucosa showed no significant irritation or any other sign of injury.Further investigation could possibly lead to a simple device development that could minimize all issues referred above in cases of critically ill with prolonged diarrhea.

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ABSOLUTE ELECTRICAL IMPEDANCE (AEIT): EFFECT OF CPAP ON ABSOLUTE LUNG RESISTIVITY AND AIR VOLUME

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INTRODUCTION. Absolute measurement of lung electrical resistance and the resulting calculation of lung volume is a new development that opens the potential to compare lung tissue measurements with normal ranges, rather than using an individual to provide there own baseline. We aimed to assess changes in absolute electrical impedance tomography (aEIT) and calculated lung volume in response to CPAP.

METHODS. We measured lung aEIT using a Sheffield mk3.5a EIT machine (Maltron UK), during facial CPAP (0, 5, 10, 15, 20cmH2O) in 9 normal subjects. We used the 8 electrode system, which is designed to be more practical than the 16 electrode system.

RESULTS. aEIT and lung volume calculated from these measurements were linearly related to CPAP level ($p<0.001$)(Table 1). However, although the coefficient of variation of aEIT measurements within an individual at each CPAP level averaged 4%, the between individual variability ranged between 20 and 30%. Therefore, although changes within an individual can be readily detected, comparison between individuals and potential normal ranges is currently only able to identify relatively large defects. The variability between individuals is partly related to thoracic shape.

TABLE 1.

The effect of CPAP on absolute resistivity (ohm. metres) and lung air vol (l)

	Absolute Resistivity Mean	SD	Calculated Air Vol Mean	SD
0 CPAP	6.39	1.57	2.59	0.55
5 CPAP	6.99	1.81	2.77	0.53
10 CPAP	8.08	2.23	3.25	0.72
15 CPAP	9.42	3.26	3.70	0.77
20 CPAP	11.06	4.21	4.20	1.12

CONCLUSION. aEIT with the 8 electrode system promises the pragmatic ability to noninvasively and near continuously monitor the lungs of the critically ill. Further refinement is needed, including further development of zones of interest and normal ranges, and more accurate allowance for variations in thoracic shape.

Poster Sessions
Drotrecogin alfa-activated (Xigris™): From clinical practice to bundle strategies 221-234

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EARLY XIGRIS IMPROVES MORTALITY DESPITE CLINICAL STABILITY (OR WORSENING) IN SEVERE SEPSIS

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INTRODUCTION. Apparent clinical stability alone may not predict survival in severe sepsis, as microvascular dysfunction can persist in at least 40% of such patients(1). Xigris (Drotrecogin alfa-activated)(DrotAA) may improve microvascular function and reduce mortality when given within the first 24-48 hours of severe sepsis and might further reduce mortality if given sooner, however clinical registry data indicates that dosing is often delayed(2).

METHODS. ENHANCE was a multi-national study of DrotAA in 2378 patients (305 in Canada) with severe sepsis. A logistic regression was performed on the Canadian data to examine independent predictors of mortality and the influence of timing of DrotAA and clinical status as defined by organ function. Only variables significant at 0.05 were retained.

RESULTS. Age, selected organ dysfunctions (expressed as change in serum creatinine and platelet count) and time to first dose of DrotAA were the most significant predictors of outcome. Patients aged </= 49 had a reduced odds ratio for death compared to those 65-74 (0.251, p=0.003) and those >/= 75 (0.269, p=0.005). Table 1 shows the effect of time to first dose of DrotAA, controlled for age and clinical status as defined by stable, worsening or improving serum creatinine and platelet count by the end of next day of treatment. Regardless of the apparent degree of clinical stability, 28 day mortality was less for all age ranges when the first dose of DrotAA was administered within the first 24 hours.

TABLE 1.

	DrotAA < 24H*#	DrotAA >/= 24H*#	DrotAA < 24H+$	DrotAA >/= 24H+$
Age </= 49	8.8%	13.6%	9.1%	9.5%
Age 50-64	11.1%	27.9%	4.4%	15.0%
Age 65-74	20.8%	36.0%	16.7%	29.6%

** p=.0409, + p=.0211 for DrotAA < 24H vs >/= 24H; #stable/worse; $stable/improve*

CONCLUSION. Despite apparent initial clinical stability in patients with severe sepsis, early treatment with Xigris is associated with reduced mortality. This may reflect the ability of DrotAA to improve microvascular dysfunction and enhance oxygen delivery thus helping to prevent the development of clinically silent or „cryptic“ shock.

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SAFETY AND EFFICACY OF ACTIVATED PROTEIN C IN SEPTIC TRAUMA PATIENTS: A DESCRIPTIVE STUDY

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INTRODUCTION. Activated protein C (APC) has been demonstrated to confer a survival benefit when used in the treatment of severe sepsis. However, its use is associated with the potential for severe bleeding. This adverse effect has led to great hesitancy regarding its use in the trauma setting(1). We have successfully used APC in several patients with traumatic injuries who subsequently develop severe sepsis. Our experience forms the basis of this descriptive study.

METHODS. Central pharmacy records and ICD-9 codes were reviewed to identify all trauma patients who had received APC between January 2002 and 2005. Medical records of this cohort were reviewed.

RESULTS. Sixteen of 1165 (1.4%) critically ill trauma patients received APC during the study period. Ten of 16 were male with a mean age of 42 years (range: 20-68 years). The majority had sustained blunt trauma (15 of 16, 94%) with a mean ISS of 24 (range: 9-43). At the time of receiving APC, they had a mean of 2 organ failures (range: 1-4) with a mean APACHE II score of 13 (range: 8-26). Thirteen of 16 (81%) had a baseline predisposition to bleeding (abnormal coagulation profile in 9, low platelet count in 7, injury to a highly vascular organ in 8 and vascular injury in 4). Infusion was begun on average 259 hours after the trauma and 76 hours following the last operative intervention. It was periodically stopped for performance of various procedures (mean: 1.75 times, range:0-4 times per patient). All patients completed the 96-hour infusion. One patient (6%) developed an intra-abdominal bleed requiring re-exploration. Thirteen of the 16 (81%) survived to discharge.

CONCLUSION. Activated protein C can be successfully used in select septic trauma patients who are remote (> 10 days) from the initial injury. Outcome in this group appears to be superior than that for historical controls. These results suggest the need for further evaluation in a prospective randomized manner.

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EFFECTS OF HUMAN ACTIVATED PROTEIN C (APC) ON HEMOSTASIS

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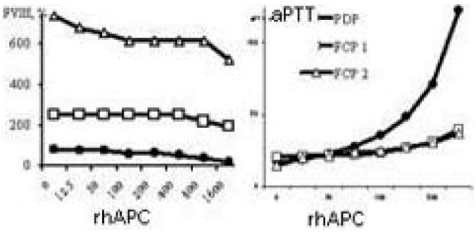
INTRODUCTION. The aim was investigation of the changes of hemostasis during treatment with APC.

METHODS. We investigated aPTT, prothrombin time (PT), the plasma activities of AT III, FVIII, protein C (PC), plasminogen (PG), Willebrand factor (FW), XIIa-dependend fibrinolysis (XIIa-F) in patient with sepsis who received APC (24 mg/kg/h for 96 hours). To study the effects of APC in vitro we spiked fresh citrated plasma (FCP) of 2 patients (pts) with sepsis and pooled donor plasma (PDP) with increasing concentrations of APC (12.5, 25, 100, 200, 400, 800, 1600 ng/ml)

RESULTS. APC infusion increased aPTT, time of XIIa-F, PC and decreased PG. APC infusion did not change levels of AT III, fibrinogen, FW, PT. In vitro rhAPC decreased FVIII and increased aPTT in PDP more than in FCP of pts with sepsis. These effects occurred in concentrations of APC, which were higher than in PROWESS study1.

TABLE 1.

	Before	12 h APC	24 h APC	48 h APC	72 h APC	96 h APC
aPTT, min	28	32	35	39	41	41
XIIa-F min	50	53	50	102	145	135
FVIII, %	203	154	123	180	170	150
PC, %	60	65	80	65	84	84
PG, %	120	130	94	69	47	54



CONCLUSION. The level of FVIII might be used to assess the influence of APC on hemostasis. In pts with sepsis the individual selection of a dose of APC is necessary.

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EARLY BENEFICIAL EFFECTS OF ACTIVATED PROTEIN C ON HEMODYNAMICS IN HUMAN SEPTIC SHOCK

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INTRODUCTION. Because Activated Protein C (APC) reduces the NO production during sepsis, it could improve the vascular tone. Our goal was to test whether APC could reduce the dose of norepinephrine (NE) required to maintain mean arterial pressure (MAP) in septic shock patients.

METHODS. Twenty-two septic shock patients with at least 2 organ failures were retrospectively investigated for MAP and the required dose of NE before (H0) and 24 (H24) hours after the administration of APC. A control group of 22 septic shock patients with at least 2 organ failures who did not receive APC, was matched on age, SAPSII, MAP and the dose of NE at the time of the theoretical start of APC.

RESULTS. At H0, SAPSII (65±16 vs 63±16), MAP (84±11 vs 88±11 mmHg), the dose of NE (1.0 interquartile range [0.26; 1.55]\mug/kg/min vs 1.1 [0.15; 1.32] \mug/kg/min) and lactates level (4.4±2.4 vs 4.8±6.6 mmol/L) were similar in treated and control patients, respectively. The MAP remained stable and was similar in both groups (86±16 vs 89±9 mmHg at H24). However, the required dose of NE increased in the control group (+38% [-41, +38%] from H0 to H24) but decreased in the treated group (-33% [-74, +11%] from H0 to H24) ($p<0.05$ from the control group).

CONCLUSION. APC rapidly improves the vascular tone in septic shock patients as assessed by a decrease in the requirement of NE to maintain arterial pressure.

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MUSCLE PO2 DURING RHAPC ADMINISTRATION IN SEPTIC SHOCK: A PRELIMINARY REPORT

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INTRODUCTION. Organ dysfunction observed in sepsis has been attributed both to tissue hypoxia and to impaired intracellular metabolism of O2. Therefore, the direct assessment of regional perfusion and oxygenation should be mandatory in patient with septic shock. To this objective, measurement of muscle PO2 by an intratissue catheter seems to provide useful information (1). The aim of this study was to evaluate the effect of therapy with recombinant human activated protein C (rhAPC) on muscle PO2 in patients with septic shock.

METHODS. In 3 patients with post-operative septic shock, we measured intramuscular (quadriceps femoris) PO2 (PtO2) by means of a miniaturized polarographic catheter (Licox, GMS) before, during and after a 96 hours-period of rhAPC therapy. Central venous SO2 (ScvO2), sepsis-related organ failure assessment (SOFA) score, standard hemodynamic and respiratory parameters and patient's outcome were also collected

RESULTS. Before rhAPC, the mean values of PtO2, ScvO2 and SOFA score were 18,3 (range 10-24) mmHg, 0,74 (range 0,68-0,85) and 15,0 (range 10-18), respectively. After rhAPC starting, PtO2 values quickly increased in all the patients to a mean vaue of 28,5 mmHg at 24 hours. ScvO2 also increased in 2 patients by about 10%, whereas in 1 patient it remained constant at a value of 0,85. At the end of rh-APC therapy, the mean values of PtO2 and ScvO2 were 38,7 (range 21-61) mmHg and 0,78 (range 0,73-0,85). In all the patients SOFA score progressively reduced and after 96 hours of rhAPC infusion the value was 11,7 (range 10-13). Twenty-four and 48 hours after the end of rhAPC, PtO2, ScvO2 and SOFA score remained quite stable. All the 3 patients were discharged by ICU (mean ICU stay was 30±8 days) and were alive 28 days after the end of rhAPC therapy.

CONCLUSION. In well-resuscitated septic shock patients, rhAPC administration induced: i) a rapid and significant increase of intramuscular PO2, ii) a slight increase in ScvO2 and iii) a consistent decrease in the extent of sepsis-related organ dysfunction. These findings can be attributable to an improvement in tissue perfusion and oxygenation. The variation of muscle PtO2 during rhAPC therapy seems to correlate better than the variation of ScvO2 with the recover of organ functioning.

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DROTREGOCIN ALFA (ACTIVATED) UPREGULATES NAP-2 IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF SEPTIC PATIENTS

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INTRODUCTION. Neutrophil-activating peptide 2 (NAP-2) is a 72-residue protein belonging to the \alpha-chemokine family. The CXC-chemokines such as interleukin-8, neutrophil-activating peptide-2 (NAP-2) are chemoattractants with high selectivity for neutrophils. During early inflammation NAP-2 are rapidly generated within the vasculature and potently induce effector functions in neutrophils, such as chemotaxis and degranulation. We investigated the effect of Drotregocin alfa (activated) on levels of NAP-2 during the time course of septic patients in blood mononuclear cells in vivo.

METHODS. We determined levels of NAP-2 in the supernatant of fresh isolated blood mononuclear cells of septic patients treated with Drotrecogin alfa (activated) (n=7) and septic patients without treatment (n=7) on day 1 and 3 of sepsis. NAP-2 supernatant levels were measured with ELISA-method. Statistical analysis with ANOVA were performed.

RESULTS. We measured significant increased levels of NAP-2 on day 3 (mean=1336.72 ng/ml ± SEM=88.13) compared to day 1 (mean=703.83 ng/ml ± SEM=171.11; $p<0.001$) in septic patients treated with Drotrecogin alfa (activated). In septic patients not treated with Drotregocin alfa (activated) the levels of NAP-2 on day 1 (mean=1775.29 ng/ml ± mean=280.57) decreased to day 3 (mean=1351.76 ng/ml ± SEM=301.19), which was not statistically significant.

CONCLUSION. The ability of rhAPC to up-regulate NAP-2 production in human blood mononuclear cells may represent a new molecular mechanism, by which rhAPC controls chemokines, thereby contributing to the efficacy of rhAPC in systemic inflammation and sepsis. Further in vitro and in vivo investigations are needed to confirm.

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ANALYSIS OF DROTRECOGIN ALFA (ACTIVATED) USE IN BELGIUM: COMPARISON TO PROGRESS REGISTRY DATA

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INTRODUCTION. As part of reimbursement conditions in Belgium, a national registry of drotrecogin alfa (activated) [DrotAA] treated severe sepsis patients was begun and data collected (9/03-9/04). PROGRESS is a separate international sepsis registry collecting data from all patients. Our objective was to compare hospital mortality of DrotAA patients from the Belgian registry to non-DrotAA Belgian patients from the PROGRESS registry (5/03-7/04).

METHODS. Logistic regression was used to assess significance and odds ratios (OR) of DrotAA treatment and hospital mortality, after adjusting for 5 organ systems and age. DrotAA patients from the Belgian registry, non-DrotAA Belgian patients from the PROGRESS registry (>1 organ dysfunction, OD), baseline data for presence or absence of OD (cardiac, respiratory, renal, hematological, metabolic), age, and hospital survival were analyzed in a regression model. After adjustments, hospital mortality was compared.

RESULTS. There were 407 DrotAA patients from the Belgian registry with a hospital mortality of 51.6%. Of these, 286 had enough baseline data to be included in the regression model with a mortality of 50.7%. Overall, 261 non-DrotAA Belgian patients (>1 OD) from the PROGRESS registry had enough baseline data to be included in the model. Of these, 167 had >2 OD with a hospital mortality of 63.3%. Logistic regression results for hospital mortality showed DrotAA treatment reduced the odds of death by 39% (OR=0.61, 95% CI=0.40-0.92, p=0.02). Using the PROGRESS non-DrotAA treated risk model, the predicted hospital mortality of Belgian registry patients, had they not been treated with DrotAA, was 63.5%. Observed hospital mortality of the 286 Belgian registry patients was 50.7%, implying an adjusted absolute mortality reduction of 12.8%.

CONCLUSION. Using Belgian reimbursement registry data, Belgian PROGRESS registry data, and appropriate statistical adjustments, apparent mortality of DrotAA-treated patients was significantly lower than untreated patients. Observed and modeled results were very similar. Though mortality of both registries was higher than previously reported, similar benefit was observed with DrotAA. While OD and age were adjusted for in the model, other differences may have been present but not included.

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PROGNOSTIC FACTORS IN PATIENTS WITH SEVERE SEPSIS TREATED WITH ACTIVATED PROTEIN C

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INTRODUCTION. Although established recommendations exist guiding the administration of activated protein C (rhAPC) for the treatment of severe sepsis, the identification of patients most likely to benefit from its use remains a subject of discussion.

METHODS. In our intensive care unit (ICU), we are performing a registration of all cases treated with rhAPC. Inclusion and exclusion criteria are derived from the PROWESS study and from the Surviving Sepsis Campaign Guidelines, and are strictly applied to all patients with severe sepsis admitted in our ICU. In this study we report an interim analysis of our data.

RESULTS. Twenty patients (11 men, 9 women) have been treated in the last 12 months since rhAPC have been approved in our institution. Mean age was 64.0 years and mean simplified acute physiologic score (SAPS) II was 54.0. Most patients were admitted with a diagnosis of septic shock (10 patients), pneumonia (9 patients) and post-operative abdominal sepsis (5 patients). Nineteen patients had septic shock, 17 were mechanically ventilated and 16 had four or more organ dysfunctions associated with sepsis at time of inclusion (mean sequential organ failure assessment - SOFA - score was 12.8). The treatment protocol (24 mug/kg/h during 96 hours) was completed in 16 patients (four interrupted the treatment due to hemorrhagic complications), and overall mortality at day 28 was 25%. Variables associated with survival were initiation of rhAPC during the first 48 hours of infection, initiation of adequate antibiotherapy during the first 24 hours of infection and reduction of SOFA score at day four of treatment.

CONCLUSION. Surveillance studies of subpopulations treated with activated protein C in different countries that may have different genetic backgrounds are needed to identify the criteria to select the patients that could afford the greatest benefit from this therapy. In our group of patients, initiation of rhAPC during the initial stages of the systemic inflammatory process related to infection, defined as the first 48 hours of clinical infection, is a major determinant of survival, irrespective to local of infection, severity, type and number of organ dysfunctions.

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CHANGES IN TOTAL SOFA SCORE TO ASSESS THE RESPONSE TO DROTRECOGIN ALFA (ACTIVATED) IN SEVERE SEPSIS

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INTRODUCTION. Drotrecogin alfa activated (DAA) is an approved treatment for patients with severe sepsis and septic shock. We sought to identify the clinical and biochemical factors that could predict a favourable course during this DAA administration.

METHODS. A total of 83 critically ill patients with severe sepsis/septic shock were treated with DAA, including 30 patients in the context of clinical trials and 53 as part of routine therapy. We defined an unfavourable course as: death within 5 days, or circulatory shock, respiratory failure or renal failure on day 5. Other patients were considered to have a favourable course. Data were analysed by an analysis of variance for repeated measurements (ANOVA) and a chi square test

RESULTS. Seven patients died within 48 hours of treatment; the other 76 patients were retained in the analysis, including 42 with a favourable course and 34 with an unfavourable course.
The total SOFA score decreased with time in the patients with a favourable course, but not in the others (Table). Only 3 of the 42 patients with a favourable course, but 12 of the 34 patients with an unfavourable course, experienced an increase in SOFA score during the first 24 hours.

TABLE 1.

	Day 1	Day 2	Day 3	Day 4
Course Favourable	8.7 ±4.1	7.3 ±4.2*	6.4 ±4.0*	5.3 ±3.4*
Unfavourable	10.1 ±3.7	9.7 ±4.0	9.3 ±3.8	9.0 ±4.3

**p<0.05 vs Day 1*

CONCLUSION. Changes in total SOFA score over time can be used to separate populations treated with DAA. A rapid decrease in SOFA score over time may help to identify those in whom treatment duration could be reduced to less than the 96 hours currently recommended.

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RHAPC IS NOT BEING USED ENOUGH IN THE ICU?

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INTRODUCTION. The use of recombinant human activated protein C in severe sepsis has a plain scientific approval, however we have observed scarce use in our unit.To see the reasons of this scant use we performed a strict and daily screening

METHODS. The study was prospective, observational performed during 71 consecutive days. Every patient was submited every day to a preliminary screening searching for sepsis data:fever, septic shock and/or disseminated intravascular coagulation. If any of these data was present a proper screening for rhAPC prescription was done

RESULTS. Two hundred and eighty four patients were evaluated with a total of 1397 observations. The preliminary screening was positive in 217 observations. The inclusion criteria were met in 73 observations but the presence of exclusion criteria reduced the indication to 33 observations (IC 95% 1,56-3,16%) (12 patients). Of this 33 observations we substract 16 corresponding to initiated treatments. Of the remaining 17 observations, (12 patients), the treatment was initiated in the first instance in 3 patients. The nine non-treated patients corresponded to: two patients with therapeutic limited effort and the remaining six patients were put on stand by awaiting evolution. Finally the treatment was started in four of the six patients put on stand by. The first instance started treatments had a mean time of waiting of two hours and corresponded to two favourable outcomes and one failed. The second instance started treatments had a mean time of waiting of twenty hours and a good outcome only was achieved in the patient with a time of waiting bellow fifteen hours. One of the two non-treated patients in wait of evolution died and the other had a stay in the ICU of 47 days

CONCLUSION. This screening resulted in a big implementation in the use of rhAPC. The reasons were the continuous vigilance and the information we offered to the physicians.We can conclude that the use of rhAPC was not completly incorporated into the daily practice in our hospital. The lack of use can also be explained by the existing contraindications.Our results also show the inclination of the physicians to “wait and see”, the evolution of the patients seems to show that this strategy is not a good method

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INCIDENCE OF USE OF DROTRECOGIN ALFA IN SEVERE SEPSIS STARTING FROM A PROTOCOL OF USE

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INTRODUCTION. Drotecogin alfa (activated) (DA) is a drug with antithrombotic, antiinflammatory and profibrinolytic effects which has demonstrated effectiveness in the treatment of severe sepsis (SS). The aim of this study is evaluate the incidence of use of the DA in SS after the implantation of agreed protocol of use in our hospital.

METHODS. During a one year period (Jan-Dec 2003), a protocol of use of DA was applied to patients who were admitted with sepsis diagnosis in our ICU. The protocol was developed by a commission of experts according to the recommendations of use indicated by the international (AMAE) and national (AEM) competent organizations; for use of DA, it was necessary the presence of 2 or more organic failures (MODS), a SOFA ≥ 6 and an evolution < 48 hours since the onset of the organic dysfunction. Sepsis and SS were defined according to the criteria of the Consensus Conference of 1991.

RESULTS. 845 patients were admitted in our ICU during the period of study, 150 of them for sepsis (17,7%). From them, 145 (96,6%) fulfilled the criteria of SS. 94 (64,8%) were men, 51 (35,2%) women. The average age was 57,75 ± 18,68 years. 12 patients (8,3%) had one organ dysfunction; 29 (20%) two; 40 (27,6%) three; 34 (23,4%) four; 27 (18,6%) five and 3 (2,1%) six organs. The mean SOFA was 7,9 ±3,35 and in 108 patients (74,5%) it was ≥ 6. APACHE II was 22,30 ± 13,54. In total, 21 patients (14,5%) received DA. This group mortality rate in ICU was 38,1%, whereas in not-treated with DA it was 44,8%. 124 patients (85,5%) didn't receive DA, either for not fulfilling inclusion's criteria: SOFA<6: 42 patients (33,9%), MODS>48 hour: 18 (14,5%), prediction of rapid improvement: 1 (0,8%), or contraindication: inmunodepression: 16 (12,9%), therapeutic effort limitation: 9 (7,3%), coagulopathy: 3 (2,4%), thrombocytopenia: 3 (2,4%), anticoagulation: 7 (5,6%), haemorrhagic risk: 11 (8,9%), liver disease: 4 (3,2%) and others: 10 (8%).

CONCLUSION. SS is an important cause of admission in critical patient's areas. DA has showed beneficial effects, despite of the adverse effects and its high cost. Following a agreed protocol model, the use of DA had a low prevalence (15,2%) in this patients, due to the lack of indication by insufficient severity or a MODS>48 hours, and/or the presence of contraindications like the inmunodepression, the haemorrhagic risk and the presence of anticoagulation.

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EXPERT TELEPHONIC ASSESSMENT FOR TREATMENT WITH DROTRECOGIN ALFA ACTIVATED

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INTRODUCTION. Treatment with drotrecogin alfa activated reduces mortality in severe sepsis (1). During the introduction period of the clinical use of Drotrecogin alfa activated, in order to overcome possible problems related to the lack of experience using this new drug, a expert telephonic assessment system was started

METHODS. During the introduction period of the clinical use of Drotrecogin alfa activated for severe sepsis (June 2003-May 2004) a team of 2 intensive care physicians and 2 clinical research nurses with previous experience in administering drotecogin alfa activated in clinical trials where full time available for telephonic questions regarding the clinical use of Drotrecogin alfa activated in Spain. Questions where made using a free toll telephone number.

RESULTS. During this one year period a total of 118 questions where answered. 100% of questions could be attended immediately. Questions where made mainly by intensivists (84%), pharmacologists (8%) and anesthesiologists (5%) regarding patients with pneumonia (42%), abdominal sepsis (31%), meningitis (10%) or other sources of sepsis (17%).
The main concerns in the clinical use of Drotrecogin alfa activated for severe sepsis where about indications or contraindications (41%), dose (16%), interruptions (26%), concomitant treatments (14%) or complications (3%). After a training period, clinical research nurses could answer 68% of questions and only 32% needed medical assessment.

CONCLUSION. Expert telephonic assessment is a useful method for improve the implementation of new drugs or technologies in critical care and give value information about main concerns in the implementation of this new technologies. During the first year of clinical use of drotrecogin alfa activated, questions about the selection criteria for treatment were the most common.

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EMERGENCY DEPARTMENT -BASED SEPSIS PROTOCOL IN A TEACHING HOSPITAL: EVALUATION USING SEPSIS BUNDLES

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INTRODUCTION. Early recognition and treatment of septic shock is associated with an increase in survival. We noted from a previous institutional database that there were delays in the identification and fluid resuscitation of septic patients and in the placement of CV catheters. A sepsis protocol based on the emergency department (ED)-centric model was instituted(1). The aim of this study is to provide an initial evaluation of the protocol after 3 months.

METHODS. 12 patients were treated using the sepsis protocol over 3 months. Performance was evaluated by assessing predefined goals, using sepsis bundles. Data were recorded from time of entry into the ED to the time the event was measured.

RESULTS. The median time to perform treatment-related events was within the goal for all 6h bundles. In the 24h bundles, there was good compliance for evaluation of steroid and APC therapy. APC was not given in 5 patients due to rapid response after fluid resuscitation. Glucose control was inadequate at 24h in 4 patients. Initial fluid resuscitation was aggressive with a median of 5L administered in the first 6h and 12.85L over 72h.

TABLE 1.

	6H Bundle Median, Hours
CVP access/monitoring	3.98
Lactate level measured	2.13
Random cortisol measured	5.85
Antibiotics administered	2.17
Blood cultures drawn	1.615

CONCLUSION. Implementation of a sepsis protocol based on an ED-centric model had a high rate of success in achieving the 6h and most of the 24h goals in this small study. It introduced an effective strategy for the early recognition and therapy of septic patients that was achieved through interdisciplinary co-operation. The protocol is easy to operate and has the potential to be expanded hospital-wide.

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THE IMPACT OF A CARE BUNDLE ON THE INTENSIVE CARE MANAGEMENT OF PATIENTS WITH SEVERE SEPSIS

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INTRODUCTION. The Surviving Sepsis Campaign aims to reduce the mortality from severe sepsis by 25% within 5 years (1). The use of sepsis care bundles has been suggested to ensure that evidence based interventions, as recommended in the Surviving Sepsis Campaign guidelines, are applied to all patients who may benefit. We implemented a sepsis care bundle on our general intensive care unit (ICU), at Chesterfield Royal Hospital, in February 2004.

METHODS. Our sepsis care bundle includes five interventions for severe sepsis - early goal-directed therapy, moderate dose steroids, intensive insulin therapy, human recombinant activated protein C and low tidal volume ventilation. We introduced a set of guidelines for the use of these interventions, along with an educational campaign to promote their use. A stamp, listing the five interventions, was made available to be used in the patient's notes as an aide memoir. The notes of all patients admitted to our ICU with severe sepsis, for a 3 month period of the year before and the year after the introduction of the care bundle, were reviewed.

RESULTS. The notes of 13 patients prior to introduction of the care bundle and 16 patients after introduction of the care bundle were assessed. No patient in either group received early goal-directed therapy. The appropriate use of moderate dose steroids increased from 0% to 88% of patients. The use of our intensive insulin regimen increased from 31% to 94%. The use of activated protein C increased four fold following introduction of the care bundle. Prior to the care bundle 5 patients apparently met the criteria for treatment with activated protein C but did not receive it, following introduction of the care bundle all patients either received activated protein C or had a documented contraindication. Mean tidal volume in the first 48hrs of admission was 8.6 ml/kg body weight before and 6.9 ml/kg body weight after introduction of the care bundle.

CONCLUSION. The use of a sepsis care bundle, in combination with an educational and promotional strategy, has led to marked improvements in our implementation of evidence based treatments for severe sepsis.

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IDENTIFICATION ON CT SCAN OF SPONTANEOUS INTRA-CEREBRAL HAEMATOMAS WITH RISK SIGNS OF BRAIN DEATH

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INTRODUCTION. Objective: To identify CT scan signs associated to the risk of evolution to brain death in patients suffering from spontaneous cerebral haematomas

METHODS. Design: Cases/control series. N 100. Study group: 50 patients with severe spontaneous cerebral hematomas admitted to ICU that evolved to brain death; Control Group: 50 survival patients, admitted to ICU after a SCH. Severe spontaneous cerebral haematoma were defined as level of consciousness lower than 12 points of Glasgow Coma Scale. Therapeutic interventions were similar in both groups. The radiological signs considered for this study were: location of the haematoma (brainstem, ganglia base, cerebellum, lobar); Existence of compression of cisterns of the base of the skull(cc), volume of the haematoma (VH) (by formula of the sphere), intraventricular bleeding (according to Graeb's scale) and midline-shift in mm. Dependent variable: Brain death. Statistical analysis using: chi's square, odds ratio(OR), and t-Student's test.

RESULTS. The location in brainstem (OR= infinite), in basal ganglia (OR=3.43), and the compression of the cisterns (OR= 5.042) were proved as CT scan signs associated to a high risk of brain death. There was a significant difference between the average of the following values: volume of the haematoma ($p < 0,05$), score of Graeb scale ($p< 0,001$) and midline-shift ($p< 0,05$). Did not exist significant difference for the rest of variables studied.

CONCLUSION. 1.- There was a powerful association between risk of BD and the existence of some CT scan signs in patients with SCH . 2.- The location of haematoma in brainstem and basal ganglia; the existence of cc, high VH, high score of Graeb's scale and high midline-shift are factors associated to risk of brain death in patients admitted to ICU suffering spontaneous cerebral haematomas .

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PROTEASOME LEVELS IN PATIENTS WITH INTRACRANIAL ANEURYSM BLEEDING: A CEREBRAL TISSUE DAMAGE MARKER

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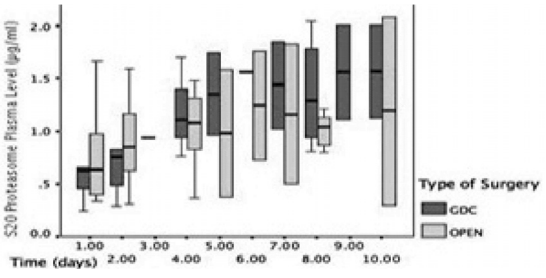
INTRODUCTION. The 20S proteasome plays an important role in the non-lysosomal pathway of intracellular protein degradation, antigen processing and apoptosis, thus being a possible marker for tissue turnover and damage. During intracranial bleeding severe tissue damage is inevitable; the aim of this study was to analyze the effect of surgery - aneurysm coiling versus clipping - on 20S proteasome plasma levels.

METHODS. We examined 14 pts (9 female, 5 male; weight: 87.7 ± 16.1 kg; Hunt-Hess 3-4) with intracranial bleeding due to aneurysm rupture. Surgery was performed immediately after the bleeding event, with either clipping (8 patients) or GDC (6 patients). Blood samples were collected postoperatively and on 9 consecutive days and 20S proteasome levels were measured with a sandwich ELISA as described by Dutaud et al.

RESULTS. As shown in figure 1, the plasma levels of 20S proteasomes in both groups increased significantly over 10 days, there was no significant difference between the groups for either timepoint. GDC patients: day 1: 0.66±0.38 µg/ml, day 10: 1.57±0.63 µg/ml; clipping patients: day 1: 0.75±0.45 µg/ml, day 10: 1.2±1.2 µg/ml (means±SD, $p<0.05$).



CONCLUSION. 1) Plasma proteasome levels rise significantly after intracranial bleeding, likely reflecting the extent of brain tissue damage. 2) There was no significant difference in proteasome levels between patients with clipped or coiled aneurysms.

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INITIAL RESULTS AFTER ESTABLISHMENT OF AN ICU-BASED MEDICAL EMERGENCY TEAM

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INTRODUCTION. The medical emergency team (MET) is a rather late invention as a complement to standard intensive care. It is intended to identify patients potentially needing intensive care due to organ failure at an early stage. If the patients can be identified earlier it may be possible to either stabilise the patient in the normal ward and thereby avoid the need for intensive care or to admit the patient to the ICU at an earlier stage. The establishment of METs has been found to decrease the number of sudden deaths in hospitals and to improve outcome in Australia and in Great Britain.

METHODS. A MET was established in a university hospital. The team was based in the ICU and called by staff in the general wards when patients with threatening organ failure were identified by the use of a Modified Early Warning Score (MEWS). The MET consisted of an ICU physician and an ICU nurse. Patients were scored according to the MEWS score by the ward nurse and by the MET. Depending of the severity of the condition patients were either admitted to the ICU or treatment to be administered in the general ward suggested. Time spent in the ward, MEWS score and number of consultations/patient were recorded. The number of cardiac arrests was recorded for a period of 15 months prior to the establishment of the MET and for a period of 10 months after the establishment.

RESULTS. The MET was consulted for 145 patients. Each inital consultation lasted for an average of 31 minutes. 26 patients were seen twice and 8 patients were seen three times by the MET. The average time spent on the follow up consultations was a few minutes shorter than the initial consultation. 54 patients (37%) were admitted to the ICU. Respiratory failure was the most common cause for consulting the MET (74 patients) followed by circulatory failure (39 patients) and sepsis (22 patients). There were 15 unexpected cardiac arrests in the ward for acute medicine during the 15 months prior to the establishment of the MET and 4 cardiac arrests during the 10 months after the establishment of the MET.

CONCLUSION. The establishment of a MET has lead to a closer collaboration between the general wards and the ICU. A transfer of knowledge between the wards has taken place. The incidence of unexpected cardiac arrests in the ward for acute medicine was reduced by 50% by the establishment of the MET. The establishment of a MET seems to improve quality of care and patient safety in a university hospital in Sweden.

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PROGNOSTIC SIGNIFICANCE OF TROPONIN I IN ACUTE PULMONARY EMBOLISM

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INTRODUCTION. Serum cardiac Troponin I (cTrop I) concentrations are useful as a diagnostic or prognostic marker in patients with massive pulmonary embolism (PE). The diagnosis of sub-massive PE is more difficult in clinical practice and there are few data evaluating the relationship between cTrop I and sub-massive PE. We therefore conducted a prospective study to determine the both the diagnostic value and the prognostic utility of cTrop I measurements in patients with PE.

METHODS. 48 patients attending the emergency room between September 2002 to January 2004 with dyspnoea, chest pain or syncope of uncertain causes and no ECG signs of acute coronary syndrome were included in the study. Patients with a low probability of PE (on the basis of pre-test clinical scale and negative D-dimer test) were discharged or admitted with a non-PE diagnosis. All other patients underwent CT scan and/or a perfusion scan to confirm the diagnosis. cTrop I concentrations were measured in all patients within 24 hours by immuno-enzymatic assay with a value of 0.4 ng ml-1 as cut-off, according to laboratory guidelines. The relationship between cTrop I and the diagnosis of acute PE, adverse in-hospital outcomes were determined by binary logistic regression and calculation of odds ratios. $P<.05$ was considered statistically significant.

RESULTS. The diagnosis of PE was confirmed in 35 patients, with 7 in-hospital deaths. There were no differences in baseline characteristics or clinical features between patients with positive diagnosis of PE and those without PE. The sensitivity and specificity of cTrop I in detecting PE was 20 % and 93 % respectively, with positive and negative predictive values of 87% and 30%. Odds ratio for the diagnosis of PE in patients with high cTrop I was 3.0 (95% C.I 0.33- 27.1, p=0.328). However, when adverse in-hospital outcomes were included, sensitivity and sensitivity were 71% and 93 %), with identical positive and negative predictive values (71% and 93% respectively). Odds ratio for in-hospital death in patients with high cTrop I was 32.5 (95% C.I 3.7-287.7, p=0.002).

CONCLUSION. These data suggest that increased cTrop I may help to detect those patients with PE who are at higher risk of mortality, in the absence of other clinical risk factors. Patients with increased cTrop I and PE may be considered for aggressive early treatment such as thrombolysis. Further studies are required to confirm these findings.

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COOLING WITH A WATER CIRCULATING BLANKET EFFICIENTLY INDUCES AND MAINTAINS NORMO AND HYPOTHERMIA

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INTRODUCTION. Controlled normothermia and therapeutic hypothermia are frequently used in neurological patients with fever and after out of hospital cardiac arrest. Little is known about the optimal cooling method for inducing and maintaining controlled normo- and hypothermia in the ICU. In this study we compared the efficacy of ice-cold infusion and icepacks, a water-circulating cooling blanket and an air-circulating cooling blanket.

METHODS. Critically ill patients with acute brain injury or subarachnoid hemorrhage who developed fever (defined as rectal temperature > 38,5ºC) despite were prospectively assigned to controlled normothermia (rectal temperature of 37ºC) by icepacks (n = 5), a water circulating cooling blanket (Blanketroll II, The Surgical Company) (n = 5), or an air-circulating cooling blanket (Caircooler CC1000, Medeco) (n = 5). Patients after out of hospital cardiac arrest were prospectively assigned to infusion of 20 ml/kg icecold fluids and icepacks (n = 5), a water circulating blanket (n = 5), or an air circulating blanket (n = 5) to induce mild hypothermia (rectal temperature of 33ºC). We compared the relative efficacy of the different cooling methods by calculating the fever burden (area under the curve, AUC) corrected for the temperature at T = 0 (delta T). In addition the percentage of time the patients' temperature was more than 0.5ºC higher or lower than the target temperature was measured. For statistical analysis the Student's T test was used.

RESULTS. Baseline demographic data, including body mass index, were comparable in all groups. In the normothermia group, the AUC/delta T was significantly lower in the patients cooled with the water circulating blanket compared to cooling with icepacks or the air circulating blanket (11.9 ± 9.4 vs 35.8 ± 8.8 (P = 0.001) vs 31.6 ± 9.7 (P = 0.01) respectively). In the hypothermia group the AUC/delta T was significantly lower in the patients cooled with the water circulating cooling blanket compared to cooling with icepacks or the air circulating blanket (1.6 ± 1.7 vs 22.8 ± 17.3 (P = 0.04) vs 15.5 ± 14.0 (P = 0.01) respectively). Using the water circulating cooling blanket the patients were significantly longer in the target temperature range in both normo- and hypothermia.

CONCLUSION. Cooling with a water circulating cooling blanket was the most efficient and reliable technique for induction and maintenance of controlled normo- and hypothermia in ICU patients.

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MECHANICAL THROMBECTOMY & CHEMICAL THROMBOLYSIS FOR HEPARIN UNRESPONSIVE CEREBRAL VENOUS THROMBOSIS

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INTRODUCTION. Management of cerebral venous thrombosis is challenging. Symptoms and severity vary depending on the extent and location of thrombus, venous collateral vessels, and rate of thrombus progression. Heparin is the first line of treatment1,2.We present 3 cases of superior sagittal sinus (SSS) thrombosis, unresponsive to heparin therapy, treated successfully by mechanical thrombectomy and chemical thrombolysis.

METHODS. Mechanical thrombectomy: the anterior part of SSS was exposed via craniectomy. A fogarty no.4 catheter was passed into it posteriorly and the bulb inflated with saline. Long bits of clot were evacuated by pulling the catheter out and procedure repeated till fresh blood gushed out. Chemical thrombolysis with intrasinus Urokinase 100,000 IU was started intraoperatively. A small catheter was left in the SSS and Urokinase 500,000 IU was infused over 24 hours.

RESULTS. Case1:21 yr male complained of headache, vomiting & focal convulsion for 2 days.He had left hemiparesis,GCS 11. Case 2:53 yr male had two episodes of focal convulsion. He had motor aphasia, no limb weakness,GCS 15. Case 3: 22 yr male had headache and focal convulsions of right side for 3 days with GCS 12. All 3 worsened within 12 hours of Heparin therapy and underwent mechanical thrombectomy. Case 1 also received chemical thrombolysis. Postoperatively heparin was given for 48 hrs. They were discharged on warfarin 10-12 days later. Case 1 & 3 were treated with hydroxycobalamine for hyperhomocystinemia due to B12 deficiency.

CONCLUSION. In patients unresponsive to heparin and where catheter based thrombolysis 2 is not possible, mechanical thrombectomy is a novel treatment option. Further studies need to be undertaken to define the exact role of these new therapies. Hyperhomocystinemia is an established cause for arterial thrombosis. Future studies to evaluate it as a cause of venous thrombosis are required.

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PREDICTIVE PARAMETERS OF DEATH IN REFRACTORY ACUTE POISONINGS WITH MEMBRANE STABILISING AGENTS

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INTRODUCTION. Acute self-poisoning with membrane stabilising agents (MSA), including chloroquine, flecainide, tricyclic antidepressants, betablockers or cocaine, are rare but may be fatal. Our objective was to identify and validate the predictive factors of unresponsiveness to conventional therapies.

METHODS. 1- Retrospective study of patients admitted during 5 years, with severe MSA intoxication and requiring cathecholamines; comparisons between survivors and non-survivors, using Chi-2 and Mann-Whitney tests; determination of the sensitivity and specificity of the predictive criteria of death. 2- Prospective validation of these criteria, including all patients admitted during 1 year. During this period, all the patients referred to our ICU and presenting a refractory shock were treated with extracorporeal life support (ECLS) and thus excluded from the analysis. This study was approved by our institutional ethics committee.

RESULTS. In the first study, 137 patients (95F/42M, 34yrs [14-84], median [extremes], mortality rate: 28%) were included. Among them, 21% presented a pre-hospital cardiac arrest, which was persistent on admission in 25% of the cases. During ICU stay, 12% presented an intra-hospital cardiac arrest. We considered the following parameters as predictive of MSA poisoning-related death: 1) persistent cardiac arrest on admission or 2) refractory shock defined by the persistence of a systolic blood pressure <90mmHg, despite adequate 1,000ml fluid loading, 375ml 8.4% bicarbonate infusion in <8h and >3mg/h epinephrine infusion, due to cardiac failure (confirmed by echocardiography or right cardiac catheter), with respiratory (PaO2/FiO2 <150mmHg) or renal failure (diuresis <20 ml/h or serum creatinine concentration >120µmol/l). Taken together, these criteria allowed us to identify the patients who died in ICU with a sensitivity of 87% and a specificity of 97%. In a second study, we prospectively validated these criteria: No death was observed in the patients (N=30) admitted with a severe MSA poisoning and who did not present any of these criteria. By opposite, all the patients (N=5) for whom an advice was sought and who validated the criteria with no possibility of ECLS, died.

CONCLUSION. Death following acute MSA intoxication is high and difficult to prevent. Characterization of predictive parameters of death may allow improvement of survival, with early recognition of situations requiring cardiac assistance.

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URINARY NGAL IS DRAMATICALLY INCREASED IN ACUTE RENAL FAILURE

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INTRODUCTION. NGAL (neutrophil gelatinase-associated lipocalin) is a 25-kDa glycoprotein first isolated from granulocytes but subsequently found to be expressed by a number of epithelial tissues, including the proximal renal tubule where expression is greatly increased after ischemic or nephrotoxic insult. Animal studies show that the level of NGAL in urine increases within 2 h of ischemic renal injury. We have developed an enzyme-linked immunosorbent assay (ELISA) for NGAL and measured NGAL in urine and serum from patients undergoing intensive care for a variety of admission diagnoses.

METHODS. A sandwich ELISA for NGAL was developed using monoclonal antibodies against recombinant human NGAL for capture and detection. The assay showed a detection limit of 6 pg/ml, a range up to 1 ng/ml, and no interference from plasma or urine. NGAL was determined in serum and urine from healthy volunteers and patients in intensive care. The results from the patients were correlated with plasma creatinine, serum C-reactive protein (CRP) and neutrophil count using Spearman's coefficient of rank correlation (r).

RESULTS. Urinary NGAL was elevated in all patients. There was significant correlation between NGAL in urine and serum (r 0.945, p <<0.001). Urinary NGAL correlated poorly with plasma creatinine (r 0.418, p 0.1) and serum NGAL did not correlate with the neutrophil count (r 0.273) or CRP (r 0.064). In particular, serum and urinary NGAL was raised in sepsis or bacterial pneumonia in patients with very low neutrophil counts due to leukemia. The highest urinary NGAL (over 15 mg/l) was found in a case of acute tubular necrosis at a time when there had been no rise in plasma creatinine. Urinary NGAL levels were also markedly but less dramatically raised in other cases of acute renal failure.

CONCLUSION. Urinary NGAL is elevated in different pathological conditions and very high values are seen in acute renal failure. Increased NGAL in serum and urine is not a reflection of neutrophilia, nor is it just an acute phase reactant, as shown by the absence of correlation with CRP. The results suggest that NGAL produced in organ damage spills over into the blood and is excreted in the urine, but renal NGAL in acute tubular necrosis also passes directly into the urine to produce dramatically elevated levels before plasma creatinine has been affected. Highly elevated urinary NGAL may be an effective early marker for acute renal injury.

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NEUROPSYCHOLOGICAL ASSESSMENT IN CARBON MONOXIDE-POISONED PATIENTS

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INTRODUCTION. Carbon monoxide (CO) is a major environmental toxicant that frequently causes death or neurologic morbidity (1).In this study, we assess cerebral function with neuropsychologic screening test in patients with different ages of carbon monoxide poisoning.

METHODS. This study was prospectively performed in 142 patients who diagnosed carbon monoxide intoxication. Patients were randomly assigned to two groups. In group I, there were 84 patients with aged <40 yr and Group II consisted of 58 patients with aged >40 yr. Neuropsychologic screening test were evaluated on admission and after 72 hours in all patients.

RESULTS. There were no significant differences between Group I and Group II with regard gender and COHb levels. On admission, there were no significant differences in neuropsychologic screening test score between Group I and Group II. In Group II, 72 hours after admission, scores were significantly decreased compared to Group I. In 2 patient in Group I (% 2.38) and 2 patients in Group II (% 3.44), delayed neuropsychologic sequelae developed at follow-up 4 weeks after poisoning.

TABLE 1.

	Group I (aged<40)	Group II (aged>40)	p-value
COHb (%) Admission	28.39±1.2	23.80±1.15	0,09
COHb (%) After 72 hrs	2.86±0.24	2.96±0.27	0.78
Neuropsychologic score Admission	24.70±1.52	22.58±1.74	0.36
Neuropsychologic score After 72 hrs	28.51±0.28	24.87±1.25	0.001

CONCLUSION. Despite the limits of our study, we can conclude no clinical history or COHb level predict which patients are at risk for neurologic deterioration but advanced age may address this group as high risk.

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MECHANICAL PROPERTIES OF EDL MUSCLE IN A RAT MODEL OF CRITICAL ILLNESS POLYNEUROPATHY

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INTRODUCTION. Critical illness polyneuropathy (CIP) remains to be delineated since it includes several nervous and muscular entities occurring after a sepsis. The aim of this study was to measure the muscular mechanical properties of the extensor digitorum longus (EDL) on a model of CIP induced by a chronic peritonitis in the rat.

METHODS. Two groups of 20 Wistar rats were submitted either to a chronic peritonitis (group S) or no surgical procedure (group C). The effects of the chronic sepsis were assessed on day 14 on EDL by stimulation of distal sciatic nerve. The following measurements were then done: 1) isometric contraction, tension-length relationship, a 2 minute fatigue test ; and 2) function of motor end plate by monitoring curarisation and decurarisation using the train of four technique after administration of 1mg/kg of atracurium.

RESULTS. Optimal length was obtained for a 32% increase of the initial length for control while it was reached for a 40% increase ($p<0.05$) in septic rats. Table 1 summarises contractile indices of EDL, (*) denotes $p<0.05$ from the other groups. Tetanic stimulation showed a higher summation in the septic rats with a maximal tension of 92g at 15s of tetanus and 71g for control ($p<0.05$). Fatigue index was 0.23 (0.11) in septic group and 0.59 (0.19) in control ($p<0.05$). Curarisation kinetics are summarised in table 2.

TABLE 1.

	Maximal tension	Contraction time	Time to half relaxation
group S	29.9 ± 5.4 *	17.3 ± 2.3 *	11 ± 2.4 *
group C	44 ± 10	29 ± 6.6	52 ± 11

TABLE 2.

	Decurarisation (min)	T4/T1 < 25%	recovery T4/T1 > 75%
Septic	36.7 * ± 9.6	12.6 * ± 5.7	22.9 * ± 8.6
Control	54.6 ± 1.7	22.3 ± 2	47.2 ± 1.2

CONCLUSION. Atrophy may account for the decreased force. Shorter delay in contraction and relaxation in the septic group may be explained by a higher cytosolic concentration of calcium as shown by Bolton. The shorter decurarisation is in agreement with the litterature and may be explained by an upregulation of acetyl choline receptors with modified electrophysiologic properties.

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FEASIBILITY OF DIFFERENT COOLING METHODS: A CRITICAL CARE NURSE SURVEY

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INTRODUCTION. International guidelines support the use of therapeutic hypothermia (TH) after out-of-hospital cardiac arrest (OHCA) and different cooling protocols have been successfully applied (1). The purpose of this study was to evaluate the feasibility of different cooling methods from the Critical Care Nurses'(CCN) point of view.

METHODS. A structured survey form was distributed in our ICU-unit and all CCN who have been involved in TH-treatment were asked to participate. The nurses'work experience and number of TH-treated patients during a 2,5 year period were recorded. A 1-to-4 rating scale (1=best/4=worst)for the various feasibility elements was applied to each TH-method used.

RESULTS. Fifty-nine CCN participated in the survey. Median work experience was 7 years (0,5-26y.), median TH-treated patients involved in was 4 (1-10).

TABLE 1.

Feasibility elements of different cooling methods

	Ease of application	Visual patient monitoring	Work load	Hygiene	Noise level
Ice-water soaked towels	1,93	2,16	3,13	2,39	1,07
Coolgard 3000	2,45	1,17	1,74	1,94	2,40
Artic Sun	2,13	2,07	1,72	1,69	2,40
Thermowrap	3,33	2,73	2,64	2,16	2,24

Mean values

CONCLUSION. The survey shows the strongpoints and weaknesses of the various currently used cooling methods from the CCN's perspective. No single method could satisfy all nursing-feasibility elements.

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CPREZY(TM): A NEW ADJUNCT TO IMPROVE QUALITY OF CHEST COMPRESSIONS BY LAYPERSONS

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INTRODUCTION. External chest compressions (ECC) are an essential part of cardiopulmonary resuscitation either by laypersons or professionals and are usually performed without any adjuncts. Although different devices have been developed in the past, none was implemented as standard during resuscitation. The CPREzyTM pad is a simple device to help the user to perform ECC.

METHODS. In a mock cardiac arrest scenario 202 laypersons were asked to perform 5 minutes of single-rescuer-CPR. Group 1 was taught classic ECC, followed by ECC with CPREzy and was tested using the CREzy. Group 2 was taught classic ECC and tested in ECC only. On the second day the groups were divided: 1a was tested in ECC with CPREzy again, 1b was tested in ECC only, 2a was taught in ECC with CPREzy and tested, 2b was tested in ECC only again. Primary endpoints were a rate of ECC between 90 and 110/min and a compression depth between 40 and 50 mm. Secondary endpoints were the rates of incorrect decompression, incorrect hand positioning and influences on rescue breathing.

RESULTS. Comparing the endpoints on day 1 (n = 111 vs. N = 91) the ECC with CPREzy was significantly improved (rate correct: 93,7% vs. 19,8%, $p \leq 0,01$; depth: 71,2% vs. 34,1%, $p \leq 0,01$). The group tested with CPREzy initially on the 2nd day (n = 36), improved significantly in the compression rate (19,8% vs. 88,9%, $p \leq 0,01$) and compression depth (34,1% vs. 75,0 %, $p \leq 0,02$). The control-group (n = 55) without CPREzy demonstrated poor performance in both evaluations (correct rate : 19,8% vs. 25,5%, depth: 34,1% vs. 43,6%).

CONCLUSION. CPREzyTM as a simple portable and re-usable device is able to improve laypersons´ performance of ECC in simulated cardiac arrest.

Grant acknowledgement. We want to thank Healthaffairs (UK) for loaning CPREzy-Pads.

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ERYTHROPOIETIN TREATMENT AFTER OUT-OF-HOSPITAL CARDIAC ARREST: RESULTS OF A PILOT STUDY

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INTRODUCTION. Numerous data suggest a neuroprotective effect of erythropoietin (EPO). We evaluated the feasibility and consequences of high-doses epoetin-alpha (EPO-\alpha) treatment after out-of-hospital cardiac arrest (CA).

METHODS. After return of spontaneous circulation, 20 pts received 5 injections of EPO-\alpha (40.000 UI every 12 hours during 48 hours). Mortality, neurologic outcome (cerebral performance category)and side effects were assessed at D30.

RESULTS. The pre-hospital rescue team enrolled 20 patients, of whom 18 were analysed (2 CA of non cardiac origin were excluded).

TABLE 1.

Patient characteristics

	Median [IQR] or number (%)
Age	58.5 [56-82]
SAPS	2 61 [50-78]
Interval between CA and ROSC (min)	20.5 [15-50]
Acute coronary syndrome	12 (67%)
Ventricular fibrillation/tachycardia	16 (89%)

TABLE 2.

Outcome and side effects

	Number (%)
Thrombocytemia (> 500x10⁶/mL)	3 (15%)
Vascular thrombosis	1 (5%)
Seizures	5 (25%)
D30-survivors with Cerebr. Perf. Cat 1	10 (55%)

CONCLUSION. We observed a high survival rate with no or minor cerebral sequelae and no major side effects. EPO treatment after CA should be evaluated in further clinical studies.

Grant acknowledgement. This study was funded by Janssen-Cilag OrthoBiotech France Inc.

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COMBINED CORE AND SURFACE COOLING IS A SAFE AND EFFECTIVE WAY TO INDUCE CONTROLLED HYPOTHERMIA

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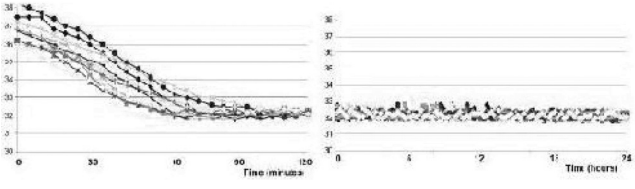
INTRODUCTION. Therapeutic hypothermia is being used with increasing frequency in the ICU for various indications. Safe and effective methods to cool and maintain low temperatures are therefore needed. We performed a feasibility study to test efficacy and reliability of a new surface cooling device, the Arctic Sun system, using hydrogel-coated water-circulating pads that stick to the skin to increase heat transfer. This was combined with infusion of refrigerated (4oC) saline for quicker induction of hypothermia.

METHODS. 10 patients with various types of neurological injury were cooled with cold fluids and 5 adhesive surface pads. Temperature was monitored centrally, rectally and/or by bladder probe. A strict protocol was used to prevent complications. Target temperature was 32oC in all patients.

RESULTS. Results are shown in Fig.1. 1980±760ml of cold fluid was infused in 45 minutes. Target temp. was reached within 120 min. in all patients. This was comparable to observations in our previous studies using 2 rubber water-circulating blankets and cold fluid infusion; however, nursing workload was significantly lower, and temperature was subsequently more accurately maintained: average temp. remained within 32±0.5oC for 96% (range 93-100%) of the next 24 hours, with no temp.<31 or >33.5oC seen in any patient.



CONCLUSION. Induction of hypothermia with cold fluids and adhesive water-circulating pads appears to be a safe and effective method to induce, and especially to reliably maintain, hypothermia in patients with neurological injury.

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MACROPHAGE CHEMOATTRACTANT PROTEIN 1 (MCP-1) AND OUTCOME IN CARDIOPULMONARY BYPASS (CPB)

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INTRODUCTION. CPB is characteristically associated to systemic inflammation, involving a number of cytokines and activated cells. MCP-1 is a chemokine that attracts and activates monocytes and T-cells and might be related to postoperative complications, despite of scarce data in the literature. This pilot-study attempted to describe perioperative circulating levels of MCP-1 and to investigate possible correlations with the intensity of postoperative organ dysfunction.

METHODS. Under informed consent, 20 patients submitted to cardiac surgery with CPB were consecutively studied. Exclusion criteria were current use of anti-inflammatory drugs, associated infectious, neoplastic and inflammatory diseases. MCP-1, macrophage migration inhibitory factor (MIF), interleukin 6 (IL6) and 10 (IL10) were assayed by ELISA-sandwich technique in peripheral blood sampled at anesthesia induction and 3, 6, 10 and 24h post-CPB. Sequential variations of blood levels were assessed by ANOVA for repeated measures and Bonferroni test. Two-tailed Spearman test was applied to assess correlations with postoperative outcomes, as measured by multiple organ dysfunction score at the third postoperative day (MODSd3). Significance was assumed for $p<0.05$.

RESULTS. Similarly to MIF and IL6, blood levels of MCP-1 significantly changed after CPB. From baseline levels (69.44 ± 15.92 pg/mL), MCP-1 reached peak values 3h post-CPB (387.11 ± 108.87pg/mL), and progressively declined thereafter. MODSd3 was associated to the levels of MCP-1 measured at anesthesia induction ($p=0.010$ rho=0.606) and at 6h post-CPB ($p=0.037$, rho=0.508). Levels of IL6, 6h post CPB, were also associated to MODSd3 ($p=0.008$, rho=0.616).

CONCLUSION. As shown for IL6, CPB can induce circulation of MCP-1, whose levels were related to postoperative outcome, as previously shown in a pediatrics population*. Interestingly, pre-operative levels of MCP-1 were also related to postoperative outcome. Although limited by the small sample size, these findings can stimulate further studies to explore the role of MCP-1 in the prediction, and also as a potential therapeutic target, in post-CPB organ failure.

REFERENCE(S). *Lotan D, Zilberman D, Dagan O,et al. Ann Thorac Surg 2001; 71:233-7

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PERIOPERATIVE DETERMINANTS FOR PROLONGED MECHANICAL VENTILATION FOLLOWING PULMONARY END-ARTERECTOMY

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INTRODUCTION. Pulmonary endartectomy is a surgical therapy for patients suffering from pulmonary hypertension due to chronic pulmonary embolism. Patients are considered candidate for surgery if they have surgically accessible occlusive thrombi and if despite optimal medical treatment, right ventricular dysfunction and invalidating dyspnoe persists. Pulmonary endarterectomy is performed with extra corporeal circulation (ECC) and intermittent deep hypothermic circulatory arrest (DHCA). We studied whether the variables ECC time, DHCA time, APACHE-II, postoperative blood loss and pO2/FiO2 ratio in the first 24 hours were related to prolonged mechanical ventilation (MV).

METHODS. A retrospective cohort study of 22 consecutive patients who underwent pulmonary endarterectomy from April 1996 to November 2002 in the St. Antonius hospital in Nieuwegein. The T-test or the Mann Whitney U test (two tailed) was used to compare groups.

RESULTS. Mean age was 48 years (sd: 15); all patients were preoperative in NYHA class 3 or 4. Median mechanical ventilation duration was 1,5 days (IQR 1-4). Table 1 illustrates mechanical ventilation parameters in two groups splitted at the 75 percentile of mechanical ventilation duration. The pO2/FiO2 ratio<200 in the first and the second twelve hours after surgery was significantly related to longer ventilation duration: median 51,5 hours vs. 20 hours ($p= 0,025$, Mann Whitney U test).

TABLE 1.

	Ventilation < 102 hours	Ventilation =/> 102 hours	P value	Test
ECC	194.4 min (mean)	311.2 min (mean)	0.004	T- test
DHCA	47.65 min (mean)	63 min (mean)	ns	T- test
APACHE	18 (mean)	22 (mean)	0.039	T- test
Postoperative Blood loss	730 ml (median)	1950 ml (median)	0.014	Mann Whitney U test
ICU-LOS	91.5 hours (median)	787.5 hours (median)	0.002	Mann Whitney U test

CONCLUSION. Results from our study suggest that a longer extracorporeal circulation time, a higher APACHE-II score, a pO2/FiO2 ratio<200 in the first 24 hours and more postoperative blood loss were related to a prolonged postoperative mechanical ventilation duration.

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EARLY THROMBOCYTOPENIA AFTER CARDIOPULMONARY BYPASS SURGERY

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INTRODUCTION. Early thrombocytopenia occurs frequently in patients submitted to cardiopulmonary bypass. However, antibodies to heparin platelet factor 4 have been reported in 25% of cardiac surgical patients and a 0.75% incidence of heparin-induced thrombocytopenia (HIT) has been reported. Before cardiac surgery, the incidence of heparin antiplatelet antibodies has been reported to be from 1% to 19% indicative of previous exposure to heparin during angiography or during hospitalization. These patients show a greater risk of developing HIT after the surgery(1). The aim of this study is to identify those patients with clinical suspicion of HIT in the first 24 h after surgery.

METHODS. Observational study, performed in the period between jan/01 to dec/31/2004. Were included all patients submitted to cardiopulmonary bypass surgery and the nadir platelet count in the first 24 hours of ICU < 150.000 cel/mm3. We considered six or more points of the „Four T´s" Score to the clinical suspicion of HIT(1).

RESULTS. Were studied 85 patients with mean age of 62.7±10.5 years and 48/85(56,5%) were male. The mean value of APACHE II and SOFA scores were 15.9±4.3 and 6.4±2.7, respectively. The comparison between the patients with thrombocytopenia (Group I, n=49) and those with clinical suspicion of HIT (Group II, n=36) is shown in table 1:

TABLE 1.

Comparison between the patients with thrombocytopenia and suspicion of HIT

	Age (years)	APACHE II	SOFA	Platelet nadir x1000	Thrombotic events (%)	Lenght of Stay in ICU	Hospital mortality
Group I	62,1±12,4	15,9±5,2	6,1±2,1	103.2±27,7	0	4,6±3,2 d	12,2
Group II	62,3±8,9	15,9±4,3	6,8±2,3	86,9±32,7	30,5	6,6±6,1 d	33,3
p value	NS	NS	NS	0,01	<0,001	0,05	0,03

CONCLUSION. The clinical suspicion of HIT in the early period after cardiopulmonary bypass surgery is associated with high rates of morbi-mortality, apart of the simmilar severity scores on study inclusion. Strategies to identify those patients with greater risk and to establish adequate treatment must be part of the management of this group of patients.

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SERUM CREATININE IN THE PATIENTS WITH MECHANICAL SUPPORT AS A BRIDGE TO HEART TRANSPLANTATION

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INTRODUCTION. Mechanical circulatory support is an important adjunct to the management of the end-stage heart failure patients, and is the standard of care for most potential heart transplant patients with life-threatening congestive heart failure refractory to conventional therapy. Proper selection of patients who would derive the most benefit from this support is essential. Severe renal dysfunction was shown to be one of the most significant risk factors for mortality, and thus low survival rate to heart transplantation in these patients.

METHODS. We retrospectively studied 11 consecutive adult heart transplant candidates (April 2003 to December 2004) with average age 52 years (range 28–61 years) who underwent implantation of biventricular assist device (VAD) as a bridge to heart transplantation. Serum creatinine levels were documented on the day before the implantation of VAD, and on the first, second, third and the fifth day after surgery. The need for CVVH after surgery and the length of this therapy were recorded. Survival rate to transplantation was evaluated with regard to preimplantation serum creatinine levels and CVVH use after VAD implantation. P values < 0.05 were considered significant.

RESULTS. Baseline serum creatinine level (mean±SD) was 193.7±87.6 umol/l. Serum creatinine levels after VAD implantation gradually decreased: on the first postoperative day serum creatinine level was 184.8±74.8, on second day 170.4±87.3, on third day 136.3±41.1, and on the fifth day 101.2±21.4 umol/l. Three patients (27%) needed CVVH which was started in all cases on the second day after surgery and lasted for 13±5.3 days. Two patients (18.2%) died before transplantation without CVVH use. Nine patients (81.8%) survived to transplantation. No association between baseline serum creatinine levels or the need for CVVH after surgery and survival to heart transplantation was found (p > 0.05).

CONCLUSION. Serum creatinine levels progressively decreased during five days after VAD implantation. It suggested mainly prerenal impairment of renal function which improved with restoration of cardiac output provided by VAD. Baseline serum creatinine levels and CVVH therapy after VAD implantation were not associated with survival to heart transplantation.

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ARE ELDERLY PATIENT AT RISK OF DELAYED EXTUBATION AFTER CORONARY SURGERY?

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INTRODUCTION. Early extubation is now widely used in cardiac surgery. Increased age is one of the main factor associated with a prolonged ventilation [1]. The aim of this study was to compared length of mechanical ventilation (MV) after coronary surgery in patients over 80 years and in patients between 60 and 70 years.

METHODS. 88 consecutive patients over 80 years (Group (Gr) 1) who underwent cornary surgery between 1996 et 2002 were retrospectively compared with a Gr of younger patients (165 patients, Gr 2, 60 to 70 years old) operated during the same period. For each elderly patient, 2 youger patients were randomly matched on sex, use of CPB, emergency, ventricular function, operative period (96-10/99 or 11/99-02)and history of COPD, stroke or arteriopathy, Statistical analysis was performed with Chi-square and t test and logistic regression; results are expressed as mean ± SD.

RESULTS. Age over 80 years was not associated with a prolonged period of MV either in univariate or multivariate analysis.

TABLE 1.

	Gr 1	Gr 2	p
Age (years)	83 ± 2	66 ± 3	<0.0001
Sex female	30 %	29 %	ns
EF (%)	60 ± 15	63 ± 14	ns
EuroSCORE	7.3 ± 2.1	3.4 ± 1.9	<0.0001
ICU > 2 days	19 %	9 %	0.005
MV (h)	6.8 ± 10.5	10.3 ± 50.5	ns
MV > 6 h	24 %	18 %	ns
Mortality	2.3 %	1.2 %	ns

CONCLUSION. Early extubation with a low mortality rate is possible after coronary surgery. However, length of stay in ICU is prolonged.

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USE OF LEVOSIMENDAN IN PATIENTS WITH PROPERATIVE LOW EJECTION FRACTION UNDERGOING CARDIAC SURGERY

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INTRODUCTION. the aim of the study was to assess the safety and efficacy of levosimendans prophylactic use in patients with preoperative low ejection fraction undergoing cardiac surgery.

METHODS. 30 consecutive patients with preoperative ejection fraction lower than 30% undergoing cardiac surgery, were enrolled in this study.All patients received a pulmonary artery catether preoperatively.All postoperative complications were recorded.Levosimendan was infused with a bolus of 12 mcg/kg immediately after the aortic clamp removal in the first 10 patients. In the others 20 patients levosimendan was infused without any bolus immediately after anesthesia induction at 0.1 mcg/kg/min.All data are reported as mean ± standard deviation. Continuous variables were evaluated by means of Students t test. Categorical data were analyzed by χ^2 test.In order to evaluate the real impact of levosimendan on the morbility and mortality we have identified a cutoff value of preoperative Euroscore using a ROC curve.

RESULTS. The mean preoperative Euroscore was 10.60 ± 4.29(predicted mortality 24.49 ± 22.61%). The mean preoperative ejection fraction was 26.5 ± 3.70%. 19 patients (63.63%) were in IV NYHA class.19 interventions were isolated CABG, 6 interventions CABG plus associated procedures, 5 valvular plasty or replacement.4 patients died (13.3%), 3 patients needed renal replacement therapy, 1 had permanent neurological damage.6 patients had IABP support, 17 patients needed major inotropic support (adrenaline > 0.05 mcg/kg/min).24 patients needed more than 24 hours of mechanical ventilation.Using the Euroscore cutoff value of 15 (specificity 100%-sensibility 75%) we have selected 27 patients with a mean euroscore of 9.52 ± 2.84 (predicted mortality of 17.97 ± 12.00%). Among this group we had only 1 dead patient (3.3%). The difference between predicted and observed mortality was statistically significative. (p<0.01)

CONCLUSION. The Levosimendan use in high risk cardiac patients seems to be safe and able to reduce the postoperative mortality, especially in the group of patients with a preoperative Euroscore within 15. The limitation of the study was the small number of patients and the wide distribution of preoperative euroscores.

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CANDIDEMIA IN PATIENTS UNDERGOING CABG SURGERY WITH AND WITHOUT CARDIOPULMONARY BYPASS

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INTRODUCTION. Off-pump coronary artery revascularization is a relatively new surgical technique in cardiac surgery with some documented advantages. On the other hand, candidemia remains a life-threatening infectious complication associated with high mortality rate.

METHODS. To determine the incidence of candidemia in adult patients undergoing coronary artery bypass grafting (CABG) surgery, with and without use of cardiopulmonary bypass (on- and off-pump), we performed an analysis of prospectively collected data from two cohorts.

RESULTS. The distributions of various variables including comorbidity and perioperative complications were similar in the two cohorts. In addition, the policy regarding the use of preventive antifungal treatment was the same (it was used only in a very small proportion of patients with several risk factors for Candida infections). Candidemia during hospitalization occurred in 15 of 3,363 and in 1 of 1,272 consecutive patients undergoing CABG surgery with and without use of cardiopulmonary bypass (0.45% versus 0.08% respectively, p=0.057).

CONCLUSION. We found a lower incidence of candidemia in patients undergoing off-pump myocardial revascularization compared to those undergoing coronary artery bypass grafting surgery with use of cardiopulmonary bypass.

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INFLUENCE OF THE AMINES ON BNP MEASURED IN PATIENTS UNDERGOING CARDIAC SURGERY

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INTRODUCTION. The prognostic and therapeutic use of B-type natriuretic peptide (BNP) levels in the postoperative (PO) management of cardiac surgery (CS) has been frequently assessed. The objective this study is correlate the BNP levels measured during the PO period of CS with the use of vasoactive amines (VA) in the first PO hour (PO1H).

METHODS. Prospective study with a classic cohort of 77 patients (pts) undergoing CS and consecutively selected between August/2003 and January/2005. Their mean age was 66.9±9.89 years, 22 (28.5%) were females, and the mean Euroscore was 4.26. The BNP level was measured in the preoperative period (BNPPre), and in the first (BNP1) and sixth (BNP6) PO hours. Hemodynamic and laboratory variables were recorded. The BNP level was quantitatively measured by use of immunofluorescence (Biosite Triage BNP Test). Patients receiving VA [(dobutamine (DBT) and/or noradrenaline (NAD)] at any dosage in the first PO hour were assessed and the use of VA was correlated with the BNP1 and BNP6 levels. The results underwent statistical analysis by using the Mann-Whitney test.

RESULTS. In our sample, 22 pts received VA in the PO1H as follows: 7 pts, NAD + DBT; 12 pts, NAD; and 3 pts, DBT. A significant correlation was observed between the use of DBT and the BNPPre (p = 0.004), BNP1 (0.024), and BNP6 (0.05) levels. In the population studied, the use of NAD did not correlate with the BNP levels. The DBT group had greater mean BNPPre, BNP1, and BNP6 levels than those in the NAD group (790x159, 1004x243, and 609x203pg/dL, respectively).

CONCLUSION. Patients using DBT had greater BNP levels than those receiving only NAD. This may correlate with a worse degree of ventricular dysfunction among those pts.

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FREQUENCY, RISK FACTORS AND OUTCOME OF HYPERLACTATEMIA AFTER CARDIAC SURGERY

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INTRODUCTION. Hyperlactatemia (HL) is common after cardiac surgery (CS), it is an indicator of systemic hypoperfusion and tissue hypoxia. It could identify patients who have the potential to further deteriorate after CS.
Objective: To determine the respective frequencies, risk factors and outcome of hyperlactatemia on ICU admission (HL0h), six hours (HL6h) after surgery and on day 1 (HL24h)

METHODS. Prospective, descriptive study with 156 consecutive patients (p) undergoing cardiopulmonary bypass (CPB) for elective cardiac surgery from August 1th 2004 to January 31th 2005. Arterial lactate concentrations were measured at ICU admission, 6 h and 24 h after surgery. Hiperlactatemia was defined as an arterial lactatemia >3mmol/l. We analysed preoperative factors (cardiovascular risk factors, severity scores,...), intraoperative factors (type of operation, CBP duration (CBPd), aortic cross-clamp duration (ACCd),...) and ICU evolution (complications: type of inotropics and hours, ventricular failure, ALI/SDRA, neurologic complication, mechanical ventilation duration (MVd), length of stay and mortality. Statistic analysis with SPSS version 11.01. Significant "p" if < 0.05

RESULTS. We collected 156 p (57 % male), mean age 66±13 years old, mean Euroscore 5.5±2.3. 60% of p. had arterial hypertension, 27.5% had diabetes, 6% had moderate-severe left ventricular dysfunction. 49 p (31.4%) had HL0h; 30 p (19.2%), HL6h; and 15 p (9.6%), HL24h. HL was associated with ICU length of stay. HL0h and HL6h were associated with low cardiac output. ICU acquired HL was associated with longer administration of inotropic/vasopressor agents and longer mechanical ventilation duration. Association between acute renal failure and HL6h were statistically significant (p 0.036). The others major postoperative complications (except acute renal failure) and the duration of mechanical ventilation (MV), hospital length of stay and mortality weren't associated with HL. Two patients died in ICU

CONCLUSION. HL is frequent after cardiac surgery and is able to identify a subpopulation of patients at higher postoperative risk with worse initial evolution after cardiac surgery

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POST OPERATIVE JAUNDICE AFTER CARDIAC SURGERY

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INTRODUCTION. The study aimed to investigate the incidence,the determinants,the significance and morbidity of post-operative jaundice in cardiac surgery.

METHODS. 128 adult patients who were submitted to open heart surgery,were divided into three groups. 50 patients who underwent CABG(1),31 who were submitted to AVR(2)±CABG and 47 patients who underwent MVR(3)±CABG. Aspartate aminotransferase (AST),alanine aminotransferase (ALT),alkaline phosphatase (ALP),gammaglutamyltranspeptidase (γGT),both types of bilirubin (bili) were determined at admission,24 hours post operation and there after according to clinical evolution.

RESULTS. Hyperbilirubinemia developed in 34 patients.The incidence was higher in patients submitted to MVR±CABG (bili: 4.39±3.61) than in CABG (bili: 1.86±2.71) and AVR±CABG (bili: 3.09±4.56). Elevated bilirubin was correlated with by-pass time (r:0.32 - p<0,001), aortic cross clamp time (r:0.33 - p<0,001),usage of IABP(4) (r:0.37 - p<0,0001),administration of inotropic agents (r:0.18 –p<0.04) and number of blood (r:0.239 – p<0.008) and plasma transfusions (r:0.30 – p<0.001).There was also difference between the morbidity of patients who developed low cardiac output syndrome and those submitted for replacement of multiple valves.Multivariate analysis identified that the aortic cross clamp time,the usage of IABP and the number of plasma tranfusions were independent determinants of the elevated bilirubin. Post-operative jaundice results mainly from an increase in conjugated bilirubin and is associated with higher mortality, especially for patients in whom highest post-operative total bilirubin occurred late after operation.

CONCLUSION. The type of operation including the specific tecnique during the performance of mitral valve replacement, a possible pre-operative hepatic dysfunction due to valvular stenosis and the decreased hepatic flow seem to determine incidence of post-operative jaundice.

REFERENCE(S). 1: CABG: Coronary Artery By-pass Grafting. 2: AVR: Aortic Valve Replacement. 3: MVR: Mitral Valve Replacement. 4: IABP: Intra-Aortic Balloon Pump.

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ATRIAL FIBRILLATION AFTER CARDIAC SURGERY: PREDICTOR VARIABLES AND ICU LENGHT OF STAY

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INTRODUCTION. Atrial fibrillation (AF) is the most common arrhythmia after cardiac surgery (CS) and administration of prophylactic magnesium (mg) reduces the incidence of this arrhytmia. The objective was to study variables associated with postoperative AF after CS during ICU stay that can identify patients at risk for AF.

METHODS. Retrospective study of 480 (male 68%) patients undergoing CS and receiving prophylactic mg. Patients with previous AF or thyroid disease were excluded. Associations between predictor variables* and postoperative AF were identified to predict AF risk. Univariate analysis and logistic regression analysis were done.

RESULTS. 82 patients (17%) developed AF after CS. Postoperative AF was associated with increased ICU lenght of stay (median; interquartile range: 3; 3-5 days) compared with LOS of non-AF patients (2; 2-5 days). Risk factors associated with AF were: advanced age (> or equal 70 years old) (odds ratio[OR] 2.13; 95% confidence interval [CI] 1.28-3.52); valve surgery (OR 1.61; 95% CI 0.9-2.88); hypermagnesemia (plasma mg >3 mg/dL) (OR 3.02; 95% CI 1.47-6.21); history of congestive heart failure (OR 1.78; 95% CI 1.00-3.15). Incidence of postoperative AF in valve surgery (24%) was significantly higher (p <0.0001) than in coronary bypass graft (CABG) surgery (10%). Hypermagnesemia was more present in patients with valve surgery (84%) than in CABG surgery (57%).

CONCLUSION. Our findings suggest that postoperative AF after CS is associated with increased ICU lenght of stay. Common risk factors for AF were identified. We believe hypermagnesemia is a confounding variable.

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CARDIAC SURGERY IN ELDERLY PATIENTS

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INTRODUCTION. The number of elderly high risk cardiac surgery patients has increased lately.
Objective: To evaluate incidence and outcome of elderly patients submitted to cardiac surgery.

METHODS. Methods: we analyse patients older than 74 years admitted in our ICU for a postoperative cardiac control, since November-00 to December-04.
We assess: type of surgery, cardiopulmonary bypass time (CPB), crossclamping time, time of mechanical ventilation, most common complications (perioperative AMI, excessive bleeding, reintervention, reintubation, acute renal failure, intestinal ischaemia, infections, definitive pacemaker), length hospital and ICU stay (LOS), readmissions, and the mortality.

RESULTS. Results: 362 patients were included from a total of 1911 (18.94%).
Type of surgery: coronary 123 (33.97%), valvular 158 (43.64%), mixed 61 (16.85%), and others 19 (5.24%). The mean CPB time was 94 min, crossclamping 63 min and mechanical ventilation 41.3 hours. 11 readmissions have been registered (3.03%).
Complications: 18 cases (4.97%) excessive bleeding, 16 (4.41%) reintervention, 11 (3.03%) perioperative AMI, 6 (1.65%) definitive pacemaker, 5 (1.38%) cardiac arrest with CPR, 7 (1.93%) cerebro-vascular accident (CVA), 6 (1.65%) intestinal ischaemia, 5 (1.38%) cardiac tamponade. Most common complications: 82 cases (22.6%) atrial fibrillation, 66 (18.23%) renal failure, 40 (11.04%) cardiac failure. The hospital LOS was 15.02 days. The ICU LOS was 5.11 days, like 5 days than total patients. Expected mortality (EuroSCORE) in elderly group was 12.7% (expected mortality in all pacients 7.97%). 26 elderly patients (7.28%) died during their hospital income (5.7% of mortality in all pacients).

CONCLUSION. Conclusion: 1- Almost a 20% of cardiac surgery patients had more than 74 years. 2-Valvular is the main type of cardiac surgery in this patients. 3- Hospital mortality in elderly patients was smaller than the expected. 4- The LOS in ICU in older patients has been similar than younger. 5- Most frequent complication were atrial fibrillation, renal failure and cardiac failure.

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INDOCYANINE GREEN PLASMA DISAPPEARANCE RATE IN CARDIAC SURGERY

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INTRODUCTION. Previous studies have demonstrated a good prognosis value of ICG-PDR (Indocyanine green Plasma Disappearance Rate) in critical ill patients (1,2). Normal value for adult healthy people is ICG-PDR > 18%/min. The objective is to assess the normal and prognosis ICG-PDR value in postoperative cardiac population.

METHODS. We used a Non-invasive liver function monitoring (LiMon, Pulsion Medical Systems, Germany) and the recommended dosage for ICG-PULSION (indocyanine green, 0'5 mg/Kg). 2 measurements were done, 12 hours (t-12) and 24 hours (t-24) after operation. Applied Kruskal-Wallis and Chi-square Tests.

RESULTS. We analyzed 103 patients. 76 had ICG-PDR > 18 (mean 29'6 ±11) in t-12 and 27 had ICG-PDR < 18 (mean 14 ±2'3). There were two deaths; one with ICG-PDR < 16 in t-12 who died in cardiogenic shock with intestinal ischemia, and the other with ICG-PDR > 18 in t-12 and t-24 who died because of a massive bleeding in the second day. Only 16 patients reminded with ICG-PDR < 18 in t-24. Their length of ICU stay (LOS) was 5'38 (±0'3) days. Mitral patients had worse ICG-PDR than coronary or aortic patients (p < 0'05).

TABLE 1.

t-12 measurements

	ICG-PDR > 18	ICG-PDR < 18	„p" value
EuroSCORE (num)	4.7 (3)	6.4 (3.6)	0.0316
LOS (days)	3.3 (2	4.4 (2)	0.0056
CPB time (min)	96 (33)	114 (62)	0.7340
Crossclamping (min)	63 (29)	80 (39)	0.0358

EuroSCORE: European System for Cardiac Operative Risk Evaluation (3)

CONCLUSION. 1. Nearly a 1/3 of patients had ICG-PDR < 18%/min in t-12. 2. Patients with ICG-PDR < 18%/min had worse EuroSCORE, had long LOS and had longer crossclamping. 3. ICG-PDR was worse in mitral patients. 4. Most of the patients normalized ICG-PDR in t-24.

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