Poster Sessions
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HIGH FREQUENCY PERCUSSIVE VENTILATION COULD REDUCE THE INFLAMMATORY RESPONSE IN TRAUMA PATIENTS

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INTRODUCTION. High frequency percussive ventilation (HFPV) is a recent ventilatory mode delivered by a Volumetric Diffusive Respirator (VDR – Percussionnaire Corporation) which combines conventional ventilatory cycles with high frequency percussions. HFPV has been described to improve gas exchanges after inhalation injury and to reduce pulmonary infections in burn patients with smoke injury (1, 2).

METHODS. We decided to compare the alveolar inflammatory response in 8 trauma patients ventilated with HFPV (HFPV group – VDR 4) compared with 6 patients under conventional mechanical ventilation (CMV group – Siemens 300). Bronchoscopy with bronchoalveolar lavage was performed for white blood cell count, protein, interleukin (IL) 1, IL 6, IL 8 and IL 10 and analyzed early (<08 hours after trauma) and late (48 hours after injury).

RESULTS. There was no difference between the two groups relative to sex, age, injury and initial PaO_2/FiO_2. There were no major outcome differences between HFPV and CMV groups relative to pneumonia, death or for oxygenation after 5 days. Both high blood cell count and protein were higher in CMV group suggesting a greater inflammatory response: neutrophils were also significantly higher in this group. The inflammatory IL 1 and IL 6 were greater in CMV group, IL 8 was not significantly different in the two groups and the anti inflammatory IL 10 was lower in HFPV group .

CONCLUSION. This observation suggests that early institution of HFPV could reduce the inflammatory alveolar response in trauma patients. Further studies are necessary to confirm these results and to determine if HFPV could reduce the morbidity and mortality in this critically ill population.

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C-GMP COULD BE A BIOCHEMICAL MARKER OF NO INHALATION RESPONSE IN ARDS PATIENTS

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INTRODUCTION. Patients with ARDS respond in a non-homogeneous way to NO inhalation. About 30% of ARDS patients are NO non-responders, in terms of PaO_2 improvement, when inhaling NO. The aim of this study was to analyze some biochemical markers of NO metabolism as predictors of PaO_2 improvement with NO.

METHODS. We obtained blood samples in 13 patients with ARDS, before and after 1 hour of 5 ppm NO inhalation during two consecutive days after ARDS was diagnosed. We measured levels of nitrites/nitrates, 6-oxo-PGF1a and cyclic guanosine monophosphate (c-GMP). We also obtained systemic and pulmonary blood samples, and systemic and pulmonary pressures to determine gasometric and hemodynamic effects of NO inhalation. Response to inhaled NO was defined as an increase in PaO_2/FiO_2 at least higher than 20 % with respect to baseline.

RESULTS. Thirteen adult patients with ARDS (6 female and 7 male) with mean age 56 ± 17 years, mean SAPS II 32.7, mean LIS 3.1. Nine patients died (mortality 69.2 %). Six were *responders* to NO inhalation the first study day and 8 patients the second study day. We obtained 52 blood samples from 13 patients during two consecutive days. The level of nitrites/nitrates were 1.52 ± 1.51 pmol/ml in *non-responders* and 1.96 ± 1.36 pmol/ml in *responders* (p NS), the level of 6-oxo-PGF1a 0.208 ± 0.093 pmol/ml in *non-responders* and 0.193 ± 0.043 pmol/ml in *responders* (p NS) and levels of c-GMP in *non-responders* 0.107 ± 0.093 pmol/ml and 0.063 ± 0.031 pmol/ml in *responders* (p 0.025).

CONCLUSION. The level of c-GMP could be a marker of oxygenation response to NO inhalation. Granted with FIS 00/0618.

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SURFACTANT PROTEIN-A AND ELASTASE IN BRONCHOALVEOLAR LAVAGE DURING MECHANICALVENTILATION

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INTRODUCTION. In the presence of phospholipids, SP-A plays a role in enhanced secretion and recycling of the surfactant,and it binds with alveolar macrophages, influenza virus indicating its involvement in the host immune defense. In this study, we wanted to evaluate the influence of Mechanicalventiration on concentration of the SP-A and Elastase in BAL and serum.

METHODS. 10 patients aged between 18~65 without smoking and steroids, who were expected to require sedation or analgesia for at least 24 hours of ventiration in intensive care. Mechanicalventiration were maintained at 30~35 mmHg $PaCO_2$, 15~20 cmH_2O airway pressure. The middle lobe was lavaged with up to 240 ml normal saline at 37degree with gentle aspiration after each 30ml aliquot. Lavage fluids cells were pellet at 1000 rpn, resuspende in medium 199, and counted under direct microscopy. Total protein, albumin, SP-A, Mucin and elastase in BAL were measured at just after intubations, 1hour, and 3 hours during mechanical ventilation. Serum elastase, and WBC in blood sample were measured at the same time.

RESULTS. Total protein concentration in BAL increased significantly and led to peak at 1689±323 mg/ml 1hour after intubations . Mucin concentration was highest at 1hour after ventilation (155.75±31.6mg/ml). BAL SP-A concentration ratio increased about 20 times after 1hour ventilation. Compare to 100mg/ml total protein, the ratio was 2.16±1.14 in 1hour later, and 4.31±2.8 in 3hours after ventilation.The change of BAL WBC level led to peak in after 1hour ventilation, but blood WBC level led to peak in 3hours later. For elastase level both peak were 3hours later in BAL and Blood.In the caller components of BAL, the neutrophyl cells were dominant in 1hour after intubation, but 3hours after ventilation, mast cells with phagocyted mucine and dusts were dominant.

	Just after intubations	1hour	3hours
SP-A ratio	1	20.15±16.82	17.30±12.81
SP-A ratio/100 mg/ml TP	1	2.16±1.14	4.31±2.8
	1hour	3hours	
WBC (BAL) /ml	89.3±98.6	179.0±106.6	171.82±107.9
WBC (Blood) /ml	5850±1793.5	6775±1813.6	11050.0±2053.5
Elastase (BAL) mg/L	311.4±392.7	1131.6±941.3	1716.0±1318.0
Elastase (Blood) mg/L	125.0±33.5	120.5±27.5	228.8±36.2

CONCLUSION. This study demonstrated that the level of SP-A and elastase in the BAL increased significantly within 1 hour during mechanical ventilation. Suggesting that both of SP-A and elastase play a role in the bronchoalveoler defense system.

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ROLE OF P38 MITOGEN-ACTIVATED PROTEIN KINASE IN THE LUNG INJURY INDUCED BY MECHANICAL VENTILATION

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INTRODUCTION. The purpose of this study was to investigate the role of p38 mitogen-activated protein kinase £¯p38 MAPK£© in the lung injury induced by mechanical ventilation.

METHODS. Fifteen healthy small pigs with continuous mechanical ventilation were randomly divided into group A (VT=16 ml/kg£¬PEEP=0), group B (VT=6 ml/kg, PEEP=16cmH2O) and group C (VT=6 ml/kg, PEEP=8cmH_2O). Immuno-histochemistry and western blot were respectively used to evaluate the expression of ICAM-1 protein and the phosphorylation of p38 MAPK levels in lung tissues 3 hours following ventilation£¬ the pulmonary histopathological change was observed as well.

RESULTS. There is a significant histological change in group A and B, whereas no significant alteration in group C. The expression of ICAM-1 protein in lung was positive in group A and B, while negative in group C. The expression level of phosphorylated p38 MAPK is significant higher in group A and B compared with that in group C ($P<0.05$), while no significant difference in the expression level of non-phosphorylated p38 MAPK among the three groups.

CONCLUSION. Acute lung injury can be induced by both high tide volume and low tide volume plus high PEEP mechanical ventilation, p38 MAPK may mediate the inflammation response in the lung injury.

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PROGNOSTIC SIGNIFICANCE OF THE HEPATOPULMONARY SYNDROME IN LIVER CIRRHOSIS

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INTRODUCTION. The hepatopulmonary syndrome (HPS) is defined as the triad of liver disease, pulmonary gas exchange abnormalities leading to arterial deoxygenation, and widespread pulmonary vascular dilatation, detected by contrast echocardiography. Mortality of patients with HPS is considered to be high, but no prospective study exists up to date.

METHODS. 111 patients with liver cirrhosis (Child-Pugh class A=30, B=32, C=49) were included in the study, HPS was defined by 1.) presence of chronic liver disease, 2.) alveolar-arterial difference for PO_2>age-related threshold value, 3.) intrapulmonary vascular dilatation, detected by contrast echocardiography.

RESULTS. Patients with HPS (n=27; 24%) had a significantly higher mortality (median survival 10.6 months) compared to those without HPS (median survival 40.8 months; P <0.05). Even if adjusted for the Child-Pugh classification, the most common classification for severity and prognosis in patients with cirrhosis, patients with HPS had a worse prognosis (Child-Pugh class C: with HPS (n=16) median survival 3.5 months; without HPS (n=33) median survival 14.7 months, p<0.05). In multivariate analysis, HPS was an independent predictor of survival beside age, total bilirubin, serum-creatinine and hepatic encephalopathy.

	Regression coefficient (b)	p Coefficient
Age	0.045634	0.000879
Bilirubin	0.067775	0.000151
Serum-Creatinine	0.744793	0.000305
HPS	0.744793	0.008933
Hepatic encephalopathy	0.429435	0.015006

CONCLUSION. Patients with advanced liver cirrhosis and HPS have a bad prognosis and should be evaluated for liver transplantation as early as possible.

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ENDOTHELIN-1 IN PATIENTS WITH THE HEPATOPULMONARY SYNDROME

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INTRODUCTION. The hepatopulmonary syndrome (HPS) is defined as the triad of liver disease, pulmonary gas exchange abnormalities leading to arterial deoxygenation, and widespread pulmonary vascular dilatation. Animal models of HPS showed that enhanced hepatic endothelin-1 (ET-1) production correlate with both pulmonary nitric oxide (NO) synthase levels and gas exchange.(1)

METHODS. Plasma ET-1 values were measured in 97 patients with liver cirrhosis (Child-Pugh class A=29, B=26, C=42). HPS was defined by 1.) presence of chronic liver disease, 2.) alveolar-arterial difference for PO_2>age-related threshold value, 3.) intrapulmonary vascular dilatation, detected by contrast echocardiography.

RESULTS. Mean plasma ET-1 was significantly higher in the 12 patients with HPS (70.5± 47.1 pmol/L) compared with the 85 patients without HPS (43±36 pmol/L; p < 0.05); normal value of plasma ET-1=1.3±0.4 pmol/L. In the patients with intrapulmonary vasodilation, detected by contrast echocardiography (n=26), ET-1 correlated significantly with PaO_2 (r=-0.52, p=0.006).

CONCLUSION. Our study proves previous data derived by animal studies that ET-1 is significantly elevated in HPS and correlates with gas exchange. Thus, elevated ET-1 produced by the injured liver may contribute to the pathogenesis of HPS by modulating NO-production and inducing intrapulmonary vasodilation.

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BRONCHO-ALVEOLAR LAVAGE (BAL) AS A METHOD FOR DIAGNOSTICS OF LUNG INJURIES.

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INTRODUCTION. Lung diffusion infiltrates in prolonged mechanically ventilation patients may be caused both by VAP and ARDS. BAL may be used as a method diagnostics of lung injuries.

METHODS. Eighty-two patients of general ICU with MOF (APACHE 11 more than 18) were on mechanically ventilation more than three days. We performed mini BAL according to European BAL Task group Protocol (1992). Total protein level (mg/ml), total cells count ($x10^6$) and PMN (%) in BAL fluid were measured. All the patients were divided into two groups according to the results of testing of BAL fluid. The permission of Ethics Committee was received before.

RESULTS. Group 1 (n=30) patients showed an increase of protein level (9,1±1,2) with slight increase of citosis (100±12,8 cells $x10^6$) and number of PMN (30±5,6%). These patients were diagnosed as having ARDS. The colonization was up to 10^4 cfu/ml. Group 11 (n=50) patients were found to have higher citosis up to 230±13,3 (p<0,05) dye to dominance of PMN in BAL fluid. Protein level was lower than in group 1 (p<0,05). The diagnosis of this group was WAP, which was proved by increasing colonization of 10^5 cfu/ml.

CONCLUSION. To exactly find out the nature of lung injury it is useful to apply the BAL fluid analysis. ARDS is characterized by increasing the total protein level, while VAP is accompanied by citosis with high colonization.

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PROCALCITONIN (PCT) AS MARKER OF INFECTIONS IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES AND ACUTE RESPIRATORY FAILURE

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INTRODUCTION. PCT is a new marker for the identification of systemic infection (1). However it is known a little about application of PCT for diagnostics of infectious and non-infectious complications in patients (pts) with hematological malignancies, including leukopenic pts. The aim of the study was to evaluate the value of PCT as a marker for diagnosis infectious inflammation in pts with hematological malignancies.

METHODS. We measured plasma PCT levels using PCT-Q immunochromatografic test (Brams Diagnostica GmbH) assay in 30 pts with hematological malignancies and acute respiratory failure (ARF) – PaO_2/FiO_2, 241.8±20.6. The results were expressed as mean values with standard error of the mean.

RESULTS. At 90% pts with bacterial pneumonia the concentration of PCT was higher 2 ng/ml, at 5 of 6 pts with a level of PCT is >10 ng/ml was bacteraemia. In pts with fungal pneumonia the concentration PCT did not exceed 2 ng/ml, only 1 pts had PCT 2-10 ng/ml, but at him was accompanying bacterial infection. Pneumocystic and CMV pneumonia in 70% associated with a level of PCT < 2 ng/ml, increase of PCT >10 ng/ml in 2 cases it is possible to explain by a combination CMV infection with bacterial infection (S. Viridans, S. epidermidis). The level of PCT did not exceed 2-10 ng/ml at ATRA syndrome and cytolitic syndrome. The most diverses in PCT concentrations were at pulmonary leukemic infiltration. There were all levels of PCT at this form of lung injury. There was linear correlation between PCT and XIIa-depended fibrinolysis (r=+0.66; p<0.01), PCT and APACHE II (r=+0.44; p<0.01). There was not correlation between PCT and PaO_2/FiO_2, white blood cells (WBC), plasma concentrations of TNF and IL-6.

	<0.5 ng/ml (n=8)	0.5-2 ng/ml (n=7)	2-10 ng/ml (n=8)	>10 ng/ml (n=7)
Bacterial pathogens (n=10)	1		3	6
Fungal pathogens (n=6)	2	3	1	
Cytolytic and ATRA syndromes (n=6)	2	2	2	
Cytolytic and ATRA syndromes (n=6)	1	2	1	2
P. carinii, cytomegalovirus (CMV) (n=13)	4	5	2	2

Number of pts with different PCT levels and different reasons of ARF (*Pts could have simultaneously a several reasons of ARF)

CONCLUSION. In pts with hematological malignancies the level of PCT raises significant at bacterial pneumonia and leukemic lung infiltrations, in the other cases its increase is expressed much less. Changes of a level of PCT does not depend on WBC.

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DESATURATION AND DIABETES – A CAUSE FOR CONCERN?

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INTRODUCTION. Coronary disease is prevalent in diabetic patients resulting in a frequency of invasive cardiac procedures four times that of non-diabetics. After cardiac surgery diabetics have twice the mortality and morbidity in early and late phases after operation. The reasons for this increased risk are poorly understood.

Diabetics exhibit complex abnormalities of lung structure and of the control of the cardio-respiratory system. These include pulmonary micro-vascular disease, autonomic neuropathy associated with an increased cardiovascular instability, an increased incidence of central and obstructive sleep apnoea and a reduced response to hypercapnia. This study was undertaken to determine whether at risk diabetic patients could be identified pre-operatively.

METHODS. 14 patients awaiting urgent cardiac surgical re-vascularisation were studied with measurement of: spirometry; percentage increase in transfer factor from sitting to lying position (TF) as an indicator of micro-vascular lung disease; overnight oximetry on air; and 24hour holter monitoring

RESULTS. Median and range

	Body Mass Index (BMI)	HBA1C	FEV1	FVC	TF	*Desaturations/hour	VentrICUlar Ectopics (VEs)/hour
Non Diabetics (n=4)	26.9 (24.3-28.0)	6.4 (5.5-6.5)	2.4 (0.9-3.1)	3.3 (1.3-4.3)	21.5 (12-31)	3.2 (0-10.5)	8.9 (0.1-144)
Type II Diabetics (n=6)	25.6 (21.7-30.6)	8.0 (6.2-11.0)	2.2 (1.7-2.4)	3.1 (2.3-3.4)	10.5 (5-19)	13.5 (7.6-44.6)	0.5 (0-82.2)
Type I Diabetics (n=4)	28.4 (26.3-30.2)	7.1 (6.6-7.8)	2.2 (1.6-2.3)	3.1 (2.6-4.1)	30.0 (20.0-32.0)	17.6 (0-41)	2.6 (1-39.8)

*Desaturations of >4% from baseline for >10 seconds

CONCLUSION. In these preliminary results, there is an increased frequency of nocturnal desaturation in diabetic patients, despite no difference in spirometry, TF or BMI. There appeared to be no association between desaturation frequency and VEs.

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RESPIRATORY FAILURE DUE TO THE PHRENIC NERVE INJURY AFTER CARDIAC SURGERY

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INTRODUCTION. Diaphragmatic dysfunction as a result of phrenic nerve injury (PNI) may follow cardiac operation. Several articles have suggested that it may induce postoperative atelectasis, dyspnea, and, even, the need for prolonged mechanical ventilation (1). The clinical relevance of this complication, however, is not well-understood.
METHODS. In this retrospective study we evaluated all patients admitted to the polyvalent intensive care unit (ICU) of a University teaching Hospital from 1998 to 2001, coming from ICU post-cardiac surgery (CS-ICU) of the same hospital and who had unexplained and prolonged diffICUlties in weaning from mechanical ventilation. The following general information was collected: age, SAPS II and SOFA on admission, causes of respiratory failure, number of days of mechanical ventilation (CS-ICU and ICU), length of stay CS-ICU and ICU (LOS), ICU and hospital mortality. We measured the maximal inspiratory pressure (MIP) in spontaneous breathing as an index of muscolar strength. Diagnosis of phrenic nerve paralysis was based on clinical presentation (inward movement of the abdomen during inspiration), low value of maximal inspiratory pressure in spontaneous breathing (MIP), chest radiography findings (diaphragmatic elevation), fluoroscopic examination of diaphragmatic motion. Data were analysed using Student's t test ($p<0.05$).
RESULTS. Eighteen patients with respiratory failure were studied. The mean age was 72±11; the overall SAPS II at admission was 40.3±15.2; the SOFA was 5.1±2.9. Clinical and radiological diagnosis of left phrenic nerve paralysis was confirmed for seven of them (38.8%). Others causes of respiratory failure were: pleuric effusion (6/18) (33.3%), pulmonary infiltrates (4/18) (22.2%) and tracheal stenosis due to malacia following prolonged intubation (1/18) (5.5%). No differences were found regarding age (74±2.9 vs 71±15, NS), SAPS II (42.5±9.7 vs 38.9±18.2, NS) and SOFA (6.1±3 vs 4.4±2.9, NS) between the patients with PNI and the others. The mean MIP value was lower in the patients with diaphragmatic dysfunction (34±12 vs 60.8±25.1,$p<0.05$). These patients had a longer period of mechanical ventilation (40.7±28.2 vs 18.9±23.2,$p<0.05$) and LOS (48.1±42.3 vs 33.9±20.6,$p<0.05$); they even had greater ICU mortality (14.2% vs 9%), but hospital mortality was similar (57.1% vs 54.5%).
CONCLUSION. We conclude that PNI is a complication even unrecognised or confused with infectious pathologies. Diagnosis is clinical and confirmation is with fluoroscopic examination; nevertheless the simple value of MIP, when it's low, can help in the confirmation of the diagnosis. Moreover PNI influence ICU and hospital mortality.
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ROLE OF ENDOGENOUS HISTAMINE ON THE PATHOGENESIS OF ENDOTOXIN-INDUCED ACUTE LUNG INJURY

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INTRODUCTION. Histamine is widely distributed in the lung. It increases in capillary permeability and the P-selectin expression on the vascular endothelial cell surfaces. We studied the role of endogenous histamine on the pathogenesis of endotoxin-induced acute lung injury (ALI) in rats.

METHODS. We instilled either normal saline (control group) or lipopolysaccharide (3mg/Kg, LPS group) to tracheas of Sprague-Dawley rats. H1-receptor blocker (mepyramine, 10 mg/Kg, H1RB group), H2-receptor blocker (ranitidine, 10mg/Kg, H2RB group), and H3-receptor blocker (thioperamide, 2 mg/Kg, H3RB group) were administered through vein or peritoneum along with intratracheal LPS. Statistical significance was accepted at $p<0.05$

RESULTS. Compared to control group, histamine level in bronchoalveolar lavage (BAL) fluid was significantly higher at 2 h after LPS instillation in LPS group. Protein concentration, PMN cell count in BAL fluid, and myeloperoxidase (MPO) activity in the lung tissues were significantly higher at 6 h after LPS instillation in LPS group. Serum histamine level was significantly higher at 2 h in H1RB-group, and significantly lower at 1 h in H3RB-group compared to LPS group. Protein concentration in BAL fluid showed no significant differences between the LPS treated groups with/without antihistamine co-treatment. However, PMN cell count in BAL fluid and MPO activity in lung tissue were significantly lower in H2RB-group compared to LPS-group.

CONCLUSION. Endogenous histamine might be involved in the recruitment of PMNs in LPS-induced ALI via H2 receptor. However, its role in ALI would not be significant in this model.

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EXTRAVASCULAR LUNG WATER MEASUREMENTS IN PATIENTS WITH ALI/ARDS

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INTRODUCTION. In patients with ALI/ARDS, the beneficial effects of fluid restriction (on arterial oxygenation and duration of mechanical ventilation and length of ICU stay) have to be balanced with the risk of worsening hemodynamics (ref. 1). The measurement of extravascular lung water (EVLW), now easily available at the bedside, could be helpful to deal with this issue. The aim of this study was to assess EVLW in patients with and without ALI/ARDS.

METHODS. Twenty six mechanically ventilated patients with severe sepsis in whom simultaneous measurement of EVLW, blood gases and chest radiographs were available have been selected for the study. EVLW was evaluated in triplicate by the single transpulmonary thermodilution technique (PiCCO, Pulsion Medical Systems, Munich, Germany). Two patients with evidence for left heart failure were excluded. 48 sets of measurements were available for analysis in 24 patients. Chest radiographs were analyzed independently by three of us. When discrepancies were observed (13/48 = 27 %) between the individual analysis, radiographs were re-analyzed for a consensual decision.

RESULTS. Bilateral pulmonary infiltrates were observed in 40 instances. The PaO_2/FiO_2 ratio ranged between 50 to 560 mmHg (mean 203±102 mmHg) and was less than 300 or 200 mmHg in 40 and 30 instances, respectively. A significant ($p<0.001$) but weak ($r2=0.28$) relationship was observed between the PaO_2/FiO_2 ratio and the EVLW. ALI/ARDS criteria were fulfilled in 37/48 (77%) instances. EVLW was significantly higher (11 ± 5 vs 6 ± 2, $p<0.01$) in the cases of ALI/ARDS. However, ALI/ARDS criteria (ALI, n=6; ARDS, n=5) were associated with a normal value (<=7 mL/kg) of EVLW in 11/37 (30%) instances.

CONCLUSION. Our findings 1) confirm the high interobserver variability of radiographic definition of ALI/ARDS (ref. 2) and the poor correlation between arterial oxygenation and EVLW, 2) demonstrate that some patients with ALI/ARDS criteria have no significant pulmonary edema. Therefore, EVLW measurement may help in decisions concerning the appropriateness of fluid restriction in patients with ALI/ARDS.

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THE EFFECT OF SURFACTANT ON THE APOPTOSIS OF NEUTROPHILS

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INTRODUCTION. The therapeutic effects of surfactant on the acute lung injury derive not only from its recruiting action on collapsed alveoli but also from its anti-inflammatory effects. Pro-apoptotic action on alveolar neutrophils can be one of the important anti-inflammatory mechanisms of surfactant.

METHODS. In in vitro study, human neutrophils were collected from healthy volunteers and equal number of neutrophils (1 * 10**6) was treated with LPS (10, 100, 1000 ng/ml), or with surfactant (10, 100, 1000 mcg/ml), or with combination of LPS (1000 ng/ml) and surfactant (10, 100, 1000 mcg/ml). After incubation for 24 hours, apoptosis of neutrophils was evaluated by Annexin V method. In in vivo study, after induction of acute lung injury by intra-tracheal instillation of LPS (5 mg/kg) in SD rats, either surfactant (30 mg/kg) or normal saline (5 ml/kg) was instilled into trachea. Twenty-four hour after LPS instillation, alveolar neutrophils were collected and apoptotic rate was evaluated by Annexin V method.

RESULTS. In in vitro study, LPS treatment resulted in the decrease of apoptosis of human peripheral blood neutrophils (control; 47.4∂5.0%, LPS10; 30.6∂10.8%, LPS100;27.5∂9.5%, LPS1000; 24.4∂7.7%). The addition of low to moderate doses of surfactant onto LPS resulted in the promotion of apoptosis (LPS1000+Sur10; 36.6∂11.3%, LPS1000+Sur100; 41.3∂11.2%). The high dose of surfactant per se decreased apoptosis (24.4∂7.7%) and augmented the anti-apoptotic effect of LPS (LPS1000+Sur1000; 19.8∂5.4%). In in vivo study, the apoptotic rate of alveolar neutrophils of surfactant-treated rats (1.38∂0.79%) was higher than that of normal saline-treated rats (0.65∂0.46%).

CONCLUSION. Surfactant promotes the apoptosis of human peripheral blood and rat alveolar neutrophils. Pro-apoptotic action on neutrophils can be one of the important anti-inflammatory mechanisms of surfactant.

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PULMONARY ENDOTHELIAL ACE DYSFUNCTION IN MECHANICALLY-VENTILATED PATIENTS

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INTRODUCTION. Early reduction of pulmonary capillary endothelium-bound (PCEB) angiotensin converting enzyme (ACE) activity, an index of pulmonary endothelial dysfunction occurs in acute lung injury (ALI) in animals and humans. In this study: i. we tested the hypothesis that mechanical ventilation (MV) per se, in the absence of ALI, might induce sub-clinical pulmonary endothelial injury, expressed as reduced PCEB-ACE activity, and ii. we attempted to define the pattern of such a potential reduction.

METHODS. PCEB-ACE activity expressed as transpulmonary substrate hydrolysis (v) and as the functional capillary surface area (FCSA) index A_{max}/K_m, was estimated by means of *indicator-dilution* techniques in 20 mechanically-ventilated, critically-ill patients. Three estimations were performed per patient, 48 hs apart each other. Nine subjects (8 men & 1 woman, 17-30 years old, Group I) had no ALI during the study, or at any other time-point prior to extubation; eleven subjects (8 men & 3 women, 11-75 years old, Group II) had or developed ALI during the study, and were on acute respiratory distress syndrome (ARDS) in at least one ACE activity estimation. Group I patients were ventilated with tidal volumes of 9-10 ml/Kg body weight.

RESULTS. There were no differences in MV days prior to 1st measurement between Groups I and II (2±0.2 vs 2.7±0.4, respectively). Logarithmic transformation of both PCEB-ACE activity parameters was performed to normalize data. Both parameters were higher in Group I than in Group II. Hydrolysis (v) decreased significantly with time (one-way ANOVA) in both groups, but in a later phase in Group I (3rd estimation) than in Group II (2nd estimation). An analysis performed using a mixed effects model revealed negative relationships of: (1) v with lung injury score (LIS) and time, and (2) A_{max}/K_m with LIS, in both groups. A second analysis was performed after adjusting for LIS, in order to exclude disease-related factors and investigate the effect of time (i.e. MV duration) only, on PCEB-ACE activity: The negative relationship of v with time was sustained in Group I (b=-0.18, p=0.05) but not in Group II (p=0.29) revealing a significant difference between the two groups (p= 0.011), and implying that v decreases were mostly related to time in Group I and to ALI/ARDS in Group II. Similarly, significantly different patterns in the A_{max}/K_m (i.e. FCSA) vs time relationships were noted between the two groups (p=0.002).

CONCLUSION. PCEB-ACE activity, a direct and quantifiable index of pulmonary capillary endothelial function, is reduced in patients on MV who have no ALI. This reduction: i. occurs later and it is slighter than the one observed in ALI/ARDS patients, and ii. probably denotes the presence of subtle endothelial injury associated with a ventilator-induced sub-clinical lung injury.

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SYSTEMIC AND PROLONGED LOW-DOSE THROMBOLYSIS IN THROMBOEMBOLIC DISEASE: A NEW THERAPEUTIC APPROACH?

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INTRODUCTION. Urokinase (Uk) systemic thrombolysis at the dose of 4000U/kg/h is a recognised therapy in case of severe thromboembolic event. However, patients (pts) may present some contraindications precluding thrombolytic use. In these pts, systemic prolonged low-dose thrombolysis (PLDT) could be an alternative therapeutic approach. We report herein on our experience of PLDT.

METHODS. Between 09/99 and 01/02, 11 pts (4 males, mean age: 48y.; range: 18-77) were admitted in our Intensive Care Unit for the treatment of 10 floating thrombus [right cardiac cavities: 5; inferior vena cava: 5] and 1 life-threatening pulmonary embolism [PE] by PLDT. Because of the bleeding risk secondary to catheter insertion or post-surgical period; or the risk of massive PE following the clots lysis, thrombolysis at usual recommended dosage was not administered. Uk infusion rate was progressively increased unless bleeding at the catheter insertion site commended the reduction to the previous Uk dosage.

RESULTS. In all cases, significant regression or disappearance of the clots was obtained at a median Uk dose of 1511 U/kg/h (Interquartile range (IQR): 1148-2164) and after a mean of 4.6 days, and thrombolysis was continued for a mean of 7 days (range:1-16days). No major complication was observed, especially no PE or significant bleeding. Adverse event was not encountered up to Uk 2000 U/kg/h. Thrombolytic activity was still present under low rate Uk infusion, as confirmed by the decrease in plasma plasminogen (mean ± SD: 98 ± 12 to 47 ± 15%) and antiplasmin (101±6,4 to 42 ± 6,7%) that we measured in 3 pt under a median Uk dose of 1046 U/kg/h (IQR: 880-2045).

CONCLUSION. Systemic prolonged low-dose thrombolysis could be an effective and safe therapeutic approach in pts suffering from severe thromboembolic disease when full dose thrombolysis is required but contraindicated.

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ELECTIVE MINI INVASIVE SURGICAL TRACHEOSTOMY. A NEW SIMPLE BEDSIDE PROCEDURE; PRELIMINARY REPORT

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INTRODUCTION. Tracheostomy is one of the oldest surgical procedures and in the past decades has become the method of choice in Intensive Care Unit (ICU) in the management of patient requiring long term mechanical ventilation (1).
The most recent articles comparing percutaneous and surgical tracheostomies techniques are not able to demonstrate a superiority of one of them in terms of feasibility or safety (2). Aim of this study is to present the new "mini invasive surgical tracheostomy technique in order to evaluate its complete efficacy in terms of safety and intraoperative and postoperative complications.

METHODS. 93 consecutively ICU patients requiring tracheostomy were undertaken to the new "mini invasive" surgical tracheostomy. All tracheostomies were performed by the staff physicians of the ICU at bedside patients. The following data were recorded: age, sex, Simplified Acute Physiology Score II (SAPS), fraction of inspired oxygen (FIO_2) before the tracheostomy, days in mechanical ventilation before the tracheostomy, bleeding, tracheal tear, subcutaneous emphysema, pneumothorax, wound infection, hypotension, lowering SaO_2 during the procedure, inability to complete the procedure and procedural mortality.

RESULTS. There were a total of 5 (5.37%) complications. Hemorrhage and wound infection were present in 2 (2.15%) and 3 (3.22%) patients respectively. Forty patients died in the ICU (43%), although none of these deaths were related to technique complications. Mean duration of the procedure was 13±0.2 min
CONCLUSION. The "mini invasive" surgical tracheostomy is a new simple and safe procedure that offers many advantage over standard open surgical and percutaneous tracheostomy.

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PRELIMINARY EXPERIENCE OF PERCUTWIST TRACHEOSTOMY AT LEEDS

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INTRODUCTION. Percutaneous tracheostomy is commonly performed in the ICU. Immediate and early complications have decreased over recent years. However trauma to the posterior tracheal wall is a concern with any percutaneous technique. Percutwist tracheostomy (Rusch UK) is a new technique with a specially designed screw-type dilator. This needs bronchoscopy to be performed. We were interested to evaluate feasibility and safety of this technique and assess the immediate complications.

METHODS. A total of 16 critically ill patients requiring tracheostomy were enrolled in this open, observational ongoing clinical trial. Assent was obtained from the close relatives. Patients with diffICUlt neck anatomy were excluded as were those requiring more than 60% FiO_2. All patients were anaesthetised and paralysed. Their endotracheal tube was withdrawn until the cuff was just seen at the vocal cords. The introducing needle was inserted below the 2nd tracheal ring under bronchoscopic guidance followed by the guidewire. The percutwist dilator was introduced by controlled clockwise rotation over the guidewire until three or four spirals were seen in the trachea. The dilator was removed anticlockwise and tracheostomy tube was placed. Operating times(needle entry to tracheostomy tube placement) for the procedure was recorded and arterial blood gases were analysed prior,during and after the tracheostomy.

RESULTS. The data of 15 patients were analysed using SPSS version 10 except one patient in whom the technique was abandoned due to increased vascularity of the neck. Patients were intubated for a median of 5 (3-7) days and had on average one failed extubation. Tracheostomy was performed on 5th ICU day (range 3-8 days). Time to perform the tracheostomy was 6.27 ± 2.3 minutes (Mean ± SD). The arterial $PaCO_2$ during the procedure (7.32±2.03 kPa) showed a significant rise ($p<.006$) over the preoperative value (5.11 ± 0.93 kPa). The blood loss was minimal (less than 5ml). There were no procedure-related complications including false passage, pneumothorax and posterior tracheal injury. In one patient there was an increase in the existing subcutaneous emphysema

CONCLUSION. The Percutwist dilator allowed a single step controlled dilatation of the trachea. It has a learning curve. The data of this preliminary study suggests that it appears to be a relatively quick procedure with a low incidence of bleeding complications. It may offer an alternative to the existing techniques of percutaneous tracheostomy.

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NON_INVASIVE MASK VENTILATION ON PATIENTS WITH ACUTE LUNG INJURY AFTER CARDIAC SURGERY

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INTRODUCTION. At present ARF is one of the most spread and serious complication of postoperation period. Practically the experience of carring NIMV on patients with ARF on early stadies of MOSF is absent. Until now, the criteria of uneffectiveness of NIMV and indications for cessation of mask ventilation and moving of patients to mechanical ventilation are not determined.
METHODS. There were included 48 patients with ALI in the examination. The cause of this condition was the MOSF, developed in postoperative period. Diagnosis of ALI/ARDS was stated on the criteria adopted The American European Consensus Conference on ARDS (1). Presence of organs failure was determined on Multiple organ dysfunction score (Table 1). NIMV was carried out by seances from 5 to 8 hours. Average duration of NIMV consisted 39.5±5.3 hours.
RESULTS. Improvement of gases change was determined on 28 patients (58%) out of 48. Though 20 patients with MOSF were reintubated, out of which 13 patients (27%) died lately as the result of MOSF progressing. The condition of gases changing functions before intubation is one of the determining factors of prognosis. The patients reintubated under satisfactory indices of gase blood composition and early symptoms of MOSF survived. Patients, who were reintubated on decreased indices of arterial oxygenation under MOSF progressing died in 100% cases (Table 2).

Respiratory failure	2.69±0.15
Cardiac failure	2380±13
Hepatic failure	2.13±0.18
Renal failure	2.57±0.22
Haematologic failure	2.31±0.14

Table1. Multiple organ dysfunction score (in points, Marshall JC, 1995)

	Group A, died, n = 13	Group B, survival, n = 7
ÐàÎ2/FiO2, mm Hg	168±15	204±17*
(A-a)ðO2, mm Hg	242±22	158±18*
Qs/Qt, %	17.4±1.5	15.1±1.8*

Table2. Parameters of lungs gases changing function

CONCLUSION. NIMV is effective method in complex therapy of ARF, developing in postoperative period after cardiac surgery, that leads to significant improvement of lungs biomechanics and gases change function. Progressing of MOSF and storage disturbance of lung oxygenation is absolute indication for intubation and applications of special regimes of mechanical ventilation.
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WEANING FROM TRACHEOSTOMY: A PROSPECTIVE PRELIMINARY EVALUATION OF A CLINICAL DECISIONAL FLOW-CHART

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INTRODUCTION. – Once the patient is liberated from prolonged mechanical ventilation (MV), the indications and timing for tracheotomy tube (TT) removal, if present, still relies on subjective criteria. We have prospectically applied a clinical decision flow-chart to test its clinical feasibility.

METHODS. 88 consecutive patients (mean age 67±12 years, SAPS II 26±8) admitted to our Respiratory Intensive Care Unit (RICU), and previously tracheotomized (70 percutaneous, 18 surgical) after at least 7 days of MV, were enrolled in the study. The primary reason for MV was: respiratory failure due to COPD exacerbation (n 27), post-operative pulmonary complications (n 27), neuromuscular disease (n 14) and refractory hypoxia (n 20). The criteria adopted in our flow-chart for TT removal were the following: 1) liberation from MV>5 days; 2) clinical stability; 3) absence of delirium or other psychiatric diseases; 4) absence of severe tracheal or glottic stenosis (assessed by means of fiberoptic bronchoscopy); 5) presence of a valid cough reflex and of a maximal expiratory pressure (MEP) ³ 40 cm H_2O; 6) adequate swallowing function (assessed by the blue methylene test or videofluoroscopy); 7) willingness of the patient. If these criteria were fullfilled, TT inner diameter was progressively downsized to 6 mm and then eventually removed; when MEP was in the range 20,39 cm H_2O or in presence of a weak cough reflex, a minitracheotomy (MT) was positioned for few days. This subset of patients was daily followed and efficacy of spontaneous expectoration was assessed by the ability of removing sputum without instrumental suctioning (< 3 suctions/day), so that in this case TT was finally removed.

RESULTS. 11 (12%) patients died while in the RICU, 45 (51%) had their TT removed at discharge (33 meeting directly all the criteria and 12 through the intermediate step of MT) while 32 (36%) had not. Reasons for TT removal failure were: need for continuous MV (18 pts), weak cough mechanism or MEP <20 cm H_2O (10 pts), supraglottic (3 pts) and tracheal (1 pt) stenosis. Patients in which TT removal failed were affected by persistent hypoxia (n 7), advanced COPD (n 14), and neuromuscular disease (n 11). Six months after discharge only 2/45 patients (4%) needed re-intubation for upper airway stenosis. Side effects following TT removal were: dysphonia (3 pts), sporadic swallowing problems (2 pts) and delayed stoma healing (2 pts).

CONCLUSION. these preliminary data support the hypothesis that objective criteria should be used in clinical practice to decide when TT weaning should be performed. Further larger prospective studies are needed to validate our decisional flow-chart.

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THE EFFECTS OF SYSTEMIC INFLAMMATION ON PULMONARY HISTOPATHOLOGY DURING MECHANICAL VENTILATION

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INTRODUCTION. The aim of this study was to determine the effects of systemic inflammation (SIRS) on pulmonary histopathological changes during mechanical ventilation.

METHODS. 24 New Zealand rabbits were randomly divided into 3 groups (n:8). All animals were sedated with ketamine, 50 mg/kg, intramuscularly. The ear vein was cannulated for fluid and anaesthesia maintenance. Group 1: (Laparotomy+SIRS group)Laparotomy was performed. Cecum was tied about 2 cm below the iliocecal valve and punctured once by 18 G needle, then abdomen was closed. Group 2: (Laparotomy without SIRS group). Only laparotomy and abdominal closure was performed. Group 3: Control group without laparotomy and SIRS. In all groups, tracheostomy was performed 1 hour after abdominal closure. The animals were curarized with 0.5 mg/kg/h atracurium infusion and anaesthesied with ketamin 10 mg/kg/h. All animals were ventilated for 3 hours with the ventilation parameters of FiO_2:1.0, PIP: 18 cmH_2O, PEEP: 5 cmH_2O and respiratory rate was adjusted to keep initial $PaCO_2$ of 35-40 mmHg by using Servo 900 C ventilator. At the end of the 3 hours, the rabbits were sacrified for histopathologic examination to evaluate lung injury. The pathological lessions were classified ranging from 0 to 4 (1).

RESULTS. Significant changes in histopathologic findings (bronchial epithelial injury, hemorrhage, alveolar edema and atelectasia) were encountered in group 1 when compared with the other groups. There was no significant difference for neutrophil infiltration and density between groups.

CONCLUSION. Systemic inflammation during mechanical ventilation effects the pulmonary histopathology changes. In our opinion, patients with systemic inflammation must be ventilated more carefully with lung protective mechanical ventilation strategies.

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REGIONAL VENTILATION AND REGIONAL PERFUSION IN HEALTHY VOLUNTEERS IN THE SUPINE AND PRONE POSITIONS

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INTRODUCTION. Regional pulmonary perfusion and ventilation have previously been studied in animals using microspheres techniques. High resolution techniques for this purpose have not previously been available for human studies. We have developed a new method using dual isotope quantitative Single Photon Emission Computed Tomography (SPECT) to simultaneously depict regional ventilation and perfusion in human subjects. The method produces spatial information on the distribution of ventilation and perfusion for the whole lung.

METHODS. The technique has been described and validated (1). Regional ventilation and perfusion were marked using inhaled Technegas and iv-administered 113mIn-MAA in healthy volunteers in supine and prone positions. The distribution of the two radiopharmaceuticals was mapped by gamma camera examination using tomography (SPECT). Corrections for photon scattering and attenuation was performed as well as correction for interfering influence between the different photon energies. Hence, the activity distribution in the gravitational plane could be analysed in quantitative terms, allowing comparisons of regional ventilation and perfusion in different postural positions.

RESULTS. Our results indicate that both ventilation and perfusion are greater in the dorsal regions regardless of whether subjects are supine or prone.

CONCLUSION. This new method allows simultaneous studies of regional ventilation and perfusion in humans with high spatial resolution. Regional ventilation and regional perfusion appear to be distributed in a similar way in healthy volunteers as previously shown in animal studies.

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REGIONAL LUNG IMPEDANCE TRACING COMPARED TO PNEUMOTACHOGRAPHY

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INTRODUCTION. Electrical impedance tomography (EIT) is an imaging technique, which offers the possibility of regional lung function studies [1]. Due to hardware improvements [2] regional lung function studies with a time resolution of up to 25 EIT-images per second are possible. The aim of this study was to compare the tracings of regional lung impedance with spirometry measured by pneumotachography in spontaneously breathing healthy volunteers.

METHODS. After approval by the local ethics committee ten healthy spontaneous breathing volunteers (weight: 55-85 (71) kg, age 18-43 (32) y, median and range) were included into the study. Simultaneous tracings of tidal volume (flow head: Fleisch No. 2, Fleisch, Lausanne, Switzerland, differential pressure transducer: Huba Control, Würenlos, Switzerland) and Electrical Impedance Tomography (EIT) (Goe-MF, EIT-Group Göttingen, Göttingen, Germany) in a transversal thoracic slice at 6. intercostal space were performed with a time resolution of 13 Hz. Impedance tracings in 912 regions-of-interest (EITregional) in the observed transverse slice were calculated during normal breathing, a vital capacity manoeuvre and forced expiration. Evaluation was done by comparing simultaneously measured data points of spirometry and EITregional. We calculated the linear correlation of spirometric volume tracings and EITregional during the breathing manouvres performed.

RESULTS. The overall linear correlation of EITregional compared to pneumotachography during normal breathing was $y=0.89x–0.0$, $R^2 =0.92$, during vital capacity manoeuvre $y=0.94x–1.0$, $R^2=0,95$ and during forced expiration $y=1.2x–26.2$, $R^2=0.97$.

CONCLUSION. We found an excellent overall correlation between the regional impedance tracings measured by EIT and spirometry during normal breathing a vital capacity manoeuvre and a forced expiration. In contrast to spirometry, however, EIT allows to monitor regional lung function.

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PERIOPERATIVE PERFORMANCE OF A NEW BIOIMPEDANCE TECHNIQUE IN CARDIAC SURGERY PATIENTS.

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INTRODUCTION. Several bioimpedance cardiac output systems have been developed in the past in order to measure cardiac output in a wide variety of clinical situations. However, open thorax surgery negatively influences the accuracy of the measurement of thoracic electrical bioimpedance cardiac output (TEB-CO) (1). The purpose of the present study was to evaluate the performance of a new bioimpedance cardiograph HL-4 (Vrije Universiteit Medical Centre Amsterdam and Hemologic Amersfoort, The Netherlands), using a new algorithm and a new electrode configuration, during open and closed chest in CABG patients, comparing TEB-CO with transcardiopulmonary thermodilution (TCPCO).

METHODS. After Hospital Ethics Committee approval and written informed consent, fourteen patients with preserved LV-function at cineangiography or echocardiography, scheduled for coronary artery bypass grafting were included. For the TEB system two current injecting electrodes were placed on the forehead and the left thigh respectively and two voltage sensing electrodes were used: one above the left clavicle at the base of the neck and the other at the level of the xyphoid in the left midaxillary line. For TCPCO, the PiCCO-system (Pulsion, Munich, Germany) was used. Hemodynamic measurements were recorded at three time points: t1 before the operation, t2 after weaning from bypass before sternal closure and t3 after sternal closure. TEB-CO and TCPCO data were compared with Pearson's r correlation coeficient. $p<0.05$ was considered significant. Bland-Altman analysis (2) with bias and precision was carried out at each of the three time points.

RESULTS. Ten males and 4 females with age 64±9 yr, body weight 78 ± 13 kg and height 172±8 cm were included. A total of 34 matched data pairs were available for analysis. Table 1 shows the results of correlation, bias and precision of the measurements at the three different time points. TEB consistently underestimated TCPCO. At all time points, there was a good correlation between both techniques.

	t1	t2	t3
r	0.68	0.82	0.84
p-value	p=0.015	p=0.001	p<0.001
Bias	-0.76 l/min	-1.53 l/min	-1.53 l/min
Precision	0.55 l/min	0.95 l/min	0.71 l/min

TEB-CO versus TCPCO

CONCLUSION. The new bioimpedance cardiographic system using a new algorithm and a simplified electrode configuration showed good agreement with the reference technique with underestimation of TCPCO. Even during the open thorax period post-bypass, there was a good agreement between both techniques. This tool may offer new perspectives in hemodynamic management during cardiac surgery.

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STARTING PRONE POSITION VENTILATION -A MOVABLE SWITCH-ON EFFECT ON OXYGENATION IN THE COURSE OF ARF?

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INTRODUCTION. In acute respiratory failure (ARF), in partICUlar acute lung injury (ALI) and respiratory distress syndrome (ARDS), change from supine (SP) to prone position (PP) can improve oxygenation by recruiting alveoli situated in dorsal dependent regions of the lung and by alteration of ventilation/perfusion ratio. The efficacy of this intervention can be demonstrated by the course of the oxygenation index. The aim of our study is to analyze the effect of proning the patient in different phases in the time course of an acute respiratory failure.

METHODS. We studied 110 consecutive patients with an acute respiratory failure, n=92 with ARDS and n=18 with ALI (mean age 66±13 [SE] years) in a clinical follow-up design at a surgical ICU in a university hospital, who met the criteria of the American-European consensus definition. All patients were ventilated intermittent in the SP and PP for supportive treatment of ARF. The patients were ventilated in the customary used supine position for different periods of time before prone position ventilation was started in a 135° left/right-side-position for at least six hours per day. We analyzed the time of supine position ventilation and the individual oxygenation index (PaO_2/FiO_2) before and after start of prone position as well as the outcome of each patient [SPSS® T-test].

RESULTS. PPV was started after a mean time delay of 11 days in a wide range from the 1st to the 81st day after the onset of acute respiratory failure. It was well tolerated in all patients, resulted in a significant increase of PaO_2/FiO_2-ratio in n=106 patients within the first six hours of PPV (SP 149±0,52 vs. PP 230±0,73mmHg [mean±SEM]) and enabled a reduction of the FiO_2. In the remaining four cases there was a positive effect within the first 24 hours. PPV lead to an 1,64±0,57[mean±SE] fold improvement of oxygenation index in essence independent of the length of time of preceding ARF. N=67 (61%) of the patients died and n=43 (39%) survived ARF. Subsequent to starting PPV n=11 patients with a more than 20 days lasting ARF showed a significant improvement in oxygenation and survived.

CONCLUSION. Starting prone position ventilation interestingly can improve oxygenation even after several days of ongoing acute respiratory failure like a switch-on effect. The timing of this non invasive technique primarily depends on the decision of the physician to turn the patient from the customary used supine to the prone position. Using this effect in the early phase of acute respiratory failure may help to reduce oxygen toxicity, aggravation of lung injury and complications due to mechanical ventilation. It should be started before the time course of pathogenic events in the overall process of ARF becomes irreversible.

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SEDATION OF ICU PATIENTS WITH ISOFLURANE USING THE ANESTHETIC CONSERVING DEVICE

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INTRODUCTION. Isoflurane sedation of ICU patients has previously been shown to be useful but has not come into wide clinical use for a number of reasons.A new device(The Anesthetic Conserving Device,"ACD") enables easy and safe administration of isoflurane in the ICU setting.We conducted a randomised, controlled study to evaluate efficacy of sedation and environmental safety during administration of isoflurane with the ACD.

METHODS. The ACD is a modified heat and moisture exchanger connected to the breathing circuit at the endotracheal tube.Isoflurane is administered via a syringe pump to a vaporiser rod in the ACD.Due to the physical properties of the ACD most of the exhaled isoflurane is returned to the patient.5 mechanically ventilated patients were randomised to receive isoflurane via the ACD.4 control patients received midazolam intravenously. All patients received morphine analgesia. Quality of sedation was assessed hourly in all patients."Adequate sedation" was pre-defined as a set interval on the Bloomsbury Sedation scale. Additionally, the patient's nurse determined if sedation over the previous hour in general had been adequate or not. Time from discontinuation of the sedative drug until the patient followed verbal command and to extubation was compared between groups. In the isoflurane group a gas evacuation system was used during isoflurane administration. Athmospheric concentration of isoflurane was measured at 0.5 m from the ACD.
RESULTS. In the isoflurane group patients were adequately sedated by the Bloomsbury Scale for 58 ± 9 % of the study period, compared to 50 ± 28 % in the control group.Nurse satisfaction in the isoflurane group was 88 % of time and 57% of time in the control group.Mean time to extubation after cessation of sedative administration was 11 min in the isoflurane group and 1864 min in the control group, mean time to patient cooperation was 55 min in the isoflurane group, and 1866 min in the control group. No significant hemodynamic changes were noted at initiation of the sedation in either of the groups. No serious complications related to sedation were noted in either group.Opioid requirements in the isoflurane group were lower, with a mean rate of 1.6∂0.9 mg/hr, compared with a mean rate of 4.2∂2.4 mg/hr in the control group.Mean isoflurane infusion rate was 2.5 ml/hr, with mean end-tidal isoflurane concentrations of 0.37% (0.19-0.82%).Environmental levels of isoflurane were generally low,with a mean of 0.43 ± 0.27 ppm, well below the recommended long-term exposure limit of 2 ppm. Brief peaks (<2min) between 2 and 15 ppm were noted during endotracheal suctioning, etc on an average of 0.1 times/hour of exposure.
CONCLUSION. Isoflurane administered via the ACD for sedation of ICU patients is environmentally safe, requires small volumes of isoflurane and may provide better quality of sedation than midazolam. It appears to be more titratable with a shorter time from adequate sedation to extubation and ability to cooperate.
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ALBUMIN CREATININE RATIO AS A PREDICTOR OF PULMONARY PROBLEMS POST CORONARY ARTERY BYPASS GRAFTING

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INTRODUCTION. Increased capillary permeability has been implicated in the pathogenesis of ARDS and organ failures. Surgery and ischaemia-reperfusion injury are both associated with stimulation of the acute inflammatory response, an early feature of which is an increase in systemic capillary permeability. The kidneys amplify small changes in systemic capillary permeability (1).The aim of this study was to explore any association between ACR during and after cardiopulmonary bypass (CPB) and subsequent pulmonary and renal function.
METHODS. Forty patients (9 female) mean (range) age 67.8 (50-85) yrs undergoing coronary artery bypass grafting were enrolled. Patients with severely impaired left ventrICUlar function (<35% EF) were excluded. Ten mL of urine was collected at intervals from the start of surgery until 48 hours post CPB. Microalbuminuria was measured by automated immunoturbidimetry and expressed as the albumin creatinine ratio (ACR: ref. range <2.3 mg/mmol). ACR was compared with pO_2/FiO_2 ratio, hours on IPPV, renal function and duration of inotropic support, using Spearman's rank correlation procedure.
RESULTS. Two patients were excluded (death at 6 hours and acute renal failure post CPB). The median (range) duration of IPPV was 15 (4-72) hours. 22 patients required inotropic support for median (range) 12 (2-96) hours. Median (range) ACR increased during surgery and was maximal 10 minutes post CPB. (Table) Two hour ACR was inversely correlated with the mean pO_2/FiO_2 ratio up to 12 hours (rs = -0.46 p = 0.0044). Two and 12 hour ACRs were both positively associated with duration of IPPV (rs = 0.46 p = 0.0071 and 0.62 p <0.0001 respectively). ACR at 4 and 12 hours were associated with serum creatinine 24 hours post CPB, (rs = 0.35 p = 0.045, rs = 0.50 p = 0.003 respectively). ACR at 2, 4 and 12 hours post CPB were associated with serum creatinine 48 hours post CPB (rs = 0.45 p = 0.033, rs = 0.59 p = 0.003 and rs = 0.49 p = 0.016 respectively). There was no significant association between duration of inotropic support and ACR at any time point up to 48 hours.

time point	pre op	pre CPB	10 min post CPB	2 hr post CPB	4 hr post CPB	12 hr post CPB
median	0.65	2.25	4.8	2.4	1.9	1.6
range	0.1-18.8	0.2-29.3	0.3-54.2	0.4-22.5	0.4-29.8	0.4-31.0

CONCLUSION. CPB leads to a perioperative microvascular insult, causing increased capillary permeability which influences later pulmonary and renal function. These rapid changes in microvascular permeability can be monitored as the ACR, and in the patient group studied, the magnitude of the ACR as early as 2 hrs post CPB is associated with later organ function. ACR may provide a tool allowing early identification of patients at risk of developing organ dysfunction, who may benefit from early intervention aimed at modifying the inflammatory response.
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FLAGELLIN INCREASES FLUID FILTRATION IN ISOLATED BLOOD-PERFUSED RAT LUNGS

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INTRODUCTION. Acute lung injury (ALI) is a major complication of gram-negative bacterial sepsis. To date, bacterial lipopolysaccharide has been held responsible for triggering ALI (1). Whether additional bacterial toxins play a role in the development of acute pulmonary inflammation during gram-negative sepsis remains an unresolved issue. Flagellin, a principal component of bacterial flagella, has been recently shown to elicit immune responses via activation of the toll-like receptor 5 (2). We have newly found that flagellin induces an expression of ICAM-1 and a massive production of IL-8 by human lung epithelial cells. In mice, flagellin produces a severe acute lung inflammation with local release of pro-inflammatory cytokines, accumulation of inflammatory cells and increased pulmonary permeability that was more pronounced than following endotoxin (3). The purpose of the present investigation was to evaluate the influence of flagellin on lung fluid filtration in rats.

METHODS. Wistar rats (250-300 g) were exposed either to intravenous injection of flagellin 0.1-2 mg/kg or corresponding volume of normal saline (controls). After 8-20 h, the rats were anesthetized and the lungs were isolated. The isolated lungs were ventilated under a normoxic condition and perfused with homologous blood (37ºC) at a constant flow for 4 h or until development of irreversible edema. Airway pressure, pulmonary arterial pressure, pulmonary vascular resistance, and changes in the lung weight were assessed. The increments in outflow pressure of 0.77 kPa for 6 min were used to determine the fluid filtration rate and filtration coefficient in the lungs every 30 min (4).

RESULTS. Flagellin induced a dose- and time-dependent increment in the lung fluid filtration rate. In parallel, flagellin markedly increased airway pressure, pulmonary arterial pressure, pulmonary vascular resistance, and filtration coefficient. In contrast to the control lungs, all the lung preparations from flagellin-treated animals developed irreversible edema within the first two hours of perfusion.

CONCLUSION. In isolated blood-perfused rat lungs, flagellin enhances fluid filtration, most likely, through elevation both of pulmonary microvascular permeability and hydrostatic pressure. The present study provides further evidence that flagellin may contribute to the development of sepsis-associated ALI.

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MECHANICAL VENTILATION INCREASES HEAT SHOCK PROTEIN 70 AND CYTOKINES IN THE SPLEEN AND INTESTINE

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INTRODUCTION. In ICU patients multiple organ failure is the most frequent cause of death among patients with the acute respiratory distress syndrome. It has been suggested that local ventilator-induced inflammatory mediators could generate distal organ failure, either by spillover of locally produced cytokines or by translocation of bacteria or bacterial toxins from the lung or the intestine into the circulation. In this study we have investigated whether mechanical ventilation in a mildly injured lung affects cytokine levels in the circulation, spleen, kidney, liver and the intestine. As a marker of cellular injury we measured heat shock protein 70 (HSP70).

METHODS. Lung inflammation was induced by intratracheal aerosolization of LPS in Sprague Dawley rats. After 24 hours we randomized the rats to the following two different ventilation strategies: 1) ZEEP group: Peak inspiratory pressure (PIP)=18 cmH2O; PEEP=0 cmH2O and 2) PEEP group: PIP=18 cmH2O; PEEP=4 cmH2O. Rats were ventilated during 4 hours in a pressure-controlled time-cycled mode, at a fractional inspired oxygen concentration (FiO_2) of 1.0, I/E ratio of 1:2 and a frequency between 20-30/minute to maintain normocapnia. Blood gases were analyzed. HSP70 was measured by Western blotting and cytokines were measured by the RNase Protection Assay and ELISA. In blood, lymphocyte subpopulations were determined by FACS analysis. Data were analyzed by Student's t test.

RESULTS. In blood, lymphocyte subpopulations were similar comparing the ZEEP group (n=10) and the PEEP group (n=7). Cytokine and HSP70 levels in the circulation and different organs were analyzed from >4 animals per group. TNF-a in the plasma was not detectable. In the spleen, IL-1b mRNA was significantly higher in the 18/0 group than in the 18/4 group (p 0.01). HSP70 was also significantly higher in the ZEEP group than in the PEEP group (p 0.03). TNF-a was not detectable. In the intestine HSP70 levels were significantly higher in the ZEEP group vs the PEEP group (p 0.01). Intestinal cytokine level measurements were not performed. However, in the kidney TNF-a, HSP70 and IL-1b mRNA levels were identical. In the liver, TNF-a levels and IL-1b mRNA expression were similar and HSP70 was not detectable.

CONCLUSION. Mechanical ventilation induces a pro-inflammatory response and provokes cellular damage in peripheral organs (spleen and intestine).

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EFFECTS OF PROTEIN C ON HUMAN EOSINOPHIL FUNCTION

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INTRODUCTION. Eosinophil counts and eosinophil percentage of white blood cells are increased in sepsis [1]. Eosinophils likely affect tissue damage and coagulation through release of toxic granule proteins and other inflammatory mediators. Eotaxin stimulates chemotaxis of eosinophils and induces release of granule proteins like eosinophil cationic protein and major basic protein which impair thrombomodulin function [2]. Protein C activation is regulated by thrombomodulin [3]. Whether protein C conversely affects eosinophil function has not yet been reported. We investigated the effects of protein C and activated protein C on chemotaxis of eosinophils. Possible involvement of endothelial protein C receptor (EPCR) in the regulation was studied by using specific EPCR antibodies.

METHODS. For preparation of eosinophils we used MACS CD+16 microbeads according to the manufactor's protocol. Chemotaxis assays were performed using a 48-well Boyden microchemotaxis chamber in which a 5-micrometer pore sized cellulose nitrate filter separates the upper and the lower chamber. Eosinophils were pretreated by various protein C preparations with or without EPCR antibodies, followed by washing and assessment of their migratory responses toward eotaxin.

RESULTS. Protein C and activated Protein C exerted no significant chemotactic effect on eosinophils. However, eosinophils pretreated with protein C or activated protein C showed a sigificantly reduced response to the specific chemoattractant, eotaxin. Moreover, this effects of protein C and activated protein C were inhibited using an antibody against EPCR.

CONCLUSION. Protein C as well as activated protein C inhibit the chemotactic effect of eotaxin on eosinophils via mechanisms involving EPCR. This result indicates that protein C as well as activated protein C may decrease the number of eosinophils in tissue and thereby inhibiting inflammation and coagulation.

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COMPARISON BETWEEN LIPOPOLYSACCHARIDE AND HIGH DOSE SELENIUM TOXICITY IN RAT

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INTRODUCTION. Deleterious effect of severe sepsis may be related to an oxidative stress, partICUlarly related to peroxynitrite. Selenium (Se) toxicity is supposed to be related to oxidative stress through reaction with thiols. We perform a study to compare these toxicities.
METHODS. 100 wistar rats were studied. After 8 day quarantine Lipopolysaccharide (LPS) or Se was administered intraperitoneally in 3 ml saline water. LPS and Se were administered in groups of 10 rats with increasing doses from 28 to 34 mg/kg for LPS, and from 0.35 to 4.5 mg/kg for Se. Mortality was observed at 48 hours. Animals were sacrificed under Halothane. Blood samples were taken in 2 surviving rats of each group. Nitric oxide (NO) and nitrotyrosine (Nit), a marker of oxidative stress especially related to peroxynitrite, were measured by Elisa techniques, and plasma Se concentration using Atomic Flame Absorption.
RESULTS. Septic rats were rapidly sick. They rolled up into a ball. Their fur was dull, and stood on end. They were asthenic and had diarrhea. At autopsy, intestinal abnormalities, and in some rats echymotics dots and hemolytic plasma were observed. Rats were dehydrated. Se rats developed an encephalopathy the first day and later recovered. Se rats were lively, and seemed to required higher level of halothane for induction. No patent visceral abnormality was observed and no sign of dehydration.

	NO mMole	Nit nMole	Lac mMole	Se mMole	GOT UI/L	GPT UI/L	Mortality
LPS 26	300	58 / 0	5.7*	3.0*	451*	389*	6 / 10
LPS 28	309	81 / 0	4.1	3.6	137	69	7 / 10
LPS 30	313	97 / 0	4.9	4.0	115	54	8 / 10
LPS 32	281	298 / 0	5.0	3.1	284	101	6 /10
LPS 34	273	0 / 0	3.5	3.1	142	50	4/10
Se 0.35	27	92 / 0	4.4	5.7	66	31	0 / 10
Se 1	26	0 / 0	3.1	5.8	81	27	0 / 10
Se 1.75	45*	0*	3	6.6	97	32	0 / 10
Se 3	28	0*	2.9*	6.6*	112*	30*	0 / 10
Se 4.5	12*	0*	2.8*	8.6*	778*	127*	4 / 10
References	15-130	0		5	55-242	26-70	

* value measured in only 1 rat, other correspond to mean, except for nitrotyrosine (Nit) Lactates (Lac), glutamic oxalacetic and pyruvic transaminases (GOT, GPT)

CONCLUSION. We observed an increase in NO plasma concentration in LPS rats ($p<0.01$), but not in Se rats. Elevated level of nitrotyrosine concentration was observed quite only in LPS rats, but this needs to be confirmed by another measurement technique. Our results are in favor of two different pathways for LPS and Se toxicity. Se plasma concentration was moderately decreased in this LPS non resuscitated rat model.

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DIAPHRAGMATIC DYSFUNCTION DURING SEPSIS

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INTRODUCTION. Diaphragmatic dysfunction has been described during sepsis in different animal models. (1)However the mechanisms responsible for this alteration remains under investigation. Depressed micochondial respiration has also been found in different tissues during sepsis.(2) The objective of this work was to study diaphragmatic function in rats after peritoneal sepsis and to correlate these findings with diaphragmatic mitocondrial respiration.

METHODS. Cecal ligation and perforation was done under general anesthesia in Wistar rats (Septic Group, n=7). After 48 hours the animals were monitored for arterial blood gases, systemic hemodynamia and body temperature. Then, they were sacrified and the diaphragm force-frequency curves were obtained in vitro before and after fatigue. Contraction time and relaxation time were also measured. Mitochondrias were isolated from the diaphragm and oxygen consumption and other respiratory indexes were studied in septic animals. The results were compared to sham operated animals (Control Group, n=7).

RESULTS. The Septic Group showed significantly lower values of aortic blood flow, arterial oxygen partial pressure, body temperature and arterial bicarbonate ($P<0.05$) when compared to the Control Group. The forces measured at the different frequencies of stimulation were lower in the septic diaphragms both before and after fatigue when compared to controls ($P<0.05$). Mitochondrial respiration evaluated by oxygen consumption and RCR indexes was found decreased in the septic animals ($P<0.05$).

CONCLUSION. Diaphragmatic contractile failure along with hemodynamic, respiratory and metabolic dysfunctions was found in peritoneal sepsis in rats. Diaphragmatic dysfunction could be explained by mitochondrial damage during sepsis. We speculate that mitochondrial injury and dysfunction could be related to oxidative stress in this animal model.

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INHIBITION OF NEUTROPHIL CHEMOTAXIS BY PROTEIN C AND ACTIVATED PROTEIN C

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INTRODUCTION. Protein C is activated by thrombin bound to thrombomodulin and this effect is enhanced in the presence of the endothelial protein C receptor (EPCR). In vivo and in vitro studies have revealed that components of this pathway may also inhibit inflammatory responses. Protein C was able to inhibit leukocyte adhesion to vascular endothelial cells and to reduce neutrophil accumulation in rat lungs [1]. Protein C inhibits proinflammatory cytokine release in monocytes [2] that were shown to express EPCR [3]. Soluble EPCR binds to proteinase-3 and CD11b/CD18 of activated neutrophils [4], which were previously shown to synthesize thrombomodulin but not to promote thrombin-dependent protein C activation [5]. If protein C directly affects neutrophil functions has not jet been sufficiently demonstrated. We investigated the in vitro effects of protein C and activated protein C on chemotaxis of isolated human neutrophils and explored wether EPCR may be involved.

METHODS. Neutrophils were obtained from forearm venous blood by standard methods. Leukocyte migration toward gradients of soluble attractants into cellulose nitrate micropore filters was measured using a 48-well microchemotaxis chamber. Cells were either directly exposed to gradients of protein C or were pretreated with protein C followed by washing; then chemotaxis toward typical attractants was tested.

RESULTS. Neither protein C nor activated protein C induce chemotaxis of neutrophils. Both inhibit neutrophil chemotaxis toward interleukin-8, fMLP and C5a and there is no significant difference in the effects of these two substances. A blocking antibody against the EPCR is able to diminish the effects of protein C and activated protein C.

CONCLUSION. Protein C as well as activated protein C is able to inhibit neutrophil chemotaxis. This indicates that an activation of protein C is not necessary for effects on neutrophils to occur or that neutrophils are able to activate protein C followed by migration. The reduction of the protein C effects by an antibody against the endothelial protein C receptor suggests that neutrophils express EPCR capable to signal anti-migratory stimuli.

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INTERLEUKIN-10 MODULATES OXIDATIVE STRESS INDUCED BY TNF-Ŭ IN ENDOTHELLIAL CELL

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INTRODUCTION. : Ischemia/reperfusion or sepsis is initially responsible of an acute activation of pro-inflammatory cytokines (e.g. Tumour Necrosis Factor (TNF-Ŭ). It is followed by a rise of anti-inflammatory cytokines (e.g. Interleukin-10 (IL-10)). In Human umbilical vein endothelial cell (HUVEC) TNF-Ŭ induces a mitochondrial release of reactive oxygen species (ROS) in a dose-dependent manner. The signalisation pathway which links TNF-Ŭ at mitochondria involves ceramide pathway (1).The goal of our study is to evaluate the action of IL-10 on the oxidative stress induced by TNF-Ŭin HUVEC and to define the mechanism of this interaction.

METHODS. HUVEC were grown on plastic cover slides. At confluence they were placed in a perfusion chamber under a microscope equipped with a digital camera connected to acquisition software. Cells were perfused with Krebs solution containing two fluorescent probes: Dichlorodihydrofluorescein diacetate (DCFH) to study the release of reactive oxygen species (ROS) and propidium iodide (PI) to study cell mortality. Three cell groups were studied: a reference group, a TNF-Ŭgroup where, after one hour stabilisation, TNF-Ŭwas added (1 ng/ml) in perfusion medium during one hour, · a group TNF-Ŭ+ IL-10 where IL-10 was added to perfusion medium 30 minutes before TNF-Ŭ Variations in fluorescence were recorded each 10 minutes for DCFH and each one hour for PI.

RESULTS. For a non lethal concentration (PI remaining unchanged), IL-10 reduces significantly the ROS production induced by TNF-Ŭ(ANOVA for repeated measures).

CONCLUSION. Interleukin-10 has an inhibitory effect on the release of ROS induced by TNF-Ŭ in HUVEC. This effect could be the result of an interaction with acid sphingomyelinase.

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ENDOTOXIN-INDUCED MYOCARDIAL APOPTOSIS AND CYCLOSPORINE A

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INTRODUCTION. The immunosuppresive drug cyclosporine A (CsA) is an inhibitor of mitochondrial permeability transition (MPT) which could afford protection against cell death [1].To test whether CsA protects against endotoxin-induced myocardial apoptosis [2], we produced 123I-Annexin V [3], a marker of apoptotic cells, and measured its myocardial uptake during endotoxaemia in CsA-treated rats. The specificity of the signal has been previously verified with caspase inhibitors and 123I-Human Serum Albumin.

METHODS. 1) 123I-Annexin V was produced with a radiochemical purity higher than 97% as confirmed by HPLC. 2) Young male Sprague-Dawley rats were either given IV : Saline (0.5ml) : control group, n=10, or lipopolysaccharide (LPS) from E Coli (30mg/kg) ± CsA (10mg/kg): LPS group, n=10 and LPS+CsA group, n=8. 6H later, all animals were given 123I-Annexin V (18MBq, 10mg protein). After 12H, hearts were harvested and divided into apex, septum, right and left ventricle (RV, LV) for determination of 123I-Annexin V myocardial uptake with a LKB gamma counter. Results were expressed as a mean percentage ± SD of the injected dose per gram of tissue (%ID/g). Statistical analysis was performed by Mann-Withney test; a p value <0.05 was considered as significant (*).

RESULTS. 123I-Annexin V myocardial uptake is significantly increased in the LPS group compared to control group; there is no significant difference between the septic groups .

%ID/g	Control	LPS	LPS+CsA
Mean + – SD	0.05 + -0.01	0.18 + -0.06 *	0.19 + -0.05 NS
Mortality	0%	25%	0%

123I-Annexin V myocardial uptake

CONCLUSION. Our results confirm that endotoxaemia is associated with significant myocardial apoptosis but fail to demonstrate that CsA can reduce the cell death signal detected by 123I-Annexin V . In spite of its action on MPT and its myocardial dysfunction reducing effect in septic rats [4], CsA provides no myocardial protection in this model . A reducing effect of CsA on endotoxin-induced mortality is not excluded but remains to be demonstrated. Further investigations are needed to clarify the effect of CsA on the inflammatory responses due to endotoxaemia.

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SEPSIS INDUCED MESENTERIC TPA RELEASE IS INHIBITED BY A PROGRESSIVE INDUCTION OF LIVER DERIVED PAI-1

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INTRODUCTION. Sepsis induced alterations in hemostasis with dysbalances in fibrinolysis may lead to capillary obstruction due to fibrin deposition. The aim was therefore to investigate regional net fluxes of the fibrinolytic enzyme tissue-type plasminogen activator, tPA, and its main inhibitor plasminogen activator inhibitor type-1, PAI-1, in response to endotoxemia.
METHODS. Anesthetized pigs (n=8) were instrumented for registration of cardiac output (CO, thermodilution) and portal (QPV), hepatic (QHA) and renal (QRA) blood flows (ultrasound flowmetry, Transonic). Blood samples were collected from the aorta and pulmonary artery as well as the portal, hepatic and renal veins. After baseline registrations, all animals were subjected to an *E. coli* endotoxin infusion for 90 min, followed by a volume/norepinephrine resuscitation for 210 min targeting baseline CO levels. Plasma concentrations of both total and active tPA and PAI-1 were determined as described [1, 2] and net organ fluxes (ng/min) were calculated based on in-/outflowing plasma concentrations and local plasma flow [1].
RESULTS. Endotoxemia induced a low CO state and a decrease in QPV. Total liver blood flow was preserved due to a concomitant increase in QHA. During resuscitation CO and QPV were restored to baseline values. Systemic plasma levels of total tPA increased over time during endotoxemia, peaking at 90 min, whereupon a decline occurred. However, plasma levels of total tPA had not returned to baseline values at the end of the registration period (300 min). Changes in systemic levels of active tPA mirrored changes in total tPA. A marked (8-fold) increase in mesenteric net release of total tPA was observed. This response was paralleled by a pronounced increase in hepatic uptake of tPA. PAI-1 described a different response to endotoxemia. By the end of the experiment plasma levels of both active and total PAI-1 increased. In contrast, no significant net fluxes of PAI-1 were observed across any of the investigated vascular beds except for the hepatic vascular bed, where a net release of both total and active PAI-1 occurred at approximately 150 min. Hepatic PAI-1 release rates then increased progressively.
CONCLUSION. Endotoxemia induced a marked increase in mesenteric release of tPA which however was not entirely responsible for the increase in systemic plasma level of tPA. The results indicate that this profibrinolytic response at later stages are counteracted by increased plasma levels of PAI-1 and this increase is mainly derived from the hepatic vascular bed. Thus, patients with altered regional endothelial functions or liver capacity prior to a septic challenge can be expected to demonstrate varying susceptibility to thrombotic events.
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ABDOMINAL LYMPH FLOW IN ENDOTOXIC SEPTIC MODEL

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INTRODUCTION. During sepsis increased vascular permeability results in fluid extravasation and edema. Lymphatics contribute in draining interstitial fluid from the abdomen to central circulation, but several factors (outflow venous pressure, pattern of mechanical ventilation) can act upon flow in the thoracic duct (1, 2). We have tested if lymph flow is affected by endotoxin infusion under different ventilatory conditions.

METHODS. 9 anesthetized pigs (29.4±3 Kg) were studied. Septic damage was induced by continuous infusion of endotoxin (lipopolysaccharide *E.Coli*, LPS). Abdominal lymph flow was continuously recorded by an ultrasound flow probe positioned on the thoracic duct at the diaphragm level; hemodynamics, respiratory system data, BGA and intra-abdominal pressure (IAP) were registered. During the first 2.5 hours of LPS infusion animals were ventilated in volume controlled mode TV 10-11 ml/Kg, RR 20 bpm, PEEP 5, FiO_2 0.5; during the next 2 hours animals were divided in group 1 (control, PEEP 5), 2 (PEEP 15) and 3 (spontaneous breathing, CPAP PEEP 5).

RESULTS. During LPS infusion lymph flow significantly increased from 2.3 to 4.6 ml/min ($p<0.05$), cardiac output and compliance decreased from 3.4 to 2.8 l/min * and 32 to 21 ml/cmH_2O * respectively, while mean pulmonary artery pressure and IAP increased from 20 to 47 mmHg * and 13 to 20 cmH_2O * (* $p<0.05$). In all the pigs a positive correlation was found between IAP and lymph flow (mean Pearson´s coefficient 0.59). No correlation was found between lymph flow and central venous pressure and airway pressure (mean Pearson´s coefficient 0.20 and 0.13). In group 1 and 2 lymph flow changes averaged -9% and +19% (versus value before randomization). CPAP increased lymph flow by 55%.

CONCLUSION. Lymph flow from the abdomen increases during LPS infusion: role of lymphatics in draining abdominal fluid could thus be significant during sepsis (~ 280 ml/h are drained). These preliminary results suggest that spontaneous breathing could improve lymphatic flow from the abdomen. Despite the following rise in intra-thoracic pressure, increase of PEEP is not associated with lymph flow reduction. Animals in PEEP 15 group have however shown different patterns of response, and more data are needed to clarify this aspect.

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ANTITHROMBIN ATTENUATES LEUKOCYTE-INDEPENDENT PLASMA EXTRA–VASATION DURING ENDOTOXEMIA.

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INTRODUCTION. Antithrombin has been shown to reduce mesenteric venular leukocyte interactions and intestine injury in a leukocyte-dependent model of endotoxemia (1). However, endothelial damage during early endotoxemia has been shown to be leukocyte-independent (2). The role of antithrombin in this setting is still unknown. Therefore, it was the aim of the study to investigate the effects of antithrombin on leukocyte-independent endothelial damage.

METHODS. In male Wistar rats, microvascular permeability (MP) and leukocyte-endothelial-interaction (leukocyte rolling, LR) were determined in mesenteric postcapillary venules using intravital microscopy at baseline, 60 and 120 min after start of a continuous infusion of endotoxin (ETX; 2mg/kg/hr, E.coli $O_2$6:B6) (group A, n=8). Therefore animals were laparotomized and the mesentery was exposed beneath an in-vivo videomicroscope. MP was measured using fluorescein isothiocyanate (FITC) labelled albumin. Leukocyte-endothelial interaction was blocked in all groups by fucoidin (25 mg/kg b.w.), a L-selectin-binding carbohydrate, 10 min before laparotomy. Animals in group B (n=8) received antithrombin (Kybernin®, Aventis-Behring, Germany; 500 IE/kg b.w.) prior to baseline measurement and additionally to the procedure described above. Animals in group C (n=8) received equivalent volumes of NaCl 0.9 % instead of antithrombin and endotoxin. Statistical analysis was performed using two-way repeated measures ANOVA followed by the Scheffé test. A p-value <0.05 was considered significant.

RESULTS. In groups A-C, fucoidin prevented LR during the entire experiment. However, in all groups MP increased significantly, starting at 60 min. Animals in group A were characterized by a stronger increase in MP and showed significantly higher values in MP in comparison to groups B and C at 120 min. There were no significant differences in MP between groups B and C.

CONCLUSION. Leukocyte-independent endothelial damage during early endotoxemia is attenuated by antithrombin.

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LEUKOCYTE-INDEPENDENT ENDOTHELIAL DAMAGE DURING EXPERIMENTAL ENDOTOXEMIA. ROLE OF NITRIC OXIDE

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INTRODUCTION. Endothelial damage during early endotoxemia has been shown to be leukocyte-independent (1). PAF (platelet-activating factor)- and serotonin-receptor antagonism has been shown to reduce leukocyte-independent macromolecular leakage significantly (2, 3). Nevertheless, the exact mechanisms involved in leukocyte-independent endothelial dysfunction are unknown. Therefore, it was the aim of the study to investigate the effects of nitric oxide (NO) on leukocyte-independent endothelial damage during endotoxemia

METHODS. In male Wistar rats, microvascular permeability (MP) and leukocyte rolling (LR) were determined in mesenteric postcapillary venules using intravital microscopy at baseline, 60 and 120 min after start of the experiment. In all groups, leukocyte-endothelial interaction was blocked by fucoidin. Rats were randomized into 7 groups, 11 animals each. The experiments were divided into two parts. Part I (NO-inhibitor): In group A, the mesentery was superfused with a L-NAME superfusion (100 mmol/L) combined with a continuous infusion of endotoxin (ETX; 2mg/kg/hr) after baseline measurement. Group B received a L-NAME superfusion of the mesentery combined with a continuous infusion of saline 0.9 %. Groups C and D were treated like groups A and B but without L-NAME. Part II (NO-donator): Group X received SIN-1 (initial bolus of 1 mg/kg b.w. followed by 0.5 mg/kg b.w. after 60 min-measurement) followed by a continuous infusion of endotoxin (ETX; 2mg/kg/hr). Group Y was treated similar to group C and group Z was treated similar to group D. Statistical analysis was performed using two-way repeated measures ANOVA followed by the Scheffé test. A p-value < 0.05 was considered significant.

RESULTS. Fucoidin prevented leukocyte-endothelial-interaction in all groups. Part I: PE increased in all groups, being significant in group D at 120 min ($p<0.05$ vs. baseline) and being significant in groups A-C starting at 60 min. Animals in group D were characterized by a slighter increase in MP and showed significantly lower values in MP in comparison to groups A and B at 60 min, and to groups A-C at 120 min. There were no significant differences in MP between groups A-C at 120 min. Part II: PE increased in all groups being significant in group Z at 120 min ($p<0.05$ vs. baseline) and being significant in groups X and Y starting at 60 min. Animals in group Y were characterized by a stronger increase in MP and showed significantly higher values in MP in comparison to groups X and Z at 120 min. There were no significant differences in MP between groups X and Z.

CONCLUSION. Leukocyte-independent endothelial damage during early endotoxemia is a nitric-oxide mediated event.

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NITRIC OXIDE SYNTHASE PROTEINS IN THE SMOOTH MUSCLE OF MESENTERIC ARTERIES IN HUMAN SEPTIC SHOCK

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INTRODUCTION. Overproduction of nitric oxide (NO) is thought to be a principal cause of the hypotension of septic shock. Two nitric oxide synthase (NOS) enzymes have been described in blood vessels: endothelial NOS (eNOS) and inducible NOS (iNOS). Constitutive activity of eNOS in the endothelium is a major determinant of blood vessel tone in health; however, in experimental sepsis it appears endothelial eNOS expression is reduced while smooth muscle iNOS expression is increased (1). In contrast, another model of human sepsis found an increase in eNOS but not iNOS in the vessel wall (2). To resolve this discrepancy, we studied eNOS and iNOS protein concentrations in arterial smooth muscle (ASM) from patients with clinical sepsis.

METHODS. ASM was isolated from mesenteric vessels from patients undergoing bowel resection for perforated viscus (who in the perioperative period met the ACCP/SCCM criteria for septic shock), and from controls with bowel cancer. After mechanical removal of endothelium and adventitia, the tissue was homogenised in protease inhibitor and frozen until sufficient samples had been accumulated. Western blotting was performed under reducing conditions, with membranes incubated in 1:2000 (iNOS) or 1:500 (eNOS) primary antibody followed by 1:2000 peroxidase labelled secondary antibody. Protein bands were quantified by computer analysis of the chemiluminescence detection film, then normalised to the protein concentration of the sample prior to dilution.

RESULTS. eNOS protein was increased in arterial smooth muscle from patients with septic shock (control 39.3 ∂ 14.7 units/mg, septic 96.5 ∂ 27.1 units/mg; n=13 controls and 11 septics; $p = 0.04$, Student's t test). In contrast, there was no increase in concentration of iNOS; indeed iNOS protein was only detectable in ASM from 2 control and 3 septic patients.

CONCLUSION. We suggest that overexpression of eNOS, rather than iNOS, in the arterial smooth muscle of patients with septic shock may be responsible for the hypotension observed in these patients.

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THE INHIBITORY EFFECT OF VASOACTIVE DRUGS ON INTESTINAL MOTILITY IS REDUCED DURING ENDOTOXINEMIA

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INTRODUCTION. Data published in the literature concerning the effect of sepsis on intestinal motility found a reduction as well as a stimulation of intestinal motility . The settings used are mostly in vivo settings, and therefore not usable to investigate intestinal motility independent from circulatory changes. The aim of our study was to evaluate the direct effect of endotoxinemia on guinea-pig small bowel motility in vitro, independent from circulatory changes, and in a second step to evaluate the effect of vasoactive drugs on motility of these septic animals.

METHODS. Two groups of guinea-pigs received 1 mg/kg E. coli LPS intraperitoneally 4 or 20 hours before the experiments started. In the following hours the animals developed severe symptoms of sepsis. A control group did not receive LPS before the experiments started. The small bowel of sacrificed guinea-pigs was excised, cleaned and kept in Tyrode's solution. After a resting period segments of 8 cm length were set up in parallel organ bathes containing oxygenated Tyrode's solution. Peristaltic contractions were elicited by perfusion of the segments with Tyrode's solution at a rate of 0.5 ml/min, against an aboral resistance of 400 Pascal. The intraluminal pressure increased gradually until it reached a pressure threshold (PT) which triggered peristaltic contractions. These contractions were recorded via a pressure transducer at the aboral end of the segments. Increasing concentrations of epinephrine, norepinephrine, dopamine, dobutamine, clonidine and dexmedetomidine were cumulatively added to the organ bath at 15 min intervals. Each drug was tested on 8 different segments. Statistics was performed using NCSS for Windows, one-way and two-way ANOVA for repeated measures were used, p values <0.05 were considered statistically significant.

RESULTS. In the control group all tested vasoactive drugs had a dose- and substance-dependent inhibitory effect on peristalsis. Higher concentrations of all tested substances led to a complete block of peristalsis. 4 hours after LPS application a pronounced reduction of the inhibitory effects of clonidine, epinephrine, norepinephrine and dopamine were found. The reduced inhibitory effect of dexmedetomidine was not significant. 20 hours after LPS application the inhibitory effect was reduced again, but for most substances this reduction was not statistically significant. Dobutamine was the only tested substance with a more pronounced effect after 4 hours than after 20 hours. Endotoxinemia per se did not affect small bowel motility in vitro.

CONCLUSION. A possible explanation for the controversy to in vivo data demonstrating an inhibitory effect on peristalsis might be that intestinal ischemia is a common event during sepsis, and ischemia in turn might cause paralysis. A described reduced sensitivity of alpha-adrenoceptors during sepsis, or a central effect of LPS additionally inhibiting peristalsis (1), might also be responsible for our findings.

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THE EFFECT OF SEPSIS ON THE KEY GLYCOLYTIC ENZYMES IN A RODENT MODEL OF ORGAN FAILURE

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INTRODUCTION. Mitochondrial dysfunction may be implicated in sepsis-induced multi-organ failure. Glycolytically-generated ATP may thus be an important alternative energy source if aerobic respiration is compromised. Little is known about glycolysis during sepsis, though both up- and down- regulation are reported[1,2]. We therefore examined changes in glycolytic activity in a long-term sepsis model.

METHODS. An instrumented, fluid-resuscitated, faecal peritonitis rat model was used. This has a 72-hour mortality rate of approx. 50%. Septic (n=57) and sham (n=35) rats were sacrificed at various time points (0, 24, 48, 72h) and liver samples harvested and assayed for maximal activity of the rate-limiting glycolytic enzymes, hexokinase (HK), phosphofructokinase (PFK) pyruvate kinase (PK).

RESULTS. Sham-operated animals showed significant up-regulation of all enzymes at 48 h, returning towards normal by 72 h. Both septic HK ($p<0.04$) and PK ($p<0.0004$) revealed down-regulation at 48h compared to sham.Data shown as mean (SE). *$p<0.05$ sham v septic, repeated measures 2-factor ANOVA

	0Hrs	24Hrs	48Hrs	72Hrs
HK sham	0.035(0.002)	0.039 (0.003)	0.092(0.016)	0.066(0.007)
HK septic*	-	0.046(0.003)	0.063(0.004)	0.067(0.008)
PK sham	1.167(0.144)	0.769(0.039)	1.1(0.06)	0.72(0.025)
PK septic*	-	0.805(0.05)	0.802(0.05)	0.68(0.028)

Activity shown in pmoles/min/mg of protein

CONCLUSION. We demonstrate an initial rise (albeit non-significant) then significant down-regulation in two rate-limiting glycolytic enzymes during sepsis. The lack of difference at 72 h may reflect prior demise of the severely ill animals. Whether the degree of glycolytic down-regulation is related to subsequent death requires further study. We presume the interesting finding of up-regulation seen in the sham animals to be a response to surgery and/or fluid loading.

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IN VIVO AND IN VITRO DIFFERENCES IN RESPONSES TO CATECHOLAMINES AND VASOPRESSIN IN RAT MODELS OF LPS

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INTRODUCTION. Recent studies have shown that low-dose vasopressin infusion or terlipressin bolus (TP, its long acting analogue; O'Brien, 2002) restores blood pressure and reduces norepinephrine (NE) requirements in septic shock. However they have no effect upon blood pressure in non-septic patients. Exact mechanisms underlying this hyperreactive effect in sepsis patients remain unknown. We chose to investigate this using our established in vivo and in vitro models of endotoxic shock in rats.
METHODS. *In vivo* – spontaneously breathing anaesthetised male Wistar rats was given either saline (sham) or endotoxin (LPS) (Klebsiella 40mg kg^{-1}) over 30 mins and then fluid resuscitated with colloid 25mls $kg^{-1}hr^{-1}$ for 210 mins. At 120 mins either a bolus of TP (1.5mg kg^{-1}) or a bolus and infusion of NE (0.5mg kg-1 and 1mg kg hr^{-1}) was administered. Measurement of flow and pressure (mean arterial pressure – MAP) were made from appropriately sited probes and transducers. *In vitro* – rings of rat mesenteric artery (RMA) were harvested, cleaned and incubated for 20 h with or without 1mg ml^{-1} LPS (S. Typhosa). They were then mounted in organ baths for measurement of isometric tension. Cumulative concentration-response curves to phenylephrine (PE: 10^{-9} to 10^{-5} M) or vasopressin (VP: 10^{-12} to 10^{-6} M) were then constructed. Statistical analysis was by ANOVA.
RESULTS. In vivo – while NE had a significantly greater effect upon MAP in shams compared with LPS rats (P=0.042), TP caused a greater increase in LPS animals than shams. A bolus of TP lasted approximately 75 mins. In vitro – LPS significantly depressed contractile responses to PE compared to control tissues (max contraction controls – 1.35±0.14g, LPS – 0.48±0.11g, P<0.001, ANOVA). However there was virtually no contractile response to VP even in control tissues after 20 h incubation.

			MAP	(mmHg)	mean±sem	
Time (mins)	120	135	150	180	210	240
Sham + NE (n=3)	107±10	156±5.7	147±2.7	143±4.7	140±6.4	142.7±8.7
LPS + NE (n=3)	97±3	107±5.2	107±6.7	104±6.2	101.3±5.9	101±7.2
Sham + TP (n=3)	95±2.1	114±4.3	116±4.9	107±2.9	101.7±2.9	102.7±3.5
LPS + TP (n=6)	92±5.1	122±5	126±7.1	103±10	110.3±8.3	87.3±7.8

CONCLUSION. Vascular hyporeactivity and decreased responsiveness to catecholamines has been demonstrated in both *in vivo* and *in vitro* models. However vasopressin (or analogue) showed *in vivo* hyperresponsiveness in sepsis, but no effect in *vitro*. We have no explanation at present for this interesting paradox that warrants further investigation.
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AUGMENTED PRO-INFLAMMATORY RESPONSE AFTER TRAUMA WITH SECONDARY SEPSIS: GOOD OR BAD?

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INTRODUCTION. The cytokine cascade activated in response to injury consists of a complex biochemical network with diverse effects on the injured host. Leukocyte activation after trauma is essential for inflammation. It is a multistep process in which chemokine – interleukin (IL)-8 has pivotal role. In two-hit hypothesis, sepsis represent a second insult to a previously injured and primed host, converting a low-grade or regulated host response into an accelerated or dysregulated host response, triggering new or progressive organ dysfunction (1). Aim of this study was to assess pro-inflammatory response to trauma with or without sepsis as a second insult.

METHODS. Twenty five patients with severe trauma (explosive and sclopetarious) who developed sepsis and 10 patients with same kind of severe trauma without sepsis were enrolled in this study. In the trauma+sepsis group 21 patients developed multiple organ dysfunction syndrome (MODS) and 14 died. In trauma group 4 developed MODS and 2 died. Blood was drown on the first, third and fifth day of trauma. Concentrations of IL-8, IL-12, tumor necrosis factor (TNF)-alpha and interferon (IFN)-gamma were determined in plasma using ELISA assays.

RESULTS. When compared trauma+sepsis group with trauma group we found statistically highly significant difference ($p<0.01$) in IL-8 and IFN-gamma and statistically significant difference ($p<0.05$) in TNF-alpha concentrations; mean values of IL-8 were 230-fold higher, IFN-gamma 360-fold higher and TNF-alpha 17-fold higher in patients with trauma with sepsis. IL-12 was not statistically different ($p>0.05$) between two groups. When compared MODS group with group without MODS, we found statistically highly significant difference ($p<0.01$) in IL-8 and TNF-alpha concentrations; mean values of IL-8 were 60-fold higher and TNF-alpha 43.5-fold higher in patients with MODS; IL-12 and IFN-gamma were not statistically different ($p>0.05$) between two groups. When compared non-survivors with survivors, we found statistically highly significant difference ($p<0.01$) in IL-8 and TNF-alpha and statistically significant difference ($p<0.05$) in IL-12 concentrations; mean values of IL-8 were 2.3-fold higher in non-survivors, mean values of TNF-alpha were 2.2-fold higher in survivors, IL-12 was also higher in survivors. IFN-gamma was not statistically different ($p>0.05$) between two groups.

CONCLUSION. There is augmented pro-inflammatory response after trauma with secondary sepsis. High concentrations of IL-8 and TNF-alpha indicated higher severity (MODS). But, fatal outcome was predicted with high concentrations of IL-8 only; survivors had higher concentrations of TNF-alpha and IL-12. Therefore, pro-inflammatory response was partly beneficial and partly detrimental to the host.

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CYTOKINES IN PATIENTS WITH CARDIOGENIC SHOCK: ARE LEVELS ASSOCIATED WITH PROGRESSION TO SEPTIC SHOCK?

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INTRODUCTION. High cytokine levels in patients admitted to the Emergency Department are associated with an increased incidence of sepsis/septic shock. Patients with cardiogenic shock (CS) who often develop sepsis during ICU-stay,have not been partICUlarly studied. We studied whether plasma levels of cytokines are better predictors of sepsis/septic shock than routinely determined laboratory parameters.

METHODS. IL-1,IL-6 and IL-10 plasma levels were determined in 51 pts with CS(Cardiac index <2.2 L/min/m², PCWP >15, mean arterial pressure <60mmHg or need for vasopressor therapy and signs of organ hypoperfusion) on admission to the ICU (median 16hrs after shock onset). 36 patients who were not surgically treated during ICU stay were eligible for the study and evaluated for development of sepsis or septic shock within 1 week after onset of CS. C-reactive protein (CRP) levels and white blood cell (WBC)-counts were routinely evaluated once daily in all patients until discharge. Data are given as median and interquartile range.

RESULTS. All pts with CS were free of demonstrable infection at time of blood sampling. Nevertheless 60% had a CRP-level >5mg/dl at time of enrollment.11 pts (31%) developed septic shock within 1 week after onset of CS. Pneumonia (54%, n=6) and catheter related infections (27%, n=3) were the leading causes of sepsis. Sepsis after CS was not associated with a higher mortality rate (82% vs. 80%, p=NS) and SIRS that was encountered in 69% of CS pts at the time of blood sampling did not predispose for development of sepsis (64 vs. 72%, p=NS).CRP levels,and WBC-counts as well as IL-1, IL-6 and IL-10 plasma levels on admission to the ICU did not differ significantly between CS-pts who developed sepsis and CS-patients without sepsis (IL-1: 0.4pg/ml [0-1.3] vs. 1.1pg/ml [0.2-1.8], p=0.25; IL-6: 303.4pg/ml [95.8-324.1] vs. 195.6 [66.5-372.5], p=0.74; IL-10: 11.3pg/ml [3.0-43.8] vs. 16.7pg/ml [8.0-57.3], p=0.47). In pts who survived for more than 24hrs (n=28) the absolute CRP levels 24hrs after admission (CRP_{24hrs}) and the increase in CRP levels over 24hrs following ICU admission (DCRP) were significantly higher in pts who developed sepsis as compared to pts without sepsis. (CRP_{24hrs}: 23.2mg/dl [11-35.6] vs. 9.4 [5.9-13.1], p=0.002; DCRP: 9.7mg/dl [7.5-11.8] vs. 4.1[0.5-5.6], p=0.011). A DCRP >6.5mg/dl in 24hrs was more sensitive than an absolute CRP level >20 mg/dl 24hrs after ICU-admission for predicting sepsis (82 vs. 73%), but both parameters had equal specificity (88%).

CONCLUSION. Although many pts with CS exhibit elevated CRP levels the increase in CRP over 24hrs ($DCRP_{24hrs}$)is a valuable parameter to identify pts at risk for sepsis. Single-point determination of cytokines on admission to the ICU is not superior to follow-up determinations of CRP for predicting sepsis.

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TISSUE OXYGEN ASSESSMENT IN INTENSIVE CARE PATIENTS WITH SEPSIS AND SEPTIC SHOCK

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INTRODUCTION. In patients with shock hypoxia is considered to be the most important cause of organ failure and death. The goal of treatment therefore is to restore tissue oxygen delivery (tDO_2). Due to impaired oxygen extraction in distributive (septic shock) the relation between tDO_2 and tissue oxygenation is less conclusive. Direct measurement of tissue oxygen pressure (ptO_2) could be of great importance in gaining a better insight in tissue oxygenation in these patients. Previously published data concerning ptO_2 in patients with sepsis/septic shock are contradictory (1,2). Furthermore the techniques used were not easily applicable at the bedside.
METHODS. In a prospective observational study we performed bedside ptO_2 measurements in 8 patients with sepsis/septic shock to gain insight in ptO_2 values and their dynamic changes related to the course of the illness, as well as investigating the practical applicability of tissue oxygen measurement in the ICU setting. PtO_2 was measured continuously during the course of the illness using polarographic Clark-type O_2 electrodes (LICOX Catheter Measurement System, GMS), which were placed subcutaneous in the upper arm. Disease progression over time was expressed as the daily calculated Sequential Organ Failure Assessment (SOFA) score.
RESULTS. Five men and 3 women with septic shock n=6 or sepsis n=2 were included. The median (range) age was 39 years (21-85), median APACHE-score on the day of admission was 15 (9-29), median duration of ptO_2 measurement per patient was 5,0 days (3-7). In none of the patients technical problems were encountered during the ptO_2 measurements. The first day of measurement the median ptO_2 of the eight patients was 49 (18-92) mmHg. In the six surviving patients the SOFA score decreased over time and this was associated with a concomitant decrease in ptO_2 to a median of 30 (16-69) mm Hg. In the 2 nonsurvivors an increasing SOFA score was associated with an increase in the mean ptO_2 to 57 mmHg on the day of death. In seven patients linear regression analysis showed a positive correlation between the daily SOFA scores and the daily mean ptO_2: r= 0.71, 0.75, 0.88, 0.93, 0.85, 0.87, 0.61. In one patient no correlation was found.
CONCLUSION. Bedside ptO_2 measurements in the ICU using the LICOX measurement system are easily performed. PtO_2 in septic patients is variable but changes with the clinical course reflected by the SOFA score: clinical improvement was associated with a decrease in ptO_2 while deterioration was associated with an increase of ptO_2. These findings suggest that in patients with septic shock decreased oxygen utilisation may play a more important role than tissue hypoxia as such.
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MACROPHAGE MIGRATION INHIBITORY FACTOR (MIF) A NEW MARKER OF SEVERITY IN SEPSIS?

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INTRODUCTION. Macrophage migration inhibitory factor (MIF) has been proposed as an important mediator of the innate immune system. MIF is released by pituitary, macrophages and T-cells in response to different stimulus, including infection and stress. Recently it was demonstrated that MIF knockout mice or mice treated with anti-MIF antibodies were protected from endotoxemia or septic shock.

METHODS. To precise the diagnostic value of macrophage migration inhibitory factor (MIF) as a marker of severity in patients with sepsis and to determine relations between MIF and Interleukin 6 (IL-6), we conduced a prospective, observational, cohort study, in two general intensive care units.

RESULTS. We analyzed 20 patients with septic shock, 17 patients with sepsis, and 10 healthy volunteers. The median MIF serum level was significantly higher in septic shock patients (2.01 ng/ml, range 0.77-12.0) than in sepsis patients (1.10 ng/ml, range 0.31-5.11) or in healthy volunteers (0.45 ng/ml, range 0.28–1.54). There was a direct correlation between MIF and IL-6 concentrations ($r=0.693$, $p<0.01$). The area under the curve (AUC) of the receiver-operating characteristic (ROC) for prediction of septic shock was 0.81 ($p<0.01$) for MIF and 0.85 ($p<0.01$) for IL-6. The AUC under the ROC curve for prediction mortality was 0.714 ($p<0.05$) for MIF and 0.707 ($p<0.05$) for IL-6.

CONCLUSION. In this trial we found significant elevated serum levels of MIF in patients with septic shock and sepsis. Moreover, MIF levels were discriminative for septic shock and mortality, and had a direct correlation with levels of IL-6 with a similar diagnostic accuracy. In conclusion, MIF appear to be a promissory marker of severity in sepsis.

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HUMAN MONOCYTE HLA-DR EXPRESSION IS ALTERED IN SEPTIC BUT NOT IN CARDIOGENIC AND HEMORRHAGIC SHOCK

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INTRODUCTION. Immunoparalysis, including monocyte deactivation assessed by decrease in HLA-DR expression, has been repeatedly described during the first stage of human septic shock (SS) (1). In order to evaluate the specificity of monocyte deactivation in SS, we compared HLA-DR expression between severe shock from various origin [SS, cardiogenic shock (CS), hemorrhagic shock (HS)] and sepsis (S) and healthy volunteers (V). Severity of shock was analysed by lactate level values and catecholamine use.

METHODS. After approval of the hospital's ethics committee, 82 patients were enrolled in a bicentric study. Monocyte HLA-DR surface expressed as % of CD14+ monocytes expressing HLA-DR, was determined at day 1 (D1), D3 and D7 by flow cytometric analysis. Data are presented as mean ∂ SEM, statistics were performed by Anova test followed by Fisher test.

RESULTS. As previously reported, HLA-DR expression is severely decreased at D1 and D3 in SS. Despite the presence of lactic acidosis and similar use of catecholamines in CS and HS, HLA-DR expression remained normal in those 2 groups. However, in 5 patients admitted for CS, HLA-DR eventually decreased when septic shock occurred in those patients.

	Age (years)	SAPS II	Lactate (mmol/L)	Catecholamine / Mortality (n / n)	D1	% HLA-DR D3	D7
SS (n=30)	61 ∂ 16	57 ∂ 20	4.8 ∂ 2.7	30¤ / 11¤	42 ∂ 26 ¤	46 ∂ 27 ¤	60 ∂ 24
S (n=19)	51 ∂ 15	29 ∂ 9 *	1.8 ∂ 1.2	0 / 1	75 ∂ 19	79 ∂ 18	76 ∂ 26
HS (n=10)	42 ∂ 14 *	42 ∂ 17	12.0 ∂ 8.2 *	6 / 1	74 ∂ 20	75 ∂ 19	84 ∂ 11
CS (n=15)	58 ∂ 13	49 ∂ 14	4.8 ∂ 3.1	9 / 5	75 ∂ 15	65 ∂ 25	67 ∂ 16
V (n=8)	61 ∂ 21	-	-	-	91 ∂ 5	-	-

* $p<0.05$ ¤ $p<0.01$

CONCLUSION. Our data confirms the transient monocyte deactivation in SS and show that monocyte deactivation is a specific marker of SS since no alteration in HLA-DR expression was observed in CS and HS.

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MODIFICATION OF HIGH DENSITY LIPOPROTEIN IN SEPTIC SHOCK: RELATIONSHIP TO OUTCOME

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INTRODUCTION. High Density Lipoprotein (HDL) modulates the inflammatory response to injury and infection via several pathways. HDL also directly binds and neutralises LPS. Administration of reconstituted HDL reduces cytokine release and attenuates shock in experimental endotoxaemia (1). The HDL associated enzymes paraoxonase (PON) and lecithin cholesterol acyl transferase (LCAT), destroy oxidised lipids that induce inflammatory changes in vascular endothelium (2). Incorporation of Serum Amyloid A (SAA), an acute phase protein, into the HDL particle during the inflammatory response, may displace these protective enzymes producing a particle with proinflammatory properties (3). Alterations in HDL composition may, therefore, be implicated in dysregulation of the inflammatory response and could influence outcome from septic shock.
METHODS. Patients with septic shock, not given TPN or propofol, were recruited. APACHE II scores and ICU mortality were recorded. Plasma and serum samples were taken within 48 hours of the onset of shock. HDL cholesterol was measured by microenzymatic colorimetric assay. Apolipoprotein AI (APO AI) was quantified by liquid phase radioimmunoassay. PON activity was determined by measuring the rate of paraoxon hydrolysis and described as percent of a control serum pool. LCAT activity was quantified by measuring the esterification rate of ^{14}C labelled cholesterol. SAA was measured by ELISA. Results were compared with those of a pool of healthy volunteers and between survivors and nonsurvivors. (Mann Whitney U test).
RESULTS. 20 patients were recruited. There were 13 survivors (S) and 7 nonsurvivors (NS). PON activity was significantly higher in S than NS: 47.6 (11.5-135.6) vs. 22.6 (5.7- 39.43), $p<0.02$. SAA concentration was significantly higher in S than NS: 1915 (90.9-14300) vs. 249 (98.1-1410), $p<0.05$. SAA concentration was negatively correlated with APACHE II scores ($r= -0.56$, $p=0.01$, Spearman's rank correlation coefficient).

	Volunteers (median, range)	Septic Shock (median, range)	p value
HDL Cholesterol (mmol/l)	0.98 (0.4-2.6)	0.22 (0.07-1.13)	<0.001
APO AI (g/l)	1.4 (1.02-1.92)	0.28 (0.11-0.94)	<0.001
PON Activity (% of pool)	102.1 (38.4-170.4)	37.4 (5.7-135.6)	<0.003
LCAT activity (nmol/l/hr)	137.5 (66.9-212.6)	20.3 (2.3-55.5)	<0.001
SAA (mcg/ml)	3.4 (1.17-33.2)	552.6 (90.9-14300)	<0.001

CONCLUSION. Septic shock is associated with profound alterations in HDL function and composition which could contribute to an uncontrolled systemic inflammatory response and oxidant stress. Some of theses changes are related to severity of illness and outcome.
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ANTI-INFLAMMATORY CYTOKINES AS PREDICTORS OF SEVERITY AND OUTCOME IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Severe trauma and sepsis are the major sources of morbidity and mortality despite the rapid development of intensive therapy. Studies have indicated that there are marked alterations in immune response in patients exposed to major trauma or prolonged surgical procedures, including altered pro- and anti-inflammatory mediator/cytokine release (1). Traumatic injury results in profound immunosuppression which predisposes the patients to sepsis and/or multiple organ dysfunction syndrome (MODS). Aim of this study was to assess the prognostic value of anti-inflammatory cytokines: interleukin (IL)-1 receptor antagonist (IL-1ra) , IL-4, IL-10 and transforming growth factor (TGF)-beta 1 regarding severity and outcome in patients with trauma and sepsis, trauma only and sepsis only.

METHODS. Twenty five patients with severe trauma (explosive and sclopetarious) who developed sepsis, 10 patients with same kind of severe trauma without sepsis and 5 patients with severe sepsis were enrolled in this study. Twenty nine patients developed MODS (of all 40 patients), 19 died. Blood was drown on the first, third and fifth day of trauma or sepsis. Concentrations of IL-1ra, IL-4, IL-10 and TGF-beta 1 were determined in plasma using ELISA assays.

RESULTS. When compared MODS group (regardless of initiating insult – trauma or sepsis) with group without MODS, we found statistically highly significant difference ($p<0.01$) in IL-1ra and IL-10 concentrations; mean values of IL-1ra were 6-fold higher and IL-10 70-fold higher in patients with MODS; IL-4 and TGF-beta 1 were not statistically different ($p>0.05$) between two groups. When compared non-survivors with survivors, we found statistically highly significant difference ($p<0.01$) in IL-1ra and IL-10 concentrations; mean values of IL-1ra were 2.7-fold higher and IL-10 1.4-fold higher in non-survivors; IL-4 and TGF-beta 1 were not statistically different ($p>0.05$) between two groups. When compared trauma+sepsis group with trauma group, we found statistically highly significant difference ($p<0.01$) in IL-1ra and IL-10 concentrations, they were higher in trauma+sepsis group (IL-1ra 3.7-fold, IL-10 42-fold). IL-4 and TGF-beta 1 were not statistically different ($p>0.05$) between two groups. When compared trauma+sepsis group with sepsis group and trauma group with sepsis group, we found no statistically significant difference in either one of 4 anti-inflammatory cytokines.

CONCLUSION. Our study shows that IL-1ra and IL-10 are excellent predictors of severity and outcome of critical illness; higher concentrations were found in group with more severe clinical status (MODS) and in non-survivors. IL-4 and TGF-beta 1 had no significance as predictors of severity and outcome what so ever.

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TROPONIN AS A RISK FACTOR FOR MORTALITY IN CRITICALLY ILL PATIENTS WITHOUT ACUTE CORONARY SYNDROMES

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INTRODUCTION. Cardiac troponins are used as specific markers for the diagnosis of acute coronary syndromes. Recent studies reported a considerable number of critically ill patients without acute coronary syndromes being troponin-positive. There is little data whether elevated troponin is a risk factor in this patient population and what mechanism may cause this phenomenon.

METHODS. Fifty-eight patients admitted to two medical intensive care units for reasons other than acute coronary syndrome were consecutively included and analyzed according to their troponin status. Thirty-day mortality, left ventrICUlar ejection fraction, the presence or absence of underlying coronary artery disease, and a panel of inflammatory cytokines were compared between troponin-positive and troponin-negative patients.

RESULTS. Thirty-two of 58 critically ill patients (55%) without evidence for an acute coronary syndrome were troponin-positive. Positive troponin levels were associated with higher mortality (22.4% vs. 5.2%, $p < 0.018$) and lower left ventrICUlar ejection fraction ($p = 0.0006$). Troponin-positive patients had significantly higher median levels of tumor necrosis factor a, its soluble receptor and interleukin-6. A subgroup of ten aplastic patients was troponin-negative at study entrance. Three became troponin-positive during leukocyte recovery and subsequently died, whereas all the others stayed troponin-negative and survived.

CONCLUSION. Elevated troponin is a mortality risk factor for medical intensive care patients admitted for reasons other than acute coronary syndromes. It is associated with decreased left ventrICUlar function, and this may be mediated by tumor necrosis factor a and mediators produced by neutrophilic granulocytes.

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COAGULATION AND COMPLEMENT INHIBITORS PREDICT OUTCOME IN PATIENTS WITH SEVERE SEPSIS AND CANDIDEMIA

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INTRODUCTION. Systemic mycosis in ICU is associated with high morbidity and mortality. In this study we propose to demonstrate the correlation among the most significant coagulation and complement system markers and the outcome of patients with Severe Sepsis associated with systemic candidemia and to state the predictive value of these markers with respect to SOFA scores and outcome .

METHODS. A prospective study has involved patients admitted (more than 48 hours) in ICU from January 2001 until March 2002 . The patients involved are those with diagnostic and clinic criteria for Severe sepsis with positive culture (candida) and 2 clinical signs of acquired systemic mycosis. We have monitored Antithrombin III (ATIII) , Protein C (PC) and Tissue Factor Pathway Inhibitor (TFPI) as coagulation inhibitor markers and a multifunctional regulator of all major kinin-generating protein cascade systems: C1 inhibitor (C1inh) . Coagulation inhibitors levels are assessed via functional (activity) , immunological (antigen) and ELISA (TFPI). C1inh was measured by a chromogenic assay (functional). We have also registered every day the SOFA score until the discharge from ICU.

RESULTS. We have enrolled 15 patients aged from 39 to 91 years . Clinical data and results for survivors (S) vs. not survivors (NS) with the levels registered at admission and at discharge (48 hours before negative outcome) are, in short, shown in table 1. Statistical analysis based on the area under the curve (ROC) and Friedman test with p-h Wilcoxon test has obtained only for these markers the highest predictive value (from- .711 to .813 and $p < .01$) with respect to these levels: AT III < 51% Protein C < 42% and C1inh >198% . These values are related to bad SOFA scores and to a negative outcome within 72 hours . No significant values are registered in this study for TFPI.

	Saps II	AT III (Admission)	P-C % (Admission)	C inh % (Admission)	AT III % (Discharge)	P- C % (Discharge)	C 1 inh % (Discharge)
Group S (6)	46.3 (31-51)	82.6 (64-110)	93.2 (86-100	84.2 (123-146)	78 (41 -82)	72 (59-76)	128 (117-142)
Group Ns (9)	48 (34-52)	74.8 (43 93)	90.5 (48-98)	112 * (94-141)	51* (37-58)	42* (32-49)	198* (188-244)

Clinical data and results (range) . SOFA > 8 in NS group at discharge. * $p< .01$

CONCLUSION. It is very interesting to notice the high correlation among protein C and AtIII activity levels and SOFA scores ($p< .01$) and the dramatic decrease of the Protein C system is already firmly present 48 hours before negative outcome (not survivors). We also register the significant alterations of C1 inhibitor specially in the group (NS) patients with severe candidemia and this marker assumes a significant role with an interesting clinical future .

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IS PLASMA LIPOPROTEIN PROFILE A VALID MARKER OF SEPSIS AT THE ADMISSION TO THE INTENSIVE CARE UNIT?

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INTRODUCTION. To study whether plasma lipoprotein pattern can distinguish septic patients from non-septic patients with systemic inflammatory response syndrome (SIRS) at the admission to the intensive care unit (ICU). In septic patients, we also evaluated if lipoproteins can differentiate Gram-negative from Gram-positive sepsis.

METHODS. One-hundred and twenty one consecutive critically ill patients were enrolled in this prospective study. Exclusion criteria were pregnancy, acute pancreatitis, sedation with propofol, cirrhosis, and end-stage renal disease. The Acute Physiology and Chronic Health Evaluation (APACHE) II score and Sequential Organ Failure Assessment (SOFA) scale were calculated considering the worst punctuation of the first 24 hours in the ICU. Mortality predicted by APACHE II was also calculated. SRIS and sepsis were defined following ACCP/SCCM criteria. Blood culture and cultures of the focus were obtained in all septic patients and classified as gram-positive sepsis, gram-negative sepsis and others. Within the first 24 hours of admission to the ICU and always before starting nutritional support, a blood sample was obtained for plasma lipid and lipoprotein determinations: total cholesterol, triglycerides, cHDL (high-density lipoprotein), cLDL (low-density lipoprotein), phospholipids, apoprotein A1, apoprotein.B. As nutritional markers, albumin, prealbumin and transferrin were also measured. Univariate and multivariate análisis were performed using chi-square test, T-test, U-Mann Whitney test and logistic regression models, using $a< 0,05$

RESULTS. Sepsis was diagnosed in 80 patients and 41 patients had SIRS without infection. APACHE II score was similar, but grade of SIRS (2.84± 0.93 vs. 2.41± 0.8; p=0.01) and SOFA at the admission (6.36±5 vs. 4.1± 3.5; p=0.006) were significantly higher in septic patients. Total cholesterol, cHDL, triglycerides, apoprotein A1, albumin, prealbumin and transferrin were also greater in septic patients. In the multivariate analysis, only cHDL (OR 21.2, 95% CI 11.2-44.3; p=0.0001) and grade of SIRS (OR 7.2, 95% CI 2-8.9; p=0.007) were independently associated with sepsis. We also calculated a cut-off point of cHDL (13 mg/dL) to define sepsis with a positive predictive value 100% and a negative predictive value 48%. None of the analyzed parameters could separate gram negative from gram positive sepsis.

CONCLUSION. We conclude that cHDL concentration at admission to the ICU could be a valid marker of sepsis. Plasma lipoprotein profile cannot be used to differentiate gram negative from gram positive sepsis.

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LACK OF ASSOCIATION BETWEEN THE -308 TNF PROMOTER POLYMORPHISM & OUTCOME FROM SEPSIS & SEPTIC SHOCK

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INTRODUCTION. Tumour necrosis factor-a (TNF) is an important pro-inflammatory mediator and high levels of this cytokine have been associated with a poor outcome from sepsis. Recently, genetic polymorphisms of the TNF locus and its promoter region have been associated with the incidence and outcome of severe sepsis[1;2], although the results have been conflicting[3]. We chose to investigate the association between a known functional single nucleotide polymorphism (SNP) in the TNF gene promoter (-308 G/A, guanine to adenine substitution) and outcome in severe sepsis and septic shock.

METHODS. Caucasian adult patients with a diagnosis of severe sepsis or septic shock on 6 ICUs in the UK and from an ICU in Sydney, Australia were recruited. Whole blood was collected in EDTA, DNA extracted and amplified by PCR using specific primers and digested with the restriction endonuclease *Nco1*. This enzyme cuts the wild type (allele G) but this cutting site is abolished by the polymorphism (allele A). The restriction fragments were then size separated, visualised and scored on agarose gels. Fisher's exact test was used for statistical analysis.

RESULTS. 167 patients were recruited. Overall ICU and hospital mortalities were 28.1% and 38.3% respectively. 54 patients had the A allele (45 heterozygous and 9 homozygous). The remainder were homozygous for the G allele. There was no difference in ICU or hospital outcome based on genotype.

	G/G (n=113)	G/A or A/A (n=54)	p
ICU Mortality % (n)	30.1 (34)	24.1 (13)	0.47
Hospital Mortality % (n)	36.3 (41)	42.6 (23)	0.5

CONCLUSION. In this study there was no association between the TNF –308 SNP and outcome from severe sepsis and septic shock. Further studies examining the extended haplotypes of the TNF locus in larger numbers of patients will be required to clarify the influence of polymorphisms of the TNF gene on the outcome from sepsis.

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TUMOR NECROSIS FACTOR GENE POLYMORPHISM AND SEVERE SEPSIS OUTCOME

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INTRODUCTION. Gender and polymorphism within the Tumor Necrosis Factor (TNF) may be related to increased TNF response and poor prognosis in severe sepsis. Male and TNF2 allele correlates to poor outcome, but clinical and experimental data appear to be inconclusive.

METHODS. We characterized the genomic distribution and allele frequency of the NcoI polymorphism in 245 adult medical Intensive Care (IC) patients which met ACCP/SCCM Consensus Conference definition for severe sepsis or septic shock, to assess its prognostic value for IC mortality. Sample are in Hardy-Weinberg equilibrium. Multivariate analysis was performed.

RESULTS. The genotype distribution in IC septic patients was comparable with healthy controls (13% B1/B1, 41% B1/B2, 46% B2/B2). There were no significant genotypic or allelic differences in IC mortality. No significant mortality difference was found among men and women genotype subgroups.

	Patients (%)	Patients age	Patients died (%)	Male	Male died (%)	Fem.	Female died (%)
B1/B1	28 (11.4)	61.0+-15.5	13(46.4)	14	6(42.9)	14	7(50.0)
B1/B2	100(40.8)	61.9+-18.4	35(35.0)	63	23(36.5)	37	12(32.4)
B2/B2	117(47.8)	64.8+-17.4	47(40.2)	75	32(42.7)	42	15(35.7)

CONCLUSION. Conclusions: From our date there is no evidence for an association of the NcoI polymorphism within the TNF locus or gender with the susceptibility to severe sepsis or mortality in adult IC medical patients.

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POLYMORPHISMS OF THE TNFRSF1B GENE: RELATIONSHIP TO OUTCOME FROM SEVERE SEPSIS AND SEPTIC SHOCK

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INTRODUCTION. Shedding of membrane bound tumour necrosis factor receptors to produce soluble molecules (sTNFRSF1A and 1B) is an important inflammatory control mechanism[1]. We and others have previously demonstrated that increased levels of sTNFRSF1A and sTNFRSF1B are associated with decreased survival from sepsis. Furthermore, there appears to be an association between polymorphisms of the TNFRSF1B locus and plasma levels of sTNFRSF1B[2]. We have therefore investigated whether polymorphisms of the TNFRSF1B gene and its promoter region might influence outcome from severe sepsis and septic shock.

METHODS. 170 Caucasian adult patients with a diagnosis of severe sepsis or septic shock from 6 ICUs in the UK and from an ICU in Sydney, Australia were recruited. We analysed 3 polymorphisms of the TNFRSF1B gene. A single nucleotide polymorphism in exon 6 (SNP 196 T/G) was studied by PCR-RFLP, a microsatellite in intron 4 (MS4) using an ABI373A sequencer and a 15 base pair insertion/deletion in the promoter region (Indel) by polyacrylamide gel electrophoresis. Analyses of associations between genotype and allele frequencies and outcome were by Fisher's exact test.

RESULTS. ICU mortality was 28%. Overall genotype and allele frequencies for each of the polymorphisms were similar to published population frequencies. There were no statistically significant differences in allele frequencies in any of the three polymorphisms between survivors and non-survivors (SNP196 p=0.19, MS4 p=0.52, Indel, p=0.42). The mortality was lower in patients homozygous for the 15 base pair repeat in the microsatellite polymorphism in intron 4 (the genotype associated with high levels of sTNFRSF1B) (mortality 20% v 32.1%) and was higher in those with the SNP196 (T/G or G/G) (mortality 34.8% v 23.2%). These differences, however, did not reach conventional levels of significance (p=0.14 and 0.12 respectively).

CONCLUSION. Larger studies will be required to confirm or refute associations between TNFRSF1B gene polymorphisms, partICUlarly MS4 15 homozygosity, and outcome from sepsis.

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CLINICAL ASSOCIATIONS OF TOLL-LIKE RECEPTOR 4 (TLR4) POLYMORPHISMS IN ICU PATIENTS WITH SEVERE SIRS

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INTRODUCTION. When associated with end organ dysfunction, SIRS is a major cause of morbidity and mortality in the intensive care unit (ICU) population (1). LPS concentrations in the gastro-intestinal tracts of these patients are elevated as a consequence of bacterial overgrowth. LPS processing in the mesenteric circulation may influence the systemic inflammatory response (2). TLR4 is an integral part of the LPS receptor complex. A TLR4 polymorphism (Asp299Gly) is associated with hypo-responsiveness to LPS in human bronchial epithelial cells. We examined the association of this polymorphism with clinical outcome in ICU patients with severe SIRS.

METHODS. Adult ICU patients with evidence of severe SIRS were studied. Patient demographics, APACHE II data, length of stay and outcome data were collected. Genotype was determined using PCR amplification. Statistical analysis was performed using SPSS 11.0.

RESULTS. 67 patients have been genotyped of whom 2 are still in ICU. Of the remaining patients, 20/65 (31%) died in ICU and 9 died in hospital after discharge from ICU, giving an overall hospital mortality rate of 29/65 (45%). Mean (SD) APACHE II score was 21 (5).The TLR4 genotype frequencies were Asp/Asp 88.1% (59/67), Asp/Gly 10.4% (7/67) and Gly/Gly 1.5% (1/67). The allele frequencies were Asp 93% and Gly 7%, similar to previously reported frequencies in Caucasians. Preliminary analysis revealed no significant differences between APACHE II scores in patients with the Asp/Asp genotype (mean 20.7, SD 5.6) and those with Asp/Gly or Gly/Gly genotypes (mean 19.0, SD 2.8) (p=0.40, Student's t-test). 5/29 (17%) of patients who died during the hospital episode carried the Gly polymorphism, compared to 3/36 (5%) of those who survived the hospital episode (p=0.45, Fisher's exact test, OR 2.3, 95% CI 0.5-10.5).

CONCLUSION. No associations with severity of illness on admission to ICU, ICU length of stay or hospital outcome were detected with the present sample size. Recruitment is ongoing, to attain sufficient power. We aim to study genes coding for components of the LPS receptor complex, which are biologically relevant to innate immunity and the development of SIRS. Detailed, prospective study of the role of polymorphisms in innate immunity has the potential to improve our understanding of the pathogenesis of SIRS, and to influence risk stratification and management of this severe complication of life-threatening infection.

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EVALUATION OF THE CHANGES IN PRELOAD BY PULMONARY VENOUS AND MITRAL FLOW VELOCITIES USING TEE

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INTRODUCTION. Optimizing patient's hemodynamics in the ICU can be challenging.The PA catheter has been used to determine preload, afterload and myocardial performance. However,insertion of a catheter is not a risk-free procedure and the values obtained can in some circumstances be misleading.The use of TEE in ICU has been increasing.Previous studies have examined the correlation between the pulmonary vein (PV) velocities and mitral valve (MV) velocities and PCWP. The purpose of our study was to evaluate the relationship between these variables during different loading conditions as assessed by TEE in ICU patients.

METHODS. Eleven (11) patients,with a mean age of 65± 10 years, requiring mechanical ventilation were prospectively studied. In all patients a PA catheter was inserted and baseline measurements were obtained.The PV velocities and MV velocities were evaluated during three different loading conditions:1) in a control situation 2) in a state of decreased preload by intravenous administration of nitroglycerin 3)in a state of increased preload by administration of fluids.In all patients we used the following indices from the PV velocity : S (systolic),D (diastolic), Decelaration Time(DT) of D wave, Apv (atrial reversal) and from MV velocity: E,A wave and Deceleration Time of E wave.

RESULTS. The decrease in preload resulted in a trend toward a lower amplidute of D wave peak velocity as compared with the control state and a significant prolongation of the Deceleration Time ($p<0,05$).There was a decrease in height of the systolic (S) wave ($p<0,001$)and the Apv ($p<0,05$). The MV curve demonstrated a significant decrease in E velocity ($p<0,05$) and prolongation of Deceleration Time ($p<0,05$).The increase in preload resulted in a significant increase in systolic and diastolic wave in PV ($p<0.01$) with a shortening of the DT of D wave.The Apv became significantly higher ($p<0,05$).The MV curves demonstrated a significant increase in E wave ($p<0,05$) with a decrease in DT.There was a good correlation between D wave and PCWP (r:0,6),Apv wave and PCWP (r:0,7) and E wave and PCWP (r:0,6).A direct correlation was present between changes in E and D waves (r:0,68) and changes in DT of E and DT of D velocities (r:0.78).

CONCLUSION. This study provides evidence that TEE gives information additive to the PA catheter in the assessment of preload in an ICU population. Examination of PV velocities and MV velocities and their changes during different loading conditions provide additional information regarding diastolic function. This may prove useful in minimizing the use of invasive methods for hemodynamic monitoring in ICU patients. Further investigation is required to correlate these Doppler measures with the invasive hemodynamic measurements.

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SEVERE PULMONARY EMBOLISM (SPE) AND ECHOCARDIOGRAPHY

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INTRODUCTION. The aim of the study was to evaluate the use of Echocardiography in severe pulmonary embolism (SPE).

METHODS. 26 patients with SPE (19 women and 7 men), with a mean age of 59 years (SD of 17; range: 21 to 83 years), were studied prospectively.
Coloured Doppler- echocardiography was performed in all cases at admission, confirming that diagnosis by perfusion gammagraphy and / or helycoidal CT scan.

RESULTS. Emboli were observed in six patients (23%): 3 in right atrial chamber, 2 in pulmonary artery and 1 in output tract of right ventricle. In 17 patients (65%) right ventrICUlar dilatation with a mean value of 38.8 mm (SD 5), and trICUspid insufficiency in 20 (74%) with mean estimated systolic pulmonary arterial pressure of 60 mmHg (SD 16). Pulmonary acceleration time was measured in 13 patients and found shortened in all of them: 52 milliseconds (SD 16), and septal abnormal movement was detected in 10 patients (39%). 25 out of 26 patients had more than one sign of severe pulmonary embolism (SPE), 10 had two sign and the other 15 had three or more signs.

CONCLUSION. Echocardiography is a simple technique, which allows the diagnosis of SPE by the detection of emboli in the right heart cavity and / or the objectivation of indirect signs of functional alteration of right ventricle.

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DEPLETION OF PROTEINS C – S AND ANTITHROMBIN AFTER SUCCESSFUL CARDIOPULMONARY RESUSCITATION (CPR)

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INTRODUCTION. Coagulopathy and systemic inflammatory response have been previously reported in patients after CPR (1). The coagulopathy includes activation of coagulation and inhibition of fibrinolysis, alterations similar to those reported in sepsis where profound depletion of anticoagulation proteins have been evidenced, and had significant therapeutic consequences (2). However, anticoagulation proteins: protein C and S (PC – PS), as well as antithrombin (AT) levels were not reported after CPR.

METHODS. Consequently, serial measurements of markers of coagulation (thrombin-AT [TAT], D-dimers), fibrinolysis (plasminogen-activator inhibitor 1: PAI-1), inflammation (IL-6) and endothelial injury (soluble thrombomodulin: sTM) were performed in 50 patients (age: 61±13 years; SAPS: 64±13) after successful CPR.Analyses on biomarker levels by ANOVA were performed.

RESULTS. Patients after CPR presented coagulopathy with consumption of anticoagulant molecules, inflammation and endothelial injury markers (sepsis-like coagulopathy). Patients with unfavorable outcome had higher levels of PAI-1 and lower levels of PC ($p<0.05$).

	Volunteers (n=7)	Septic patients Day 0 (n=5)	CPR patients Day 0 (n=50)	CPR patients Day 1 (n=48)	CPR patients Day 5 (n=31)
TAT (ug/l)	0.2±0.3*	11.6±3	74±21	40±14	12±2†
D-Dimers (ug/l)	0.3±0.07*	6.6±3.4	11.5±2.7	6.8±1	5±1†
PAI-1 (AU/ml)	11±1.5*	60±6	30±4	50±5	28±5
Protein C (%)	134±10*	48±11	75±6	80±6	86±9
Protein S (%)	117±7*	51±10	67±5	61±4	76±7
AT (AU/ml)	112±4*	63±10	85±3	84±2	91±4
IL-6 (ng/ml)	0.04±0.01*	3.5±1.4	2.1±1.9	4.3±2.7	0.3±0.3†
sTM (ng/ml)	43±3*	137±31	62±18	76±11	119±31

*p<0.05 volunteers vs CPR patients on Day 0; † p<0.05 CPR patients on Day 1, or 5 vs Day 0

CONCLUSION. The data suggest that patients after CPR had significant depletion of anti-coagulation proteins. Further studies are required to test the hypothesis that repletion of anticoagulant proteins may improve organ failure, especially cerebral outcome.

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LOW DOSE ALBUMIN INFUSION ATTENUATES INFLAMMATORY RESPONSE FOLLOWING ABDOMINAL SURGERY

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INTRODUCTION. The present study was designed to evaluate the effect of low dose albumin infusion vs. control on the local inflammatory response following abdominal surgery. Albumin loss during surgery is a well described phenomenon. In previous experiments a loss of plasma proteins, resp. albumin was observed during abdominal surgery. Intravital microscopy for five hours was used to evaluate the effect of low dose albumin on the mesenteric microcirculation.

METHODS. Urethan-anesthetized Sprague-Dawley rats underwent median laparatomy and placement of a doppler flow probe around the abdominal aorta. An ileal loop was prepared for eventration onto a microscopic stage using a plastic foil technique and the mesentery was immersed with Krebs-Henseleit buffer(5%CO_2 in N2). Low dose albumin (0.001 g/(kg BW*h)) was given vs. control (NaCl 0.9%) during the experiment. Heart rate, MAP, aortic blood flow were registered on a beat-to-beat basis. ABG's were drawn hourly for analysis of metabolic(BE), respiratory (pO_2, pCO_2) and hct values.

RESULTS. Rolling and adherent leukocytes significantly increased in the control group until the end of the experiment, whereas they constantly remained on a low level in the albumin group. Velocity and shear rate in the mesenteric microcirculation were significantly higher in the albumin group which was supported by increased abdominal flow and stroke volume vs. control.

CONCLUSION. Low dose albumin infusion significantly reduces the inflammatory response on the mesenteric microcirculation following abdominal surgery. Beneficial effects on systemic hemodynamics, mesenteric microcirculation and attenuation of leukocyte rolling and adhesion in mesenteric venules could only be observed in the albumin group, whereas the inflammation progressed in the control group.

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THROMBOLYTIC THERAPY IN PULMONARY EMBOLISM

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INTRODUCTION. The aim was to evaluate the effect of thrombolytic therapy in massive and submassive pulmonary embolism

METHODS. 22 patients (16 women and 6 men), with a mean age of 59 years (SD 18), range: 21 to 83, studied prospectively. Diagnosis at admission was confirmed with spiral CT scan and/or Ventilation–Perfusion (V/P) Gammagraphy. A study protocol was performed in all patients consisting of: complete analysis, electrocardiography, thorax radiography and echocardiography.One hundred milligrams of rt- PA was infused in 2 hours due to severity of the clinical presentation: haemodynamic instability (4 cases) and/or severe hypoxemia or echocardiographic abnormalities (8 patients).

RESULTS. Clinical improvement was seen in the entire group. Studied variables Pre and Post-thrombolysis are shown in the table. Mean arterial pressure (MAP); right ventrICUlar diameter (RVd), systolic pulmonary arterial pressure (sPAP), acceleration pulmonary time (APT), oxygen saturation (OS), fibrinogen, hematocrit and heart rate (HR). Postthrombolytic changes in electrocardiogram were objectivated, showing that some abnormalities had disappeared, such as: right bundle heart block in 8 out of 19 patients (42%), S1Q3T3 pattern in 5 out of 20 (25%), T wave alterations in 6 out of 21 (29%), and the pulmonary P in 2 out of 4 (50%). Minor hemorrhagic complications were observed in 7 cases; only one needed transfusion. One patient had hematuria, one other hemarthrosis, and another one suffered pericardial blood effusion (after coronary by-pass graft).

	Prethrombolysis	Postthrombolysis	p
MAP (mmHg)	72∂21	87∂14	0.0001
RVd (mm)	39∂5	27∂8	0.0001
sPAP (mmHg)	60∂ 16	36∂10	0.0001
APT (ms)	52∂ 16	82∂17	0.0001
OS	89∂ 7	98∂1	0.0001
Fibrinogen (ml/dl)	3.1∂5	1.1∂0.9	0.0001
Hematocrit (%)	37∂5	33∂6	0.0001
HR (bpm)	121∂25	89∂18	0.0001

CONCLUSION. rt-PA Thrombolytic therapy of massive and submassive pulmonary embolism has shown, in our experience, utility and effectiveness with minimal complications, even in old patients.

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RATE OF DECREASE OF GUT INTRALUMINAL REDOX POTENTIAL AFTER VASCULAR OCCLUSION

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INTRODUCTION. We have previously shown that the measurement of gut intraluminal redox potential (Eh) during progressive bleeding and reperfusion is useful to monitor changes in oxygen transport[1]. Eh could provide with a different type of information from other parameters of tissue oxygenation, such as lactate and intramucosal pH. Our goal was to show the rate of decrease of Eh after the occlusion of superior mesenteric artery blood flow ($Q_{intestinal}$).

METHODS. Eight anesthetized and mechanically ventilated sheep were studied. Eh was measured as a voltage difference using a milivoltmeter with a platinum electrode, against a reference electrode. $Q_{intestinal}$ was measured with an electromagnetic flowmeter. After basal measurements, superior mesenteric artery was occluded and Eh was continuously registered during 30 minutes. Data (mean ± SD) were analyzed with repeated measures of ANOVA followed by Dunnett's test. Response time was defined as a decline greater than three SD from basal values.

RESULTS. Response time was 78 ± 82 seconds.

	BASAL	5'	10'	15'	20'	25'	30'
Eh (mV)	358 ± 342	274 ± 355*	228 ± 349§	191 ± 342§	165 ± 338§	146 ± 333§	128 ± 330§

* $p < 0.05$ vs. basal. § $p < 0.001$ vs. basal.

CONCLUSION. Our results demonstrate that Eh adequately and rapidly reflected changes in tissue oxygenation during ischemia.

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HEART RATE VARIABILITY IN ESRD PATIENTS

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INTRODUCTION. Assessment of heart rate variability (HRV) has been used in risk stratification after acute myocardial infarction, in congestive heart failure, and in the early diagnosis of diabetic neuropathy. Patients with end-stage renal disease (ESRD) constitute a population of increased cardiovascular morbidity and mortality. Hemodialysis patients often show signs of autonomic neuropathy. Data on HRV are usually derived from 24-hour Holter recordings. However, short term RR interval variation as measured on standard 12-lead ECG holds important prognostic implications in subjects with dilated cardiomyopathy. The purpose of this study was to look at short term RR variation in ESRD patients, and its modification after dialysis.

METHODS. 47 (32 male, 15 female) patients were included in the study.All of them were in three times a week hospital hemodialysis. Twenty control subjects, of similar age and gender distribution, with normal renal function and blood pressure, were recruited among ward stuff. The RR intervals were measured from a continuous 2-min recording of lead II. RR variation was calculated as the standard deviation of the RR intervals (RRSD), and the coefficient of variance of the RR (RRCV), i.e. standard deviation divided by the mean RR and expressed as percentage. ECGs were also analysed for left ventrICUlar hypertrophy (LVH).

RESULTS. RRSD and RRCV were significantly decreased in dialysis patients compared to controls. RRSD was 11.28±8.13 vs 39.832.12 p=0.000, and RRCV was 1.56±1.13 vs 4.63±2.75, p=0.000. RRSD and RRCV were not affected by dialysis, but were significantly decreased in those with ECG evidence of LVH, compared to those without. RRSD was 6.87±6.1 vs 10.9±8.8 (p=0.043), and RRCV was 0.95±0.76 vs 1.36±1.26, (p=0.033). RRCV was associated with Mg and K postdialysis. RRSD and RRCV were inversely correlated with Cornell voltage, an ECG index of LVH.

CONCLUSION. Hemodialysis patients present with low short term RR variation in comparison with control subjects. Electrocardiographically detected LVH among ESRD patients is also associated with depressed RR variability.

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ELECTROCARDIOGRAPHIC CHANGES IN PATIENTS WITH BRAIN TUMORS

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INTRODUCTION. Increased intracranial pressure,as that was seen in patients with large cerebral tumors, reduces frequency of the pulse.Prolapsus of the brain masses in tentorial incissura of foramen magnum and consequently bradycardia,respiratory arrest,coma and death might occur in these patients. The aim of this study is to examine the ECG changes in patients with brain tumors in regard to the kind of tumors and localisation .

METHODS. : The study group was consisted of 31 patients (15 male and 16 female) of average age 57,9 years (range 30 to 83). There were 10 patients with temporal lobe tumor (4 left and 6 right), 9 patients with frontal lobe tumor (5 left and 4 right), 9 with parietal lobe tumor (3 left and 6 right) and 3 with occipital lobe tumor (2 left and 1 right). ECG changes were evaluated during the first 72 hours from receiving in the ICU. Large cerebral tumors confirmed with CT, and definitive diagnosis was made pathohystologicaly.

RESULTS. The most common ECG abnormalities associated with central lesions that we found were: prolongation of the Q-T interval in 64.7% patients with right and 50% with left cerebral hemisphere tumor; elevated, peaked, or notched T waves in 52.9% patients with right and 42.8% with left cerebral hemisphere tumor; and increased P-wave amplitude in 23.5% with right and 28.5% patients with left cerebral hemisphere tumor. The most frequent ECG changes that we registered among rhythm and conduction disturbances were: narrow-QRS tachycardia with regular rhythm; sinus tachycardia in 35% with right and 28% patients with left cerebral hemisphere tumor, sinus bradycardia in 11.7% with right and 14% with left cerebral hemisphere tumor, and incomplete/complete right bundle branch block (BBB) in 28% patients with left cerebral hemisphere tumor. We did not find any specific differences according to the pathohystologicaly type of the tumors.

CONCLUSION. ECG abnormalities associated with central lesions in the patients with brain tumors are not depend from the kind of tumors and side of the brain where tumor is located. In the patients with brain tumors on left side of the brain prevails incomplete and complete right bundle branch block (BBB).

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CATACHOLAMINE USE IN CEREBRAL VASOSPASM AFTER SAH; OUTCOME AND COMPLICATIONS

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INTRODUCTION. Cerebral vasospasm is a, potentially, life threatening phenomenon after aneurysmal subarachnoid hemorrhage (SAH). As part of "triple H" therapy, fenylephrine and norepinephrine in combination with dobutamine and dopamine, are used most frequently to elevate systemic arterial blood pressure (ABP) in order to preserve optimal cerebral blood flow. In obtaining increased arterial blood pressure during episodes of vasospasm we altered medical therapy from fenylephrine to norepinephrine but experienced an increasing incidence of paralytic ileus. In a retrospective cohort study we evaluated clinical outcome and the incidence of paralytic ileus.

METHODS. In 1991-1999, a consecutive series of 146 patients had surgery (aneurysmal clip ligation) within 72 hours after SAH. 80 patients with clinical vasospasm, were subdivided into two groups with respect to medication used. Group A (N=48) was treated with a combination of dobutamine, dopamine and fenylephrine (mean increase syst. ABP 40.0±20.5 mm Hg). In group B (N=32) norepinephrine was used instead of fenylephrine (mean increase in syst. ABP 57.8 ± 27.3 mm Hg). We compared basic variables of the two treatment groups, and investigated the clinical outcome using the Glasgow Outcome Scale (GOS), one year after initial SAH. Complications were registered and compared between these treatment groups.

RESULTS. The two treatment groups were evenly matched concerning age (p=0.28), WFNS-score at admission (p=0.89), amount of subarachnoid blood on CT-scan (Fisher) (p=0.75), and observed prognostic variables as hypertension (p=0.50) and smoking (p=0.65). The clinical outcome, was not influenced by the kind of medication used (p=0.55). The incidence of paralytic ileus differed between the two groups (group A: 2/48 vs group B: 12/32, p<0,001). Paralytic ileus occurred mainly in patients treated with norepinephrine (12/32=37.5%, Odds Ratio=13.8). No relationship was found in height of systolic ABP or dosage of norepinephrine administered to these patients. We observed a significant difference in duration of administration of norepinephrine in patients, who did develop a paralytic ileus (see table). We observed no difference between groups in cardial or pulmonary complications.

	N Ileus	Mean (SD)	C.I. 95%	Sign.
Medication dose (mcg/kg/min)	20 no / 12 yes	0.34 (0.22) / 0.40 (0.25)	-0.23 / 0.12	p=0.528 (NS)
Height syst. ABP (mm Hg)	20 no / 12 yes	201 (23.1) / 216 (24.1)	-23.16 / 2.80	p=0.097 (NS)
Time medication administered (days)	20 no / 12 yes	9.27 (4.2) / 17.83 (6.4)	-12.14 / -3.42	p=0.002

Table: norepinephrine use in cerebral vasospasm; patients with or without paralyticileus.

CONCLUSION. -The use of norepinephrine in patients with cerebral vasospasm after SAH did not influence clinical outcome, although higher blood pressure levels were reached. -Norepinephrine administered during longer periods than 12 days, increases the risk of paralytic ileus.-Fenylephrine is recommended in the treatment of cerebral vasospasm after SAH.

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KIDNEY DISEASE DOESN'T COMPROMISE ULTRAFITRATION-INDUCED IMPROVEMENT IN END STAGE CARDIAC FAILURE

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INTRODUCTION. Slow discontinuous ultrafiltration (SDUF) is nown recognized as an effective complementary treatment for congestive refractory end stage cardiac failure(ESCF). However, an organic kidney disease is often associated with heart failure and may worsen the prognosis. This study was undertaken to compare the effects of SDUF in ESCF patients with and without previous kidney disease.

METHODS. 39 patients fullfilling ESCF criteria with fluid overload and oliguria (grade IV NYHA) were treated by SDUF. SDUF was performed with a double head pump monitor (BSM 22, Hospal), blood flow rate: 150-200 ml/mn, ultrafltration rate: 0.2 to 1 l/h. Vascular access was provided by femoral silicone twin catheters. A renal replacement therapy was institued when indicated. Age, sex, cardiopathy, and nephropathy were collected in each patient. Patient follow up before and after SDUF: systolic arterial pressure, heart rate, diuresis, total fluid volume removed, cardiothoracic index, creatinemia, blood urea nitrogen, natremia, natriuresis, mortality and average survival. Datas were compared between two groups: Group 1without and Group 2 with nephropathy.

RESULTS. Mean age was 65±9 yo and sex ratio was 1/4,3. Myocardiopathy origin was: ischemia (11), hypertension (6), valvulopathy (4), primary non-obstructive cardiopathy (7), multifactorial (11). Oliguric renal failure: fonctional in 20 patients (Group 1) and associated with mild chronic nephropathy in 19 patients prior to heart attack (Group 2). No significant differences in clinical and biological datas were observed between the two groups except for blood urea nitrogen: 26,2±15 in group 1 vs 39,2±16,8 mmol/l in group 2. During SCUD, hemodynamic stability was observed in both groups; diuresis and natriuresis significantly increased and remained stable at the end of the treatment despite significant decreased diuretic doses. Mean sessions of SDUF was 3,8±2,4 in group 1and 5,6±5,6 in group 2 (ns). Renal replacement therapy was institued in both groups but the number of sessions was significantly higher in group 2: 3,8±4,7 vs 0,95±1,3. Mortality during hospitalisation was 25% in group 1 and 21%in group 2. From the surviving patients, 4/15 patients in group 1 and 6/15 patients in group 2 underwent a chronic hemodialysis treatment. Average survival was higher but not significant in group 2 (21,3±36 vs 7,7±9 months).

CONCLUSION. Our study sugests that SDUF remains a long term beneficent treatment for patients with both ESCF and renal failure. Paradoxically, prognosis is slightly better than in patients with isolated refractory congestive heart failure. Organic renal failure could artificially worsens cardiac function by increasing diuretic resistance which may be improved by SDUF.

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HAEMODYNAMIC VARIABLES AFFECTING KIDNEY ALLOGRAFT FUNCTION

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INTRODUCTION. Studies on haemodynamic factors influencing graft function in kidney transplant have traditionally focused on the mean arterial pressure (MAP), central venous pressure (CVP), fluid therapy and dopamine. Recent studies show a relationship between renal artery blood flow and graft function (1). This study aims to evaluate the influence of factors affecting renal blood flow including MAP, CVP, pulmonary artery wedge pressure (PAWP), cardiac index (CI), systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR) on immediate graft function.

METHODS. 15 consecutive patients undergoing live-related kidney transplant were included. Prior to anaesthesia, a 7.5F continuous cardiac output pulmonary artery catheter was placed via the right internal jugular vein. A continuous cardiac output monitor (Baxter Edwards PX 1800) was used for haemodynamic monitoring. Baseline values of the MAP, CVP, PAWP, CI, SVR and PVR were computed. Data was collected at 30-minute intervals thereafter and immediately before and after release of the vascular clamps. The ischemia time, intravenous fluids, dopamine use and blood transfusion were noted. If warranted by low preoperative haemoglobin or increased surgical blood loss, blood was administered as 200 ml packed cell units using leukocyte filters. The outcomes chosen for graft function were the urine output on table (UO-OT), 24-hour urine output (UO-24), fall of serum creatinine from the preoperative value on day 1 (Creat-1) and day 7 (Creat-7). Using SPSS statistical software, multiple linear regression analysis was done to find the variables significantly affecting the outcome.

RESULTS. The only variable found to have a statistically significant influence on UO-OT was the MAP. No variable had any effect on the UO-24. Blood transfusion had a negative influence on the fall of creatinine on day 1 and day 7 (Table 1).

	Effect on intraoperative urine output	Effect on fall of creatinine on day 1	Effect on fall of creatinine on day 7
MAP	Increases by 25.37 ml/ mmHg rise in MAP (p<0.001)	No effect	No effect
CVP, PAWP, SVR, CI	No effect	No effect	No effect
Blood transfusion (1 unit)	No effect	Fall of creatinine reduced by 1.6 mg/dl (p<0.005)	Fall of creatinine reduced by 1.2 mg/dl (p<0.05)

Table 1. Effect of haemodynamic variables on early graft function

CONCLUSION. Mean arterial pressure and blood transfusion had the maximum impact on kidney function in the early postoperative phase. There was no influence of CVP, PAWP, CI, SVR and PVR. A study with a larger sample size is required to corroborate these findings.

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VARIABLES ASSOCIATED WITH PROLONGED MECHANICAL VENTILATION SUPPORT IN HEART SURGERY

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INTRODUCTION. Prolonged mechanical ventilation support (MV) is associated with increased morbidity and less cost – effective admissions in the postoperative period (PO) of heart surgery (HS). Study conducted to identify variables associated with prolonged MV in patients that underwent HS.

METHODS. Cohort study; 293 consecutive patients enrolled from 1/12 to 11/17 of 2001. Inclusion criteria: patients submitted to HS and admitted to Intensive Care Unit (ICU) in use of MV. Exclusion criteria: non–cardiac surgery, admission to ICU in spontaneous ventilation or death during the first 12 hours of the PO. Variables that could be associated with prolonged MV were pre-selected for analysis and grouped according to the period it represented. Preoperative period: in–hospital stay duration, age, body mass index, gender, severity of left ventrICUlar dysfunction (LVD), pulmonary hypertension, chronic obstructive pulmonary disease, redo, urgency for the procedure. Peroperative period: surgery, extracorporeal circulation (ECC) and aortic clamping duration, fluid and blood input/output differences, type of surgical procedure, combined procedures, need for post–ECC intraaortic balloon counterpulsation (IAB). Admission to the ICU: oxygen alveolar/arterial difference, blood oxygen partial pressure/oxygen inspired fraction ratio (P/F). First 24 hours of PO: dobutamine or norepinephrine (NOR) use, blood drainage volume, lowest blood lactate measurement and prognostic scores SOFA, TISS and MODS. For dichotomyc variables, Mann-Whitney Test was applied; for continuous variables we used Kendall's Tau Non–Parametric Correlation Test; Cuzick Tendency Test was used to evaluate association with LVD.

RESULTS. Median MV duration: 8 hours; mean duration time 37.8 hours (1 to 742). Increased MV duration was associated with emergency surgery (p=0.0117), coronary artery bypass graft surgery (p=0.0307), need of IAB counterpulsation after ECC (p=0.0005), use of NOR (p<0.0001). Increases in MV duration were associated with increasing values of some variables (Positive Correlation): age (p<0.0001), surgery duration (p=0.0058), blood input/output difference (p<0.0001) and SOFA, TISS and MODS scores (p<0.0001). Negative Correlation was presented for fluids input/output difference (p=0.0142) and P/F (p<0.0001). Increased linear tendency for MV duration correlates with worsening of LVD (p=0.012).

CONCLUSION. More sophisticated statistical analysis should be applied in order to determine the cause-effect correlation for these variables. Interventional studies will be conducted in the following months.

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IMPACT OF CORTICOSTEROID OVER ACUTE PHASE RESPONSE FOLLOWING CARDIOPULMONARY BYPASS

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INTRODUCTION. Since clinically adopted during cardiac surgery, cardiopulmonary bypass (CPB) has been implicated in complement activation and postoperative acute phase reaction. Corticosteroids are usually employed as an attempt to dampen these phenomena and related postoperative morbidity.
METHODS. After informed consent previously approved by the local ethical committee, we included 62 adult patients submitted to cardiac surgery under CPB at a non-emergency setting. Preoperative risk stratification employed Euroscore (ES) and Cleveland Clinic Score (CCS). Methylprednisolone (MP) – 15mg/kg, was added to CPB priming solution for Group 1 (n=31) but not for Group 2 (n=31). Blood samples were collected from all patients at anaesthesia induction (T0), 3(T3), 6(T6) and 24-hour postoperative (T24) for measurement of total C3 and C-reactive protein (CRP) levels, by nephelometric technique. Postoperative multiple organ score (MODS) were daily registered.
RESULTS. The groups were considered comparable concerning to preoperative risk stratification, length of CPB and postoperative organ dysfunction at 72h postoperative (MOD72, as well. Starting from similar levels of C3 and CRP, we did not observe significant differences between groups 1 and 2 concerning to postoperative levels of C3. Nevertheless, patients treated with MP (Group 1) exhibited higher CRP levels at 24h postoperative, as shown bellow:

	Group 1	Group 2	p
CCS	3.12 ± 3.181	2.09 ± 1.599	0.903
ES	5.741 ± 2.966	4.645 ± 2.388	0.582
MOD 72	1.94 ± 3.136	1.58 ± 1.336	0.600
	Group 1	Group 1	p
C3 – T0	116 ± 33.38	104.43 ± 34.48	0.413
C3 – T3	91.19 ± 27.66	94.00 ± 29.78	0.727
C3 – T6	93.97 ± 35.93	96.97 ± 34.62	0.235
C3 – T 24	110.03 ± 118.97	98.5 ± 32.45	0.337
CRP – T0	1.56 ± 2.50	1.96 ± 3.24	0.669
CRP – T3	3.23 ± 4.40	3.02 ± 4.59	0.916
CRP – T6	4.40 ± 3.93	3.19 ± 3.74	0.434
CRP – T24	11.24 ± 6.34	6.57 ± 6.20	0.001

CONCLUSION. Perioperative administration of MP failed to show evidences of beneficial effect over postoperative organ failure and complement activation. The acute phase response, expressed as CRP systemic levels, instead of softened, was significantly enhanced among patients to whose CPB priming solutions was added MP. These results support a larger randomised trial to reassess routine use of corticosteroids during CPB.

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IMMUNOGLOBULIN-ENRICHED COLOSTRUM MILK FOR REDUCING ACUTE PHASE REACTION IN CARDIAC PATIENTS

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INTRODUCTION. Objective: To evaluate the influence of enteral application of an immunoglobulin enriched bovine milk preparation on endotoxin plasma levels, endotoxin neutralizing capacity of plasma (ENC) and the acute phase response (IL-6, CRP) during and after cardiac surgery in a pilot study.

METHODS. Design, patients and methods. 60 patients who were treated by coronary bypass operation were enrolled in a controlled randomized study. The patients were treated by enteral application of 40g of a bovine colostrum milk preparation per day for 2 days preoperatively. Endotoxin and ENC were sequentially determined intra- and postoperatively by a chromogenic modification of the limulus amebocyte lysate test. Interleukin-6, CRP, transferrin, alpha-2-macroglobulin, albumin, apo-A, apo-B, IgG, IgA, IgM were determined by "ELISA" and nephelometrically. The clinical course was followed up by daily evaluation of the Apache-II-score.

RESULTS. Main results: Demographic data were comparable in both groups. No differences of the Apache-II-score (6.5 ∂ 1.9 verum group, and 6.8 ∂ 1,8 control group, on admission) were observed. Endotoxin plasma levels and ENC showed high levels at the end of the procedure and seemed to have a trigger function for the acute phase response but were not significantly reduced throughout the observation period in patients receiving the milk preparation as calculated by comparing the area under the curve. Plasma levels of endotoxin binding proteins did not differ significantly. Plasma levels of IL-6 increased to maximal median values of 655 pg/ml in the verum and 786 pg/ml in the control group 2 and 6 h after surgery. A tendency to lowered IL-6 levels was observed throughout the whole observation period for the verum group. CRP-levels showed their maximum values 48h after the procedure and were significantly reduced in patients of the verum group ($p = 0.034$).

CONCLUSION. This study revealed that endotoxemia occurs early during an elective surgical intervention, which is followed by a subsequent increase in mediators of the acute phase reaction. The prophylactic enteral application of a bovine milk preparation for two days in cardiac patients did reduce postoperative CRP-plasma levels but contrary to a former prospective double blind study in abdominal surgery did not reduce perioperative endotoxemia. One reason could be the too low application of the bovine colostrum milk preparation.

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NATION-WIDE EPIDEMIOLOGICAL DATA ON HEAD TRAUMA IN GERMANY 1999 COMPARED TO 1996

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INTRODUCTION. To compare a possible effect of improved therapeutical approaches in head trauma, epidemiological data should be compared at certain time points. Due to the legal obligation to document all in-patient treatments in Germany and to forward these data in an anonymous form to the Office for Statistical Affairs (Statistisches Bundesamt) it is possible to provide a nationwide epidemiological analysis of head trauma and to compare the yearly obtained data.

METHODS. The incidence, the mortality, and the duration of hospital stay for the treatment of all hospitalized patients suffering from head trauma were calculated and compared to the data from 1996 while considering the data obtained from the Office for Statistical Affairs in Bonn and Wiesbaden. The data were investigated while separating them according to the International Classification of Diseases 9 (ICD-9; No. 800-804 and 850-854). To further elucidate the causes of altered mortality and duration of hospital stay the number of CTs and MRIs in German hospitals in 1996 and 1999 were compared. In addition, data indicating the number of patients admitted to neurological rehabilitation centers were analyzed.

RESULTS. The incidence of head trauma did not change between 1996 and 1999 and was calculated to be at 340/100.000. The mortality, however, decreased from 11.6/100.000 in 1996 to 9.4/100.000 in 1999 (9412 vs. 7705 patients). In addition, the duration of hospital stay declined in all ICD-9 encoded subgroups including mild brain trauma. This could be due to the increased number of CT devices and MRIs in German hospitals (CT: 732 vs 904/ MRI: 227 vs 350) while comparing 1996 and 1999. The number of patients transferred from hospitals to neurological rehabilitation centers increased from 35800 in 1996 to 61088 in 1999 (+ 71%).

CONCLUSION. It could be speculated that both improved knowledge on the field of brain trauma therapy and a higher number of technical devices allowing rapid diagnosis of brain injury or potential intracranial complications following head trauma accounted for the reduction in mortality due to brain trauma in Germany from 1996 through 1999. The decline of the duration of hospital stay especially in patients with more severe head injury could also be due to a more rapid transfer of patients with head trauma from hospitals to rehabilitation centers.

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EFFECTS OF THERAPEUTIC HYPOTHERMIA ON INTRACRANIAL PRESSURE AND OUTCOME IN PATIENTS WITH SEVERE HEAD INJURY

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INTRODUCTION. Therapeutic hypothermia may improve outcome in patients with severe head injury, but clinical studies have produced conflicting results. We hypothesised that severe side effects of artificial cooling might have masked positive effects in earlier studies, and treated a large group of patients with severe head injury with hypothermia, using a strict protocol to prevent the occurrence of cooling-induced side effects.

METHODS. 136 consecutive patients admitted to our hospital with severe head injury (Glasgow Coma Scale (GCS) <8) in whom ICP remained above 20 mmHg in spite of therapy according to a step-up protocol described previously [1] were included in our study. Those who responded to the last step of our protocol (barbiturate coma) constituted the control group (n=72). Those who did not respond to barbiturate coma (n=64) were treated with moderate hypothermia (32oC-34oC).

RESULTS. Average APACHE II scores were higher, and average GCS at admission slightly lower in the hypothermia group, indicating greater severity of illness and more severe neurologic injury. Predicted mortality was 86% for the hypothermia group vs. 80% in controls. Actual mortality rates were significantly lower: 62% vs. 72%, $p<0.02$. The difference in overall mortality between hypothermic patients and controls was statistically significant ($p<0.05$). The number of patients with good neurologic outcome was also higher in the hypothermia group: 15.7% vs. 9.7% for hypothermic patients vs. controls, respectively ($p<0.02$). These differences were explained almost entirely by the subgroup of patients with GCS of 5 or 6 at admission (mortality 52% vs. 76%, $p<0.01$; good neurologic outcome 29% vs. 8%, $p<0.01$).

CONCLUSION. Artificial cooling can significantly improve survival and neurologic outcome in patients with severe head injury, when used in a protocol with great attention for the prevention of side effects. These effects are especially clear in patients with GCS of 5 or 6 at admission. Because there is likely to have been bias against the hypothermia group in this study, the positive effects of hypothermia might even have been underestimated.

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THE HYPOTHALAMIC-PITUITARY-ADRENAL (HPA) AXIS RESPONSE TO TRAUMATIC BRAIN INJURY (TBI)

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INTRODUCTION. The neuroendocrine adaptation to TBI has been an area of interest for decades and studies have shown considerable variation in hormonal responses.

METHODS. To further clarify this issue, 16 patients (14 men), having a mean (±SD) age of 31±12 years were investigated. They all sustained severe TBI, requiring hospitalization in the ICU for 28±16 days (range 10-60 days). Patients participated in the study within a few days following ICU discharge. Endocrine evaluation included measurement of morning corticotropin (ACTH) and cortisol plasma levels. Furthermore, all patients underwent a short, low-dose (1 mcg) ACTH stimulation test; those who had a stimulated plasma cortisol of at least 18 mcg/dL were defined as having an adequate adrenocortical response.

RESULTS. Mean ACTH was 38±19 pg/ml (range: 3-76 pg/ml, normal values: 9-50 pg/ml); ACTH levels were found to be normal (n=13), high (n=2) or low (n=1). Morning baseline cortisol was 16.7±5.7 mcg/dL (range: 4.2-25.4 mcg/dL) and stimulated cortisol was 21.6±6.2 mcg/dL (range: 6.8-31.9 mcg/dL). Overall, 3 of the 16 patients (19%) had an inadequate response to the low-dose ACTH test; in two patients ACTH levels were within normal limits, whereas in one patient ACTH was low (3 pg/ml).

CONCLUSION. In summary, adrenal cortisol production after stimulation with ACTH is deficient in about 20% of patients with severe head trauma, suggesting that the HPA axis should be routinely evaluated after TBI.

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HAZARDS ASSOCIATED WITH THE LICOX BRAIN TISSUE OXYGENATION DEVICE

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INTRODUCTION. As recent technology advance in neuromonitoring, brain tissue oxygenation (p_tO_2) monitoring was introduced in neurointensive care. The Licox system (GMS, Kiel, Germany) offers implantation of a p_tO_2 catheter, either alone or with up to two additional probes via burr hole technique in the frontal white matter. To analyze the hazards associated with the device, we retrospectively reviewed our patient collective for complications after implantation of a Licox brain tissue oxygenation monitoring device since the introduction of the system in our department in 1997.

METHODS. The records and CCT scans of 77 patients with 84 implanted Licox devices were reviewed. Main diagnoses included severe subarachnoid hemorrhage (50 patients) and traumatic brain injury (20 patients). With 39 probes, only p_tO_2 was monitored, for 11 probes a two-way device for p_tO_2 and intracranial pressure (ICP) was used and 34 probes included brain temperature monitoring additionally to p_tO_2 and ICP.

RESULTS. Mean monitoring time per patient was 7.6 days. In all but one patient, measurement data were reliable in a clinical sense. One probe was unwantedly extracted, two probes broke when disconnection was attempted. Four patients showed small intracranial hemorrhage with a diameter of 0.5 cm around the insertion site of the probe, two patients suffered median-sized intracranial hemorrhage of 1 cm diameter around the probe. Five of the described events of intraparenchymal hemorrhage occurred after insertation of a three-way device. Additionally, in two patients a small bony fragment from the tabula interna was pushed on the cortex. None of these patients needed surgical intervention due to the implantation of the Licox probe.

CONCLUSION. Although neuroimaging depicted lesions after implantation of a Licox probe, none of these lesions were clinically relevant. In our opinion, the Licox three-way bolt system is a safe method for neuromonitoring in patients with severe intracranial pathology. However, further studies are warranted whether a three-channel bolt system is needed in every patient.

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MARKED STEPWISE INCREASE IN BETA-AMYLOID IN VENTRICULAR CSF AFTER SEVERE TRAUMATIC BRAIN INJURY

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INTRODUCTION. Severe traumatic brain injury (TBI) causes marked acceleration/deceleration forces that results in widespread shear damage to axons, termed diffuse axonal injury (DAI). Alzheimer's disease (AD) is characterised by synaptic and axonal degeneration together with senile plaques (SP), which are composed of aggregated b-amyloid (Ab), a breakdown product of the amyloid precursor protein (APP). Besides that TBI is a risk factor for AD, a link exists between TBI and AD, since upregulation of APP with accumulation in damaged axons is found after TBI, and deposition of Ab in the brain has been shown both in patients with TBI and in experimental models of head injury.

METHODS. We measured the 42 amino acid form of Ab (Ab42) and the two soluble isoforms of APP (a-sAPP and b-sAPP) in ventrICUlar cerebrospinal fluid (VCSF) from patients with TBI. Inclusion criteria were; 1) severe TBI, i.e. a Glasgow Coma Scale (GCS) score of <8 at admission & a pathological cerebral computer tomography scan (CT), 2) CSF drainage performed on therapeutical indication, i.e. unmanageable ICP, (>20 mm Hg) and 3) more than 2 CSF samples during the study period. Fifteen patients, (5 female, 10 male, age 19-82 years), met these criteria.

RESULTS. As compared with Day 0-1, there was a stepwise increase in VCSF-Ab42 at day 2 (260%), to day 3 (441%), day 4 (570%), and day 5 (624%), after which VCSF-Ab42 levels declined at day 8-11 (515%). There was also a marked stepwise increase in VCSF-a-sAPP, peaking at day 3 (449%). VCSF-b-sAPP showed a less marked increase, also peaking at day 3 (178%).

CONCLUSION. This study is the first in which both Ab42 and the APP isoforms have been examined in longitudinal CSF samples from patients with TBI. Our findings show that there is a stepwise increase in the expression of both APP and Ab after TBI. The time course supports that an upregulation of APP precedes the increase in Ab. These findings further support that APP expression increases after axonal injury. It is debated whether the disturbance in Ab metabolism in AD is the primary central
pathogenic event, or whether it is secondary to the axonal degeneration. Our findings show that increased Ab expression may occur as a secondary phenomenon after TBI with axonal damage.

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PREDICTING NEUROLOGICAL OUTCOME AT 3 MONTHS USING SERUM NSE AND PROTEIN S-100 AFTER CEREBRAL INJURY

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INTRODUCTION. Serum neurone specific enolase (NSE) and glial protein S-100 may be useful markers of neurological outcome after cardiac arrest[12] or stroke.3 Following ischaemic insult or head injury long-term functional outcome may be more important than short-term survival. Our aim was to assess the value of serum NSE and S-100 in predicting neurological outcome at 3 months following cerebral insult.

METHODS. A prospective, blinded, pilot study of adult patients admitted to ICU with Glasgow coma scores (GCS) of <9 due to either head injury with no surgically remediable lesion, (10 patients); a period of hypoxaemia (p02 <7kPa) or hypotension (systolic blood pressure <90 mmHg), (10 patients); or drug overdose and a pre-hospital history strongly suggesting a period of hypoxaemia (3 patients). Serum NSE and S-100 were measured at 12, 24, 48 and 72 hours after insult. Glasgow Outcome Scores (GOS) were recorded at ICU discharge and 3 months post-insult. Data were analysed using the Mann Whitney U test.

RESULTS. Analysis was possible on 20 of 23 patients who fulfilled study entry criteria. 9 patients died in ICU, 11 had died by the 3-month follow-up point. For each analysis the 24-hr value of NSE and S-100 and the highest recorded value were used. There were no significant correlations between NSE or S-100 at 24 hours and the GOS at either discharge from ICU or at 3 months. There was a significant correlation between the highest recorded NSE (but not S-100) and the GOS at ICU discharge (p=0.035), but not for the outcome at 3 months. Subgroup analysis of those patients with head injury, and those with hypotension/hypoxia, showed no significant correlations between NSE or S-100 and outcome within either subgroup. Subgroup analysis of those patients with good outcome (GOS 4 or 5) n=8 [mean NSE at 24 hrs 17.1 ìg/L (range 6.6-26), mean S-100 at 24 hrs 1.9 ìg/L (0.1-12.55)] and those with poor outcome (GOS<4) n=12 [mean NSE 32.03 (5.7-113), mean S-100 1.2 (0.24-6.65)] revealed no significant difference in either marker between the two groups. However, power analysis suggests a sample size of 120 is needed to detect a difference of 15 in NSE values with 80% power based on a standard deviation of 30 for NSE.

CONCLUSION. NSE and S-100 did not predict neurological outcome at 3 months following cerebral injury due to trauma, hypoxia or ischaemia. However, the highest recorded NSE correlated with the functional outcome at ICU discharge and there is a trend suggesting that the 24-hour NSE may predict outcome at 3 months.

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INCREASES IN SPINAL FLUID OSMOLARITY INDUCED BY MANNITOL

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INTRODUCTION. Mannitol is widely used in hospitals worldwide to treat patients with high intracranial pressure (ICP) and/or cerebral edema. The main mechanism by which mannitol is thought to affect ICP is by increasing the patients' serum osmolarity, but not the osmolarity in the brain or cerebrospinal fluid. In this way mannitol is thought to increase the osmolarity gap between the brain and the blood, which in turn leads to removal of excess water from the brain. However, little is known regarding long-term effects of mannitol on osmolarity of the brain and cerebrospinal fluid (CSF). We therefore sought to determine effects of mannitol administration on the osmolarity of cerebrospinal fluid.

METHODS. Serum and CSF osmolarity were measured before and during Mannitol administration in 10 patients treated with Mannitol for more than 72 hours (group 1), 10 patients treated for 24 – 48 hours (group 2), and 10 controls (group 3).

RESULTS. Serum osmolarity increased quickly in all patients receiving mannitol (groups 1 and 2), while remaining constant in controls. CSF osmolarity also increased in all patients receiving mannitol; CSF osmolarity rose from 291.5 ± 4.0 to 315.5 ± 4.5 mosm/kg after 96 hours in group 1 ($p<0.01$), and from 288.9 ± 3.5 to 296.9 ± 6.2 mosm/kg after 48 hours in group 2 ($p<0.01$). CSF osmolarity remained constant in controls ($p<0.01$ for group 1 vs. group 3 and for group 2 vs. group 3, respectively). In group 1 the gap between serum and CSF osmolarity initially increased (which was the desired effect), but later decreased first to baseline values and then to below-normal levels.

CONCLUSION. Long-term administration of mannitol can induce significant increases in CSF osmolarity in patients with severe head injury. This is an undesirable and potentially dangerous effect. Therefore, CSF osmolarity should be measured regularly in all patients receiving mannitol for longer than 24 hours, and doses of mannitol should be decreased or discontinued if CSF osmolarity rises.

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S 100 B IS INCREASED IN HEMORRHAGIC-TRAUMATIC SHOCK AND INFLUENCED BY THE SEVERITY OF SHOCK

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INTRODUCTION. S 100 B, a glial calcium-binding protein, is a serum marker of cerebral damage. Posttraumatically, however, S 100 B in increased in all patients suffereing from hemorrhagic-traumatic shock, regardless of whether trauma is cerebral or extra-cerebral. The aim of this experimental study was to determine whether the posttraumatic S 100 B increase is caused by extra-cerebral trauma or by hemorrhagic shock and whether it is influenced by the severity of shock.

METHODS. Hemorrhagic shock was achieved by bleeding anesthesized rats to a mean arterial pressure (MAP) of 30-35 mm Hg through a femoral catheter and maintaining this MAP until incipient decompensation. Subsequently, MAP was either increased immediately to 40-45 mm Hg (moderate shock) or maintained at 30-35 mm Hg until 40% of shed blood had been returned (severe shock), and then increased to 40-45 mm Hg. Resuscitation was provided after 40-45 mm Hg MAP had been maintained for 40 min. Trauma was achieved by midline laparotomy.

RESULTS. Hemorrhagic-traumatic shock caused an early S 100 B increase at the onset of decompensation. S 100 B in serum was highest at the end of the 40 min. period during which MAP was maintained at 40-45 mm Hg and was significantly higher at all time points after severe shock than after moderate shock. In contrast, trauma (laparotomy)without hemorrhagic shock did not cause any increase of S 100 B in serum.

CONCLUSION. The posttraumatic S 100 B increase in serum appears to be caused by hemorrhagic shock rather than by extra-cerebral trauma. Regardless of whether the source of S 100 B is cerebral, indicating cerebral damage linked to shock, or extra-cerebral, the main determinant in the clinical setting remains the severity of shock.

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HIGH TROPONIN I LEVELS IN NON-TRAUMATIC SUBARACHNOID HEMORRHAGE ARE ASSOCIATED WITH A WORSE PROGNOSIS

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INTRODUCTION. In patients with non-traumatic subarachnoid hemorrhage (SAH), the development of myocardial abnormalities has been widely described. However, the true incidence of myocardial injury in this group of patients is unknown yet. We analyze the incidence of myocardial injury, in this population, using cardiac troponin I (Tn I) assay and also we assess if the increase in Tn I concentration has prognostic value.
METHODS. Prospective study, including all patients with non-traumatic SAH admitted to our intensive care unit (ICU), from December 1999 to December 2001. Serum Tn I concentration was measured, at least once, within the first 72 hours after onset of symptoms. Inmunoassay based on the "sandwich" principle was employed. The Chi-squared test and Fisher exact test were used for statistical analysis.

RESULTS. Of the 96 patients admitted, 14 were excluded (admission later than 72 hours, absence of TnI determination, previous cardiopathy or renal failure). Eighty-two patients were included in the study (50 women). Mean age 50±15 years. The TnI concentration was increased in 24/82 patients (29%). Sixteen (19.5%) patients died in ICU. Twelve of the 24 (50%) with a high TnI concentration and 4/58 (7%) with a normal TnI concentration died [relative risk (RR) 7.25 (2.6 to 20.2; 95 % confidence interval (CI); $p<0.001$]. Thirty-seven (45 %) patients had a Hunt-Hess (HH) grade greater or equal to III. Poor grades of SAH (HH>or = III) were associated with a higher incidence of raised TnI concentration [RR 3.17 (2-4.9; CI 95 %); $p<0.001$]. Among this group of poor grade patients, elevated Tn I levels were associated with a higher mortality [12/21 (57%) with a raised TnI compared with 3/16 (19%) with a normal TnI concentration; RR 3 (1.03-9; CI 95%); $p<0.05$]. However, mortality in every case was related to neurological problems. Seven patients (8.5%) suffered from pulmonary edema and all had elevated TnI levels. Echocardiography was performed in all 7 patients, being abnormal in 5 of them.

CONCLUSION. In our series, the incidence of myocardial injury in SAH was 29 %. This cardiac injury was more frequent among patients with severe grades of SAH. Elevations in Tn I levels had prognostic value, being associated with a higher mortality. Therefore, we should closely monitor those patients with SAH who develop an increase in the TnI levels.

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ACUTE RESPIRATORY FAILURE INCIDENCE, ETIOLOGIES AND OUTCOME IN MIDDLE CEREBRAL ARTERY AND BRAINSTEM

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INTRODUCTION. Respiratory failure is one of the major complication of acute stroke (1). We have investigated the impact of the location stroke on respiratory failure incidence, cause of intubation and outcome.

METHODS. We reviewed 40 consecutive patients with acute stroke admitted to ICU from 1998 to 2001. Following data were collected, glasgow coma score (GCS), cause of ICU admission, presence of acute respiratory failure (ARF), reason for intubation, presence of aspiration, length of mechanical ventilation (LOMV), severity of hypoxia, length of stay in ICU (LOS) and mortality. Continuous data were compared by paired t-test and nominal data by chi-test. Explicative variables for ARF were assessed by univariate analysis.

RESULTS. 24 patients had a middle cerebral artery (MCA) stroke and 16 had brainstem stroke (BS). Age (MCA 50±13SD yrs vs BS 52±13SD for), GSG score (MCA 8±3SD vs BS 10±3SD for), length of stay in ICU (12±15SD days for MCA vs 15±13SD) were not significantly different. 68% BS and 33% MCA patients were admitted in ICU for respiratory failure ($p=0.01$). Admission to ICU with loss of consciousness was significantly higher in MCA (19/24, 80%) than in BS (0/16) ($p=0.001$). Indication for intubation was always for aspiration pneumonia that was the leading cause of ARF (0.0007) associated with swallowing paralysis in BS ($p=0.001$) and to unconsciousness in MCA ($p=0.03$). There was no difference for the LOMV, the severity of hypoxia between the 2 groups. ARF, intubation or reason for intubation were not associated with mortality in the 2 groups ($p=0.1$). The major cause of death was the presence of cerebral herniation in the 2 groups ($p=0.004$).

CONCLUSION. Pulmonary complication due to aspiration more predominant in BS than MCA stroke, represents the major cause of intubation and ARF for BS patients. In the contrary, loss of consciousness in MCA stroke group predominates for ICU admission. Outcome in all patients (MCA and BS) was not influenced by presence of respiratory failure or reason for intubation. The major cause of death for stroke's patients is the neurologic state, and especially the presence of herniation.

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ACUTE ISCHEMIC STROKE CODE. STILL IMPROVING?

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INTRODUCTION. Stroke code (SC) is a guidelines of united actuatio between out of hospital enmergency services from Barcelone and the most four important hospitals of the city; which aim is to optimize the sequence time for stroke treatment; this allows to increase the number of candidates for reperfusion therapy. The present study aim is to evalute differents times sequences in the acute strokes in which trombolysis has been practised according to the acute stroke code first priority; and secundary to describe findings in the CT scan of these patients

METHODS. Cross-sectional of a sample 48 patients obtained during the period from abril 2001 to march 2002 in a teaching hospital whom SC was actived. Cohort Study after applying the SC in 2001 with the fist SC applied in a teaching hospital from Barcelona in 1997. The analysis of the numeric variables has been achieved by "T Student test".

RESULTS. During this period 233 patients with stroke diagnosis were carried to hospital. SC was actived in 48 patients (20.6%). 7 of them (14.58%)recieved fibrinolytic therapy. The cerebral CT results showed 34 (70.8%) ischemic strokes, 8 (16.6%) haemorrhaged strokes, 4 (8.3%) little strokes and 2 (4.1%) were tumors. About acute ischemic ones, 10 (29.4%) were caused by heart embolism of middle cerebral artery (MCA), 7 (20.58%), heart embolism top of basilar, 1 (2.9%) heart embolism basilar artery (BA) (2.9%) thrombosis BADuring this period 233 patients with stroke diagnosis were carried to Hospital. SC was actived in 48 patients (20.6%). 7 of them (14.58%) recieved fibrinolytic therapy. The cerebral CT results showed 34 (70.8%) ischemic strokes, 8 (16.6%) haemorrhaged strokes, 4 (8.3%) little stroke and 2 (4.1%) were tumors. In 7 cases (20.58%) fibrinolytic therapy was applied. The mean time between onset of symptom and hospital arrival was 50.8∂13.4 minutes; between onset of symptom and initial neurologist specialist performance 55.7∂17.1 minutes; between onset of symptom and CT achieved 76.8∂19.9 minutes; between hospital emergencies arrival and initial neurologist specialist performance 4.8∂8.5 minutes, this result was statistical significant (P=0.04) and better than a sample patients whom SC was applied the first year it was going on; between initial neurologist specialist performance and CT achieved 22 ∂ 20.8 minutes; between hospital emergencies arrival and CT achieved 26∂17.9 minutes.

CONCLUSION. The SC allows to follow time suggestions from the National Institute of Neurologic Disorders and Stroke (NINDS). The sequence time from hospital emergency arrival to initial neurologist specialist performance has been improved during SC application.

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NEUROPROTECTIVE EFFECTS OF ERYTHROPOIETIN IN TRAUMATIC BRAIN INJURY IN THE RAT

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INTRODUCTION. Pro-inflammatory cytokines, such as TNF and IL-1 are released in the brain within hours after closed head injury (CHI). They were shown to have deleterious effects, mainly when active in the early post-injury period. A variety of anti-inflammatory and anti-apoptotic modalities have been shown to ameliorate the outcome of CHI. Erythropoietin (EPO) is a kidney-derived cytokine regulating haematopoiesis both by acting as a growth factor and by inhibiting apoptotic cell death. Recently it has been shown to be produced in cultured neurons, brain astrocytes and neurons under hypoxic/ischemic conditions and in response to oxidative stress. Other studies have shown that the erythropoietin receptor (EPOR) is present under normal conditions on neuronal and brain capillary endothelial cells. EPO has been found to have newly discovered neuroprotective properties in different models. These models include neuronal cultures against glutamate toxicity, global glutamate toxicity and rodent models of cerebral ischemia. In addition it induces brain endothelial cell proliferation and stimulates neovascularization in vivo. The present study was designed to test the protective effects of EPO in rats udergoing controlled CHI.

METHODS. CHI in rats was induced using a weight-drop device. Clinical status was evaluated by the Neurological Severity Score (NSS), which tests 10 tasks including reflexes, behavior and motor activity. A point is awarded for failing to perform a task so a higher score corresponds to a more severe trauma. Study animals were treated with 2 doses of i.p. 5000 units/dose (1 ml) of rhu-Epo, 1 h and 24 h after CHI (treatment group) or with 1 ml of vehicle injected i.p. at the same time points (control group). NSS was evaluated by an observer blinded to the different groups at 1, 3 and 7 days post CHI. NSS scores were compared using a two tailed student t-test.

RESULTS. Control and study rats were subjected to CHI of similar severity, (1h NSS 10.4+0.78 and 10.22+0.46 respectively, p=0.86) and followed at 1d, 3d and 7d following CHI. Clinical recovery was facilitated in the treatment group starting at 24 h after CHI and reached statistical significance at 7 days post CHI. The treatment group's 7 d NSS was 5.0 (n=8) vs. 6.625 in control animals (n=9) p=0.037. The present findings point to a neuroprotective role of EPO in traumatic brain injury. Brain tissue of treated and control animals is currently being analyzed for parenchymal cytokine levels.

CONCLUSION. We have examined the role of post trauma treatment with EPO of rats undergoing CHI. As has been shown in other models of brain injury (stroke, ischemia, glutamate toxicity) EPO seems to have a neuroprotective effect in head trauma. The exact mechanism of this protection has yet to be elucidated. This is the first time, to our knowledge, that EPO has been studied in an animal model of traumatic head injury.

Poster Sessions
Assessing the surgical patient – 405-418

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EVALUATION OF TWO DIFFERENT SCORES TO PREDICT OPERATIVE RISK

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INTRODUCTION. Possum has been used to calculate operative risk, but it is quite unfeasible to perform in clinical setting, due to its complexity. Aim of this study was to create a new model, ASA based, to predict mortality

METHODS. Data were taken in two different hospitals and all surgical specialities were included but for cardiosurgery. Parameters considered for the new model were: ASA, Age, type of surgery (scheduled surgery, not scheduled surgery, emergency surgery) and surgical categories (less compelling surgery = 1; medium = 2; more compelling surgery = 3). The development data set was based on 2100 surgical patients, while the validation data set was based on 590 patients. Goodness-of-Fit Hosmer-Lemeshow test and ROC curve were performed in both data set to test calibration and discrimination. In the validation data set the new model was compared to POSSUM for calibration and discrimination

RESULTS. Table I shows the variables which were calculated for this model. Calibration and discrimination was good both in the development data set and in the validation data set. Finally this new model was better calibrated and with a better discrimination than POSSUM. In fact POSSUM was not calibrated (chi-square = 31.81466; p=0.00043) and ROC curve was 0.968 (IC0.935-1.001) for new model and 0.930 (IC 0.876-0.935) for POSSUM.

Independent Variables	
ASA	1.09
Age	0.03346
Type of operation:	
Scheduled	-0.821068
Not scheduled	0.004768
Emergency	0.8163
Surgical cat. (1)	-1.2056
Surgical cat. (2)	0.5317
Surgical cat. (3)	0.6739
Constant	-8.067

CONCLUSION. This new model is simple ASA based and can be used routinely in the operative room to predict the operative risk, both for scheduled and not scheduled surgery.

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ANAEROBIC THRESHOLD AND AORTIC ANEURYSM MORTALITY

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INTRODUCTION. Elective abdominal aortic aneurysm (AAA) surgery has an in hospital mortality of 7.3% in the United Kingdom (reference 1). Our hospital mortality for the last 3 years (1998-2000) is 4.7%. It is diffICUlt to know how to apply these figures to individual patients. We have used the Anaerobic Threshold in a prospective observational study to try and identify patients with an increased risk of mortality.

METHODS. Forty-five patients scheduled for elective AAA repair had their Anaerobic Thresholds measured pre-operatively. The Anaerobic Threshold is the patient's oxygen consumption in ml/kg/min when anaerobic metabolism occurs(reference 2). It is calculated by using a bicycle ergometer and a metabolic cart.

RESULTS. A low pre-operative Anaerobic Threshold was associated with a higher postoperative death rate; 5/17 versus 1/28(Fisher exact test 0.02).

	AT > 11ml O_2 /kg/min	AT < 11ml O_2 /kg/min
Number of patients	28	17
Age	74 (55-90)	74 (62-83)
APACHE II	15 (6-27)	16 (5-27)
SAPS II	29 (14-51)	32 (16-53)
Critical Care Days	1.8 (1-5)	3.4 (1-17)
Hospital Mortality*	1/28 (4%)	5/17 (29%)

Anaerobic Threshold and Mortality

CONCLUSION. An Anaerobic Threshold of less than 11ml O_2 /kg/min is associated with increased mortality and possibly lengthens stay in the Critical Care Unit after elective AAA repair.

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ACUTE ABDOMINAL AORTIC ANEURYSMS; LONG-TERM OUTCOME OF 308 PATIENTS

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INTRODUCTION. The mortality in acute abdominal aortic aneurysms remains high. Recent series still report a hospital mortality rate of more than 50% (1,2). Despite the large number of published studies on hospital outcome, long-term outcome after ICU admission has hardly been studied. Here we present hospital survival and long-term outcome in 308 patients with an acute abdominal aortic aneurysm.

METHODS. The records of all patients operated for aneurysm surgery between 1990 and 2001 were retrospectively reviewed. In 308 patients surgery was performed for an acute abdominal aortic aneurysm. All operation reports were analysed. For complete follow-up the general practitioner was contacted if necessary. After arrival in the emergency department and confirmation of the diagnosis by physical examination and/or ultrasound all patients were immediately brought to the operation room. In our hospital even patients with cardiac arrest on arrival in the operation room are treated without delay, and were thus included in our study. All surviving patients were admitted at the intensive care. In case of postoperative haemodynamic instability, multiple organ failure, sepsis or diarrhea a sigmoidoscopy was performed to assess the presence of ischemia or infarction.

RESULTS. Three hundred and eight patients were operated for an acute abdominal aortic aneurysm, 266 men and 42 women. Operative mortality was 13% (39/308). Calculated from the moment of ICU admission, 30 day survival was 78%. Cumulative survival rates calculated with the Kaplan Meier method at 1, 3, 5 and 10 years were 65%, 55%, 46% and 28% respectively. In 23 patients in whom sigmoid resection was performed, 30 day survival was 35% compared to 83% in the other patients.

CONCLUSION. Mortality in ruptured abdominal aortic aneurysm remains high, 30 day survival was 78% in our group. Sigmoid resection was associated with lower survival but sigmoidoscopy should be augmented to exclude sigmoid necrosis. Outcome in these patients is not invariably poor. Long term follow-up shows that also after discharge from the hospital these patients have a high mortality.

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PATIENTS PROFILE AND PROGNOSTIC MARKERS FOR HEART SURGERY IN A PUBLIC TERTIARY HOSPITAL

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INTRODUCTION. Prognostic markers developed in Europe and North America cannot be applied in Latin America where life expectancy is 30 % lower according to World Health Organization. The objective of this study is to analyze patients profile submitted to heart surgery (HS), type of surgery distribution and the impact of variables, previously reported in medical literature, in the mortality and duration of Intensive Care Unit (ICU) stay in a public tertiary hospital.

METHODS. Cohort study of patients submitted to HS from January 1998 to April 2001. Patients profile, type of surgery distribution and many variables were analyzed. Variables that were studied: age, gender, body mass index (BMI), body area (BA), preoperative in-hospital stay (PREOP), extracorporeal circulation (ECC) duration, ventrICUlar function (VF), surgical indication, combined procedures (COMB), urgency for the surgery, presence of diabetes mellitus (DM), systemic arterial hypertension (AH) and cigarette smoke (CS). The profile and patients variables were analyzed and compared in two different groups. Group A (GA): patients discharged from ICU or in-ICU stay lower than or equal to 3 days (median in-ICU stay in this study). Group B (GB): death during ICU admission or in-ICU stay longer than 3 days. T-student, Mann-Whitney, Chi-squared and Fisher Tests were used in the statistical analysis.

RESULTS. 374 patients were enrolled, GA 204. General mortality 4.8%. Mean values for patients profile: age 53.1 years old, females 42.7%, BMI 23.2 kg/m2, BA 1.83 squared meters, PREOP 24 days, ECC duration 93.3 minutes, normal VF 72%, stable angina 33%, unstable angina 22%, miscellaneous diagnosis 45%, COMB 7.7%, elective surgery 93.8%, DM 22.2%, AH 45.7%, CS 19%. Surgery distribution/absolute risk: coronary artery bypass graft 56.8%/0.47, valvular heart disease correction 33.1%/0.46, adult congenital defects correction 8.8%/0.27 and aortic surgery 1.3%/0.8. Variables associated with mortality or longer ICU admissions: age (p=0.006), BMI (p=0.009), PREOP (p=0.0035), ECC duration (p=0.004), surgical indication (p=0.003), emergency surgery (p=0.017).

CONCLUSION. there is a rather singular distribution of surgeries in this group. Many of the previously described variables showed correlation with mortality or longer admission in the ICU. Prospective studies will be held in order to adjust these variables and determine new ones more relevant to underdeveloped countries.

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TRAINING IN BASIC CARDIOPULMONARY RESUSCITATION FOR RELATIVES OF AT-RISK PATIENTS IN INTENSIVE CARE

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INTRODUCTION. In our setting, the diffusion of Institutional Education in Basic Cardiopulmonary Resuscitation (BCPR) is low. The number of patients admitted to our Units after resuscitation following Cardiac Arrest is rising due to the population demand on the Out-of-Hospital Emergency Services, 061. The patients with neurological sequelae secondary to incorrect BCPR in the first 10 minutes are common.

METHODS. Through the Association of Ex-Patients of the Intensive Care Medicine Department, and with the psycho-social support of voluntary helpers on patient discharge, relatives are offered BCPR as part of the Quality Care Programme. Every three months, professionals from the Department organise this course for 20 relatives in the form of a 5 hour module. The concepts of the prevention of Ischaemic Heart Disease are presented together with the content of the National Plan for BCPR. Practical sessions are undertaken in small groups of 6 to 8 persons, using dummies.

RESULTS. A total of 294 relatives in 14 courses have received this training over the past 5 years. The mean age of the students was 38.3 (SD 15) years (11-75), 72% women, 32% with middle and higher education, 20% housewives, and 15% manual labourers. The evaluation of the scores obtained in the 16 item test before and after the course is shown in the tables below.

	N	Before Course Mean	SD	N	After Course Mean	SD	p*
Males	83	6.1	2.6	82	10.7	2.4	0.000
Females	211	5.5	2.5	206	10.7	2.5	0.000
Educational Level 1	77	4.3	2.5	77	9.7	3.2	0.000
Educational Level 2	117	6.3	2.5	114	11.4	2.2	0.000
Educational Level 3	58	6.6	2.5	56	11.1	2.3	0.000
Educational Level 4	42	7.1	1.8	41	11.8	2.7	0.000
Total	294	5.6	2.5	288	10.7	2.4	0.000

* t-Test

CONCLUSION. The participation of relatives of at-risk patients (Acute Coronary Syndrome, Bronchial Asthma, Neuromuscular Pathology) in this technique is considered to be a priority action, whether in the hospital setting or in Primary Care.

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CAN THE PATIENT UNDER VERTICAL BANDED GASTROPLASTY BE CONSIDERED AS A CRITICALLY ILL PATIENT?

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INTRODUCTION. To analyze if morbid obesity (MO) is associated with critical pathology in relation to patients undergoing vertical banded gastroplasty (VBG).

METHODS. All critical patients (CP) suffering MO, with a mean body mass index = 50,61, receiving programmed surgical treatment, and admitted in the ICU during the next period: 1st Oct. 96 to 25th Feb. 02, were prospectively included.
· Surgery procedures.
*Restrictive: VBG according to Masson's technic.
*Derivative: VBG + GIP according to Salmon's technic.
VBG + GIP according to Capella's technic.
·Type of study: Descriptive.

RESULTS. · Number of CP:116 (90 fem., 26 male).
· Mean age: 30.0 yrs. (SD = ±5)
· Mean lenth of stay: 1.38 days (SD = ±2,197). 2 outlayers were excluded.
· Surgery information
-VBG (Masson): 58 CP.
-VBG + GIP (Salmon): 34 CP. -VBG + GIP (Salmon): 24 CP.
-VBG in association to other surgical procedures: 16 CP
(16 cholecystectomies, 1 right inguinal herniorhaphy, and other 3 procedures).
· Mortality: 2 CP:
-Septic shock
-Multiorganic disfunction
· Readmission: 2 CP (subphrenic abcess and ARDS).
Complications
1. Hypoxemia: 69 CP (60% of the total)
1.1. 1.1. Not secondary to hypoventilation: 52 CP (72.5%).
1.2. 1.2. Associated to hypoventilation: 52 CP (72.5%)
2. Need for noninvasive mechanical ventilation: 25 CP (22%)
3. High blood pressure: 61 CP (52.0%).
4. Disturbances of cardiac rythm and conduction: 8 CP (7%).
5. Metabolic acidosis: 13 CP (11%).
6. Other complications: 16 CP (14%).

CONCLUSION. 1- The MO patient undergoing VBG, with or without GIP, rather than a patient bound to the reanimation or recovery room, is indeed a patient who requires admission in the ICU for, at least, 24-36 hours. 2- Hypertension of diffICUlt management and hypoxemia not due to hypoventilation nor shunt are the most frequent complications. 3- An important percentage of CP requires also mechanical ventilation. 4- Complications related to surgery are exceptional.

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PREOPERATIVE PROGNOSTIC PREDICTORS IN VALVULAR HEART DISEASE SURGERY.

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INTRODUCTION. Clinical presentation and evolution of valvular heart disease (VHD) patients have great significance in determining the best moment for surgical correction but lacks correlation with surgical outcome in most cases. This study tries to determine the preoperative variables associated with mortality in the course of surgical treatment of VHD.

METHODS. Cohort study conducted from January 2001 to February 2002. Inclusion criteria: patients submitted to VHD surgery during the period of study. Exclusion criteria: VHD surgery combined with non – VHD procedures. Data were analyzed with Chi – squared, Fisher and Mann – Whitney Tests.

RESULTS. One hundred five patients met the inclusion criteria. The preoperative variables associated with surgical mortality were: systemic arterial hypertension (p=0.016), peripheral vascular disease (p=0.031), redo (p=0.031), age (p=0.051), blood creatinine level (p=0.042), left ventrICUlar dysfunction (p=0.02).

CONCLUSION. Based on these data, efforts will be held in order to develop a prognostic score index for mortality in VHD surgical patients.

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MORTALITY AND RESCUE ANGIOPLASTY IN ACUTE MYOCARDIAL INFARCTION

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INTRODUCTION. In our setting, the diffusion of Institutional education in Basic Cardiopulmonary Resuscitation (BCPR) is low. The number of patients admitted to our Units after resuscitation following Cardiac Arrest is rising due to the population demand on the Out-of-Hospital Emergency Services, 061. The patients with neurological sequelae secondary to incorrect BCPR in the first 10 minutes are common.

METHODS. Through the Association of Ex-Patients of the Intensive Care Medicine Department, and with the psycho-social support of voluntary helpers on patient discharge, relatives are offered BCPR as part of the Quality Care Programme. Every three months, professionals from the Department organise this course for 20 relatives in the form of a 5 hour module. The concepts of the prevention of Ischaemic Heart Disease are presented together with the content of the National Plan for BCPR. Practical sessions are undertaken in small groups of 6 to 8 persons, using dummies.

RESULTS. A total of 294 relatives in 13 courses have received this training over the past 5 years. The mean age of the students was 38.3 (SD 15) years (11-75), 72% women, 32% with middle and higher education, 20% housewives, and 15% manual labourers. The evaluation of the scores obtained in the 16 item test before and after the course is shown in the tables below.

	N	Before Course Mean	SD	N	After Course Mean	SD	p*
Males	83	6.1	2.6	82	10.7	2.4	0.000
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* t-Test

CONCLUSION. The participation of relatives of at-risk patients (Acute Coronary Syndrome, Bronchial Asthma, Neuromuscular Pathology) in this technique is considered to be a priority action, whether in the hospital setting or in Primary Care.

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MULTISYSTEM ORGAN FAILURE (MSOF) AFTER OPEN-HEART SURGERY: INCIDENCE, PROGNOSIS AND RISK FACTORS

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INTRODUCTION. Multiorgan system failure (MOSF) is an infrequent but very serious complications after cardiac surgery, with high rates of mortality. This study was undertaken to determine the frequency, prognosis and risk factors for MOSF

METHODS. This study was performed in a twelve-bed Cardiac Surgery Intensive Care Unit over a 24-month period. All adult consecutive patients undergoing coronary, valvular and combined (valvular and coronary) surgery were prospectively studied (n = 2102). All patients were assessed by the "Modified" Parsonnet score

RESULTS. MOSF developed in 138 (6.57%) patients, of whom 51 (36.9%) died. This was the main cause of overall hospital mortality (51/92, 55.4%). In a logistic-regression anlysis, the development of sepsis, postoperative low cardiac output syndrome, mechanical ventilation more than 72 hours, a "Modified" Parsonnet score more than 25 and and preoperative ventilatory support were independantly associated with the development of MOSF. An organ system failure index (OSFI) of 3 or more was most significantly associated with ICU mortality (p<0.001).

CONCLUSION. In our series MOSF was a leading cause of mortality after open-heart surgery. The development of MOSF with an OSFI of 3 or more was the main predictor of postoperative mortality.

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CLINICAL AND EPIDEMIOLOGICAL FEATURES OF YOUNG AND ELDER PATIENTS UNDERGOING CARDIAC SURGERY

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INTRODUCTION. The comparative study of clinical, epiemiological and angiographic characteristics of young and elder patients admitted to the I.C.U after coronary artery bypass surgery (CABG) was the aim of the present study.

METHODS. We studied 211 patients who underwent CABG surgery. Fifteen patients (13 male and 2 female) were younger than 45 years and 196 patients (147 male and 49 female) were older than 65 years. Perioperative death occured in one patient from the <45 years group and in 10 patients from the >65 years group (P=NS). Categorical data were compared using the chi-square test and numerical data were analysed using the Student t-test. Differences were considered significant at P<0.05.

RESULTS. The characteristics of patients admitted to the I.C.U. after CABG surgery according to their age are listed in the table below:

	Patients <45 years	Patients >65 years	P
Hyperlipidaemia	9	101	NS
Hypertension	2	146	<0.001
Smoking	13	78	0.05
Hereditary History	5	56	NS
Diabetes Mellitus	3	118	<0.001
History of Myocardial Infarction	6	85	NS
Ejection fraction	51.67±8.66	47.52±11.58	NS
Left main or three-vessel disease	4	32	NS

CONCLUSION. According to the results of the present study, among patients admitted to the ICU after CABG surgery, smoking is the main predisposing risk factor in those who are <45 years, while hypertension and diabetes mellitus are the main risk factors in patients >65 years.

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EFFECT OF IMPLEMENTING A PAIN EVALUATION AND TREATEMENT GUIDELINES FOLLOWING CARDIAC SURGERY

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INTRODUCTION. In a n investigation conducted in ours ICU, 38% of patients hospitalised after elective cardiac surgery presented a pain score > 30 (min score 0 ; max 100) . These results were considered inadequate. A quality improvement initiative was undertake. The aim of the present study was to test if pain evaluation and treatement improved following pain guidelines implementation in a surgical ICU.

METHODS. The design consisted in observing de pain evaluation both before and 1 month after implementation of guidelines. These guideline are divided in two item : first introduction of a regular pain evaluation using a visual analogue scale (VAS) and second in a proportional VAS-derived analgesic prescription protocol. Recommendation were given during repetitive meetings, feedback sessions and regular poster information on the ICU walls. Pocket guideline and VAS tool was distributed. Pain intensity evaluation of the nursing team was checked by an independent observer and compared with the nurses-charted VAS. Improvement of pain control was tested based on the following criteria: utilisation of the algorithm at least twice per working shift; corresponding analgesic drug to observed VAS; and follow up check of VAS after analgesic administration. The independent observer measure VAS at 8 a.m. and at 4 p.m. postoperative day 2 and 3. Proportion of algorithm adherence before and after introduction of the recommendation were tested using Fisher's exact test. Variance of median VAS was tested using Mann-Whitney test.

RESULTS. Demographic data: 10 patients per période, 17 days of observation before , 16 days after; 61 working shift before and 59 after.

	Before	After	p
Number of 2 Vas evaluation per shift (%)	27 (44%)	38 (64%)	0.0297
Number of VAS evaluation per period	67	86	
Number of VAS evaluation >30 (%)	25 (37%)	41 (48%)	
Number of corresponding drug of VAS >30 (%)	6 (24%)	17 (41%)	0.1881
Number of control VAS after drug administration	2 (8%)	14 (34%)	0.0189
Median VAS Nurse Team	20	20	0.6474
Median VAS Independent Observer	31	20	0.2807

CONCLUSION. These preliminary results indicate that the implementation of an algorithm on pain intensity evaluation and treatment increases the number of pain evaluation and re-evaluation after drugs administration. Although the administration of analgesic drugs increased, the number of patients with insufficient pain treatment stays still high.

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PAIN FOLLOWING CARDIAC SURGERY IS PRESENT FOR AT LEAST ONE MONTH

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INTRODUCTION. Acute pain after surgery may contribute to chronic pain and may worsen quality of life after a successful intervention. The aim was to assess pain intensity after cardiac surgery during intensive care (ICU) stay, and during convalescence.

METHODS. Prospective cohort study in a tertiary teaching hospital. Pain evaluation and treatment of the health care provider was not standardized; pain intensity was evaluated daily by an independent observer during ICU using visual analog scale (VAS). An adapted, validated questionnaire of the American Pain Society on pain during ICU was applied at ICU discharge, and on pain during convalescence at one month after surgery. For proportions, Fisher's Exact tests, for nonparametric data, Mann-Whitney tests, for correlations, Spearman Rank Tests were used.

RESULTS. Eighty patients following cardiac surgery of 62∂13 years (mean∂S.D.), male:female 79%: 21% were included consecutively. Median VAS at rest during ICU was 24 mm, median VAS at mobilisation 50 mm. Table 1. VAS at rest and at mobilisation measured on day 2 correlated with NRS at rest during convalescence(r=0.36, p=0.008; r=0.38, p=0.005). VAS at mobilisation (cut-off 60 mm) on day 2 predicted NRS at rest (cut-off 3) during convalescence [0.94 (95%CI 0.81 to 0.99); specificity 0.29 (95%CI 0.10 to 0.56); p=0.03]

	During ICU (N=69)	During convalescence (N=56)	p
Median pain at rest	4	3	0.0001
NRS of pain >3 at rest	40 (58%)	18 (32%)	0.0023
Median pain at mobilisation	7	4	<0.0001
NRS of pain >3 at mobilisation	59 (86%)	34 (61%)	0.0001
Often or always pain	7 (10%)	7 (13%)	0.7784
Never painless	35 (50%)	11 (20%)	0.0002

NRS, numeric rating scale (minimal 0, maximal 10)

CONCLUSION. High pain intensity levels are reported by the patients during ICU after discharge. Pain after on month is reduced compared with ICU discharge. However, one third suffer from moderate to severe pain at rest, two thirds at mobilisation during convalescence. There is a correlation between pain during ICU and pain during convalescence. VAS at mobilisation on day 2 is predictive for pain after one month

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EARLY COMPLICATIONS IN THE POSTOPERATORY CARE OF LIVER TRANSPLANT, A PROSPECTIVE OBSERVATIONAL STUDY

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INTRODUCTION. The prognosis of liver transplant has improved the last few years due to advance in surgical techniques and immunosuppressive regimes, but early complications show a high prevalence affecting morbi-mortality in these patients

METHODS. A 42 beds ICU in a teaching 3rd level Hospital. Prospective observational study on all patients with the mentioned condition treated in our centre from October 2000 to October 2001. Follow up during ICU stay. We have collected data from 46 patients (47 grafts) with a mean age of 52.4±9.6 years, 28.3% women, mean APACHE II on admission 17±4.1, median Child score 7,5 (7-8) and mean SOFA score 5.8±1.8. Surgical data were as follows: fluids balance 478±2570, hours of graft ischemia 7.6±2.1, reperfusion syndrome in 21% and fibrinolysis in 4.3%. At admission mean core temperature was 35.3±1 ºC. Median ICU stay 3.5 (3-4, max. 17) days and median hours under mechanical ventilation 10 (7.5-16, max 67). The prescribed immunosuppression was cyclosporine in 50% and tacrolimus in 50% of patients

RESULTS. ICU mortality was 6.5% (3 patients). Complications were present in 78% (45.7% of them more than two episodes). 2 patients had to be reoperated, one because early graft dysfunction treated with MARS and retransplantation (death because a new graft dysfunction), and the other because abdominal haemorrhage. One patient developed an early rejection. Metabolic complic 60.9% (high insulin requirements 41.3%) – Renal failure 45.7% (renal replacement 6,5%)- Cardiac complic 30.4% (CHF 8.7%, HBP 10.9%) – Respiratory complic 19.6% (10.9% SDRA) – Bleeding 13% – Neurological complic 10.9% (myelinolysis 1 patient) – Infection 2.2%.
Patients who died had higher APACHE II, Child and SOFA scores, lower serum albumin levels, longer graft ischemia, higher percentage of fibrinolysis and reperfusion syndrome during surgery and higher percentage of acute renal failure an need for renal replacement (not statistical analysis due to the low mortality rate

CONCLUSION. 1.- Early complications are frequent but generally mild. 2.- Mortality in the ICU is mainly related to surgical aspects. 3.- Severity scores classify adequately patients with higher risk of death

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SLEEP IS DISTURBED AFTER CARDIAC SURGERY FOR AT LEAST ONE MONTH

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INTRODUCTION. Sleep is an important parameter of quality of life. The aim was to assess the impact of cardiac surgical insult and ICU environmental factors on sleep observed over one month.
METHODS. Prospective cohort study in a tertiary teaching hospital. Exclusion criteria: major comorbidities, dementia, chronic pain, insomnia, chronic intake of hypnotics, antiepileptics or antidepressants. A validated French translation of the Pittsburgh Sleep Quality Index questionnaire (1) was applied before surgery, at the end of ICU stay, and one month after surgery. For parametric data, unpaired t-test and one way ANOVA, for nonparametric data, Mann-Whitney or Kruskal-Wallis tests were used.
RESULTS. Eighty French speaking patients of 62 ±13 years (mean ± S.D.), male:female 79%:21%, were included consecutively. 44% had coronary artery bypass grafting, 13% aortic valve replacement, 6% mitral valve replacement, 29% combined, 9% other cardiac surgery. Compared with before surgery, patients presented significantly more cough, nycturia and pain disturbing their sleep after one month. Compared with before surgery and after 1 month, patients presented significantly more pain and bad dreams at the end of ICU stay. Eleven of 55 patients (20%) reported a new regular intake of hypnotics after one month. Four of 55 patients (7%) who did use hypnotics before surgery stopped doing so one month after.

	Before surgery N = 80	End of ICU stay N = 17 §	After one month	p
Time going to bed/preparing sleep (hh:mm)	22:37 ± 1:13*	21:08 ± 1:58	21:55 ± 1:08	< 0.0001
Sleep time (h)	7:24 ± 1:40	4:47 ± 2:39°	7:21 ± 1:25	< 0.0001
Time falling asleep (min)	29 ± 35	17 ± 29	32 ± 36	0.4478
N of >2 awakenings per week/ICU stay	26 (33%)*	10 (59%)	38 (69%)	< 0.0001

§ 63 patients presenting complete insomnia, temporal disorientation, amnesia or delirium were temporarily excluded ; * significantly different from end of ICU stay and after 1 month ; ° significantly different from before surgery and after 1 month.

CONCLUSION. Cardiac surgery and ICU stay are followed by an impairment of quality of life due to sleep disturbances for at least 1 month. They lead to a new postoperative intake of hypnotics in 20% of the patients. Disturbances, i.e. more frequent sleep interruption, are mainly related to more nycturia, coughing and pain compared with the preoperative status.
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HUMAN PROTEIN C CONCENTRATE IN THE TREATMENT OF SEPTIC CHILDREN AND NEONATES

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INTRODUCTION. We report the effects of substitution with a virus-inactivated protein C (PC) concentrate in disseminated intravascular coagulation (DIC) in preterm infants and children with sepsis (meningococcal in the children and aldolecent; staphylococcal and enterobacter in the preterms) associated with purpura fulminans.

METHODS. This was a prospective open-label study. A total of 16 patients,9 paediatric and adolescent patients age 0.2 to 18.25 years with DIC associated with severe acquired PC deficiency (range 0.02 to 0.48 IU/mL; median, 0.22 IU/mL) in meningococcal septic shock and purpura fulminans; and 7 preterm infants with severe acquired PC deficiency (range 0.01 to 0.1IU/mL; median, 0.02 IU/mL) due to staphylococcal and enterobacter sepsis were studied. Replacement therapy was initiated with a virus-inactivated PC concentrate with an initial intravenous bolus of 80 to 120 IU/kg followed by 50 IU/kg up to six times per day as an adjunctive therapeutic regimen to otherwise optimal intensive care treatment.

RESULTS. After initial PC administration, plasma PC levels rose to normal ranges and were maintained under PC replacement therapy. Improving or even normalising global hemostatic parameters were assessed in all patients. Markedly elevated plasminogen activator inhibitor type 1 (PAI-1) levels prior to treatment, reflecting a reduced fibrinolytic potential, decreased rapidly under PC substitution. Concomitantly improving signs of purpura fulminans reflected by decreasing size of skin lesions, demonstrated a restoring microcirculation. Seven of the nine paediatric and all of the neonatal patients survived. One patient (paediatric) required limb amputation; two patients died because of multiorgan failure. Both presented with a severely low plasma PC activity of 0.02 IU/mL on admission to the hospital. No adverse effects were observed with the PC concentrate administration.

CONCLUSION. AIt can be concluded that the administration of PC concentrate had a marked benefit on the deranged coagulation status of patients with purpura fulminans and septicaemia. Normalisation or even partial correction of haemostasis as well as improvement of microcirculation accompanied by improving signs of purpura fulminans were demonstrated in all patients

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SPINE SURGERY. SURGICAL AND MEDICAL COMPLICATIONS

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INTRODUCTION. The main purpose of this study is to report medical and surgical complications of spine surgery in a third level universitary pediatric hospital with a reference spine surgical program.
METHODS. Study design is a retrospective clinical series of 73 pediatric spinal surgeries.All spine surgeries performed on children under 18 years of age between January 2000 and January 2002 were included. Patient were grouped in four diagnostic categories (idiopathic, neuromuscular, congenital scoliosis and miscellaneous) and procedure performed (posterior (P) fusion, anterior/posterior (AP) fusion, anterior (A) fusion, (IW) instrumental withdrawal). Next data were recorded from clinical chart:age, gender, needs of transfusion products, volume demands during first postoperative day,days on mechanical ventilation,medical and surgical complications.
RESULTS. Study sample included 73 patients, 47 female and 26 male. Age ranged between 4 and 18 years with average of 12.7 years. Characteristics were: Idiopathic 29, Neuromuscular 26,Congenital scoliosis 7,miscellaneous 11. Procedures performed were:P fusion 53,AP fusion 17,A fusion 1,IW 2. .Average lenght of stay in Pediatric intensive care unit were 1.3 days (range 0-25).Average days on ventilatory support 0.46(range 0-2.5). No patient required intubation after weaning.Major complications were: Deep wound infection(2), respiratory distress(1), large intraoperative blood loss (1),and paraplegia (1).No deaths were observed.Minor complications were: atelectasis(6), Pleural effusion(4), pneumonia(2), pneumotorax(1), superficial wound infection(4), urinary tract infection(3) and electrolitical disturbances(17). Postoperative transfusion needs were 8.4 ml/kg (95% confidence interval (CI) 4.1-12.8) for AP fusion, 6.8 ml/kg (95% CI 4.8-8.7)for P fusion; A fusion and IW doesn't need postoperative blood replacement. Total blood transfusion was 40.7 ml/kg (95% CI 29.7-51.8)for AP fusion, 23.2 ml/kg (95% CI19.3-27.1)for P fusion; 6.9ml/kg for A fusion and 7.6 ml/kg for IW.Volume demands(no blood products)during first postoperative day were 81.4 ml/kg (95% CI 50.5-112.2)for AP fusion, 59.1 ml/kg (95% CI 48-69.7) for P fusion;38ml/kg for A fusion and 44.8 ml/kg for IW.
CONCLUSION. Spine surgery has few major complications rate in a reference spine surgery pediatric hospital. Minor respiratory complications affect 15% of our patients without repercussion in outcome. Total blood loss is greater in AP fusion than in other procedures, but postoperative blood replacement in PICU didn't differ between procedures.
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INTRAABDOMINAL PRESSURE IN PEDIATRIC POPULATION IN THE PICU: METHODOLOGY AND VALIDATION

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INTRODUCTION. Background Elevated intra-abdominal pressure (IAP) adversely affects pulmonary, cardiovascular, renal, splanchnic and central nervous system physiology, and it determines the common clinical picture called "the abdominal compartment syndrome". Nevertheless the direct monitoring of IAP is not always practicable, because it requires an abdominal drainage. A lot of Authors demonstrated in the adults that the bladder pressure is a reliable index of IAP, but there are not studies on pediatric population. The aim of this study is to evaluate the level of significance of this index in a pediatric population.

METHODS. Population: We enlisted a group of pediatric patients, sedated and paralysed (3 OLTX, 3 abdominal surgery, 1 cardiac surgery), Age 20.8 ± 16,3 (range 4-48) months. METHODS. The bladder pressure was measured with the patient in supine position, with a trasduction circuit connected to the bladder catheter and to the abdominal drainage (3 JPratt, 3 Pig Tail, 1 catheter for peritoneal dialysis). To obtain a good transduction of pressure, a volume of saline was pushed into the bladder. The volume of saline was variable according to the weigth and age: we obtained a scheme (Table 1) from our empirical evaluation of the pediatric bladder compliance and urodinamic data.

RESULTS. As reported in Table 2, there aren't significative differences between the level of pressure measured in the bladder and in the peritoneal cavity (p= 0.50).
Mean:0,00∂DS:1,15

Weigth	< 5 Kg		6-20 Kg		21-40 Kg		>40 Kg
Volume	2.5 ml / Kg		2 ml / Kg		1.5 ml / Kg		100 ml Total
Abdomen	6	10	11	7	9	8	22
Vescical	7	11	9	7	10	7	22
Delta	1	1	2	0	1	1	0

CONCLUSION. Our data, although numerically limited, suggest that the bladder pressure is a reliable index of the IAP in pediatric patient population admitted to PICU.

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NON-INVASIVE POSITIVE-PRESSURE VENTILATION (NPPV) IN ACUTE NEUROMUSCULAR PEDIATRIC PATIENTS

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INTRODUCTION. From 1998 to 2001, 7 pediatric patients (age range 0.58 to 10 years, mean 3.91 years) were treated using NPPV during distinct episodes of acute respiratory failure (ARF) of neuromuscular origin. In all patients immediate intubation for an acute, life-threatening presentation was avoided and respiratory status improvement was achieved. Few data are available up to now about NPPV application and indications in the acute setting in infants affected by neuromuscular disorders (NMD).
METHODS. A prospective observational study was carried out on 7 non-consecutive neuromuscular patients admitted to PICU because of ARF and managed with NPPV in the acute phase;remarkably, 4 out of 7 were <15 months aged. All the patients were treated by a flow-triggered intensive care mechanical ventilator (Siemens Servo 300 ventilator, Siemens-Elema, Sweden) through a tight fitting face mask. NPPV was administered for at least 24 hours post-admission. A pressure-control mode was adopted for better compensation of leaks around the mask. Flow-sensitive trigger permitted a better synchronization of patient's spontaneous breathing, limiting the need for deeper patient sedation (low-dose midazolam drip). Initially, a relatively low ventilator frequency delivery was set (8-10 b/min). Peak inspiratory pressure was titrated upward to obtain an exhaled tidal volume of 5-6 ml/kg maintaining a $PaCO_2$ value <65 mmHg and a pH >7.25; PEEP value was adjusted to maintain an oxygen saturation >91-92% with a required FiO_2 <0.6.
RESULTS. All patients were referred to PICU on spontaneous breathing: those admitted with ET tube already positioned were not considered eligible for this study. An oxygenation improvement was obtained in all patients within 3 hours from the onset of NPPV . The PaO_2/FiO_2 increased from 86.29 ±16.13 to 235.6±32.32 ($p<0.05$) and 292.6 ± 25.75 ($p<0.001$) on selected time points (3 and 12 hours after NPPV introduction, respectively); conformly, alveolar-to-arterial oxygenation difference ($A\text{-}aDO_2$) decreased from a 462.3 ± 77.77 to 195.7 ± 59.67 ($p<0.05$) and 101.8 ± 23.92 ($p<0.001$) respectively.
CONCLUSION. NPPV resulted a safe and effective therapeutic approach in both hypoxemic and hypercapneic ARF episodes in this children group affected by NMD. Even in cases of emergency presentation or when resuscitation is needed, it is of importance to identify NMD children with residual ventilator-free breathing ability thus performing a NPPV trial. Life-threatening respiratory distress and young age should not preclude NPPV application in a PICU setting.
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HERPES SIMPLEX ENCEPHALITIS IN CHILDREN. ANALYSIS OF 11 CASES.

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INTRODUCTION. Herpes simplex encephalitis (HSE) is a severe sporadic encephalopathy mainly caused by herpes simplex viruses (HSV)1 and 2.It brings a high morbility, so a quick diagnosis, early specific treatment and accurate management in the acute phase are essential for the prognosis.

METHODS. Restrospective analysis of the patients diagnosed of HSE from 1991 to 2001. Variables: Symptoms at onset; HSV diagnosis: HSV specific polymerase chain reaction (PCR)in cerebrospinal fluid (CSF), serum and CSF serologies, CSF composition; Electroencephalography; Neuroimaging; Therapeutics: Paediatric intensive care unit (PICU) admission, acyclovir administration, treatment of seizures, corticotherapy, cerebral oedema treatment, mechanical ventilation, inotropic support; Sequelae.

RESULTS. 11 cases (45% girls, 55% boys). 45% < 1 year (age range from 4m to 12y). 63% at springtime. Symptoms at onset: Fever (100%), vomiting (73%), focal seizures (54%), consciousness decrease (36%), headache (27%) and diarrhoea (27%). Others (< 20%): behaviour changes, asthenia, ataxia, damaged cranial nerves signs, meningism, abdominal pain, paraesthesiae and cough. PCR for HSV in CSF was used in 81% and positive in all. Serum and CSF serologies were made in 72%, 50% were positive. Early examination of CSF was done in all patients, being normal in 18%, abnormal in 82%(predominance of lymphocytes 36% and of granulocytes 36%). Cranial ultrasound (3 cases) was normal in all. When the computerized tomography (CT) was undertaken within the first 24 hours (6 cases) it was normal in 83%, whereas undertaken afterwards (3 cases) all were pathological. Magnetic resonance imaging (MRI) (8 cases) was abnormal in 87,5% (obtained after 3 days of illness). EEG (10 cases) was altered in 80% (done within the first 24 hours in 55%). 82% of the patients were admitted in PICU, meaning 1,2 o/oo of the admissions in our unit. The mean length of PICU stay was 9 days and of hospital stay was 30 days. Acyclovir was given to 90% of the patients (20mg/kg/8h iv, mean length: 17 days), 55% received anticonvulsant therapy and 27% corticoids. 2 cases needed mechanical ventilation. No need of inotropic support nor of cerebral oedema intensive treatment. There was no death, yet a high morbility. After discharge, there were sequelae in 72%: motor (72%), cognitive (42%), epilepsy (42%). In the follow-up the patients showed severe sequelae in 36%, slight sequelae in 27% and no sequelae in 36%.

CONCLUSION. 1- HSE is infrequent, with higher incidence in infants and at springtime. 2- The main symptoms are fever, vomiting, focal seizures and consciousness decrease. 3- Detection of HSV by PCR of CSF is a quick effective method to reach the diagnosis. 4- A normal CT within the first 24 hours doesn't exclude future alterations. 5- MRI has a high efficiency. 6- Most patients need admission in PICU. 7- Despite specific treatment for HSV and intensive management in the acute phase, morbility is very high.

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INVESTIGATION OF PHOTOPLETHYSMOGRAPHIC SIGNALS IN NEONATAL AND PAEDIATRIC PATIENTS

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INTRODUCTION. Pulse oximeters are widely used in paediatric intensive care but they have some severe limitations. The technique relies on the presence of adequate peripheral arterial pulsations, which are detected as photoplethysmographic signals (PPG). When peripheral perfusion is poor as in states of hypovolaemia, hypothermia and vasoconstriction oxygenation readings become extremely unreliable. Hence, pulse oximetry becomes unreliable in a significant group of children just at the time when accurate readings are most needed. To overcome this limitation, the oesophagus has been investigated as a potential measurement site on the hypothesis that perfusion may well be better preserved at this central site. Studies on adult patients have shown that measurable PPG signals at red and infrared wavelengths can be detected within the whole depth of the oesophagus. A new system to investigate the quality of oesophageal PPG signals is being constructed with the aim of developing a neonatal and paediatric oesophageal pulse oximeter.

METHODS. A reflectance optical sensor has been constructed comprising miniature infrared and red emitters and a photodetector. The sensor was design to fit into a conventional disposable transparent stomach tube, 12 French gauge. The oesophageal PPG sensor within the stomach tube was inserted through the nose into the oesophagus of a 2 kg, 17 day old neonate. The stomach tube was advanced into the oesophagus under direct vision until the probe was 25 cm from the nose. PPG traces from the oesophagus were recorded for approximately 5 minutes at this depth on a laptop computer. Measurements were repeated at 20 and 15 cm from the nose.

RESULTS. Measurable PPG traces of good quality were obtained in the oesophagus at all three depths. The PPG signals in the mid to lower region of the oesophagus on average had larger amplitudes at both red and infrared wavelengths than the PPGs recorded in the upper oesophagus. Artefacts on both wavelengths due to oscillations as a result of high frequency ventilation. Filtering successfully eliminates the artefact.

CONCLUSION. The new oesophageal reflectance optical sensor has allowed PPG measurements to be made within the whole length of the neonatal oesophagus. The red and infrared wavelengths used are suitable for pulse oximetry. These results are the first to demonstrate that pulse oximetry may be feasible in the neonatal or paediatric oesophagus. Further studies are required to develop a neonatal/paediatric pulse oximeter.

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FAVORABLE RESPONSE TO PROTEIN C IN VENOOCCLUSIVE DISEASE AFTER ALLOGENEOUS STEM CELL TRANSPLANTATION

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INTRODUCTION. Venoocclusive disease (VOD; syn: sinusoidal obstruction syndrome) may be a severe, lethal complication occuring after stem cell transplantation. The underlying pathomechanism is an endothelial damage of small liver sinusoids. Recently, trials with defibrotide showed promising results. The use of Protein C (PC)has not been evaluated thoroughly.

METHODS. We used protein C (Ceprotein; Baxter -Immuno) in two patients with moderate or severe, therapy-resistant VOD.

RESULTS. Patient 1 (E.G, swiss, 1,75 y) suffered from an acute myelogenous leukemia (M 7 with t(1;22) of early infancy After complete first remission by conventional chemotherapy an allogeneic stem cell transplantation with a matched unrelated donor was performed. Conditioning comprised busulfan, VP16 and cyclophosphamide. Patient 2 (M.K, iranian, 11 y) suffered from beta-thalassemia major with secondary moderate hemosiderosis, as well as chronic persisting hepatitis C infection with liver fibrosis. He received a matched related bone marrow transplantation, using i.v. busulfan , reduced cyclophosphamide dose and fludarabine. Both patients received low dose heparin (100 IU/kg) and antithrombin III substitution. In addition, pat. 2 got prophylactical defibrotide (20 mg/kg) and N-acetylcystein. Two weeks after transplant both patients developed VOD (severe (pat 1); moderate to severe (pat 2))with weight gain, hepatomegaly, massive ascites and severe thrombocytopenia. Maximal bilirubin was 15 mg/dl (pat 1) and 2 mg/dl)(pat 2). Therapy with defibrotide (60 mg/kg) was started immediately. In pat.1 the pulmonary situation deteriorated rapidly with massive aszites and oxygen need and a reversed portal venous flow. Defibrotide was stopped after 5 days. Thrombolytic therapy using rTPA and a continuous PC substitution (PC level 16%; bolus 100 IU/kg, followed by 100 IU/kg every 4h)) were started. Lysis therapy had to be abandoned due to respiratory tract bleeding Global coagulation (PT 34 %, aPTT 250 sec) and PC level normalized within hours after PC substitution. A normal centripetal portal flow could be achieved by high dose defibrotide (120 mg/kg) and continued PC substitution after several weeks. Pat. 2 showed only a temporary improvement under defibrotide treatment. Due to clinical deterioration (hepatic pain, increased ascites) and low PC level (38%) a continuous PC substitution (50 IU/kg every 6 h) was initiated. There was a prompt recovery after adding PC with a dramatic reduction of ascites, weight and abdominal pain within 2-3 days after start of PC infusion. Elevated bilirubin levels returned to normal in both patients.

CONCLUSION. In our 2 patients neither prophylactic administration of AT III nor of defibrotide were able to prevent moderate to severe VOD.Our data indicate that PC substitution may be a useful adjunctive treatment in severe VOD. Until controlled studied will be initiated we recommend a stratified treatment in VOD, starting with defibrotide, and adding PC in unresponsive cases.

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TIMING, INDICATION AND OUTCOME OF TRACHEOSTOMY IN PEDIARIC ICU PATIENTS

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INTRODUCTION. Tracheostomy is a procedure usually done to facilitate prolong ventilation or chronic airway management. To review the role of this procedure in PICU patients, we conducted a study looking at prevalence, indication, timing and outcome of tracheostomy in our PICU patients.

METHODS. A retrospective analysis of PICU patients who underwent tracheostomy from 1996-2001.

RESULTS. 35 children averaging 4.7±0.5 year and representing 2% of all PICU admission underwent tracheostomy during the study period. Upper airway obstruction associated with traumatic and non-traumatic brain insult was the main indication for tracheostomy. 25/35 patients were disconnected from ventilator after tracheostomy. 2/35 patients needed prolong ventilation. The mean ventilation days pre and post tracheostomy were 17.4±2.2 and 6.6±3 respectively. A total of 27 patients survived (77%): 15/27 patients were discharged home, and the remaining 12/27 needed rehabilitation. The mean length of PICU stay pre and post tracheostomy were 21.5±2.6 and 10.8±3 days respectively. 8/35 (23%) patients expired in the hospital: 2 from causes related directly to tracheostomy and 6 from other causes.

CONCLUSION. Upper airway obstruction is the leading indication for tracheotomy. Most of the pediatric patients tolerat the procedure well. Tracheostomy may facilitate weaning from ventilator and shortens the length of PICU stay in patients requiring prolong intubation. Although life threatening complications related to tracheostomy are seldom, it should be well recognized. Mortality in tracheostomy patients is mainly due to underline pathology.

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ORAL SILDENAFIL FOR THE TREATMENT OF REVERSIBLE PULMONARY HYPERTENSION IN CHILDREN

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INTRODUCTION. There are anecdotal reports of sildenafil, a type 4 phospodiesterase inhibitor, being used to reduce pulmonary artery pressure in children with mainly cardiac induced pulmonary hypertension (PHT).

METHODS. We have given oral Sildenafil to 10 children on our paediatric intensive care units with PHT from various causes. Diaphragmatic hernia (3), AVSD (2) VSD (1) PDA (1), PPHN (2) pulmonary hypoplasia (1). The median age of the group was 1m (IQR 1-6m). 7 were receiving inhaled nitric oxide during sildenafil. Median dose was 0.5mg/kg (IQR 0.3-0.53mg/kg 8hrly) and duration was 7 days (IQR 3-29). Pulmonary artery pressures were directly measured in 3 of the 4 cardiac children and deduced from Doppler echocardiographic measurements of the TR jet in 5 children.

RESULTS. PAP decreased significantly ($p<0.05$) following oral doses of sildenafil (n=7). Mean pulmonary/system (P/S) ratios decreased from 0.99 to 0.75 (n=8) within 3 hours of the oral dose. Systemic pressure was unaltered in all children. In one child with pulmonary hypoplasia the P/S ratio was unaffected.

CONCLUSION. Oral sildenafil can significantly reduce raised PAP in children when there is a reversible etiology. This may be partICUlarly useful in children and neonate with PPHN.

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ASSESSMENT OF ANTIBIOTIC SERUM LEVELS OF AN ANTIBIOTIC IMPREGNATED CENTRAL VENOUS CATHETER IN PICU

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INTRODUCTION. Central venous catheters (CVC) are an important means of securing intravascular access in pediatric intensive care unit patients. One of the major morbidity's in use of CVC is catheter-related infection (CRI). The incidence of bacteremia with CVC use is approximately 5.3/1000 catheter days and mortality as high as 25%. One approach to reduce the incidence of CRI has been to decrease catheter bacterial colonization (CBC). Reduction in CBC is achieved by coating or impregnating antimicrobial substances into the catheter material. Use of minocycline/rifampin treated catheters has been shown to reduce the rate of CRI in critically ill patients. The concern in pediatric population is the use of minocycline. Tetracycline and its derivatives (minocycline), when used in young children, carry the risk of dental and sceletal abnormalities. The problem of potential eluting of minocycline from minocycline-impregnated catheters may pose a risk for young children. Our study examined whether detectable levels of minocycline and rifampin were present in the serum of the pediatric intensive care unit patients with indwelling minocycline/rifampin impregnated CVC.
METHODS. Patients admitted to PCCU age 8-18 years and in need of CVC were eligible for study. Six patients were enrolled. Each patient had two samples of blood 2 and 2.5 ml withdrawn for rifampin and minocycline assays respectively. Collection times were at the time of catheter insertion and 24h thereafter for seven days or until catheter removal, whichever came first. Rifampin serum samples were processed prospectively soon after colection by standard HPLC. Minocycline serum samples were stored frozen in -80 centigrade and assayed in one batch using reverse phase HPLC.
RESULTS. Demographic data are in table. Ranges with mean values in ( ).
None of the minocycline samples had detectable level of antibiotic. The limit of sensitivity for minocycline was 0.4 mg/l. Therapeutic levels are 1.4-1.8 mcg/ml. One patient had 4 consecutive samples 3 to 6 with low therapeutic levels of rifampin (4-5 mcg/ml). Therapeutic levels of rifampin are 4-32 mcg/ml. Rifampin sensitivity was 1 mcg/ml. Rifampin has distinct peak time and no interfering substances were identified.

Sex Male 6	Age (y) 8-16 (12.3)	Cath.Insertion site Fem. Vein-5, Int.Jug. V.-1	Duration of stay (d) 2-7 (5.3)	No of samples assayed 36

CONCLUSION. Minocycline/rifampin impregnated catheters do not produce detectable levels of minocycline and may be safely use in infants and young children.
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HYDROCORTISONE EFFECTS ON BLOOD PRESSURE IN PRETERM INFANTS WITH CATECHOLAMINE RESISTANT HYPOTENSION

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INTRODUCTION. About 20% of preterm neonates admitted to neonatal intensive care units (NICU)become hypotensive during first days of life (1). Because hypotension in very low birth weight (VLBW) neonates is correlated with development of deleterious sequeles, such as intraventrICUlar haemorrhages (IVH), cerebral ischemia (2) or necrotizing enterocolitis (NEC) (3), the emergence of this consequences required fast and corrective treatment. An inotropic agents commonly used in VLBW infants such as dopamine and norepinephrine in some cases do not produce elevation in blood pressure despite using of very high dose. In this study I would like to exam the influence of hydrocortisone administration in VLBW infants with hypotension unresponsive to stndard catecholamine treatment.

METHODS. I have reviewed the cardiovascular response to hydrocortisone therapy in 16 preterm infants. Mean gestation age was 27.1 (25-29) weeks, postnatal age 4.8
(1-9)days, mean birth weight 1070g (710-1420). Eight of them suffered from respiratory distress syndrome and eight from sepsis. The first line of hypotension therapy was always volume administration (normal saline or albumine) and catecholamine infusion. Hydrocortisone at the dose 2mg/kg was administered when dopamine at the dose 10mcg/kg/min (12 patients or norepinephrine 0.5mcg/kg/min (4 patients)failed to normalized arterial blood pressure.

RESULTS. Mean blood pressure increased from mean 23.7mm of mercury (21-26) to 27.1 mm Hg (25-31) 2 hours after hydrocortisone administration and to 28.4 mm Hg (26-32), 29.7 mm Hg (27-34) and 31.3 mm Hg (28-35) by 4, 6 and 8 hours of hydrocortisone injection, respectively. After 24 hours blood pressure remained still stable. The dose of dopamine and norepinephrine decreased during the first day after the hydrocortisone treatment and the mean dose was 7.8mcg/kg/min (4-10) and 0.34mcg/kg/min (0.2-0.5), respectively. During the first 24 hours after the treatment urine output increased in 14 patients. Twelve of total sixteen patients survived. Two of them died because of Gram negative sepsis, one developed IVH IVdegree and one died because of severe brochopulmonary dysplasia

CONCLUSION. VLBW neonates suffered from circulatory failure with catecholamine resistant hypotension can response to single dose of hydrocortisone with rapid stabilization of cardiovascular status. This effect results in decrease of catecholamine requirement.

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PNEUMOCOCCAL MENINGITIS IN CHILDREN. REVIEW OF 32 CASES

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INTRODUCTION. Pneumococcal meningitis is an important cause of morbility and mortality in children. We describe the epidemiological characteristics and clinical features of pneumococcal meinigitis in children admitted to a children's hospital in Barcelona.

METHODS. Medical records of 32 children with a diagnosis of pneumococcal meningitis based on identification of S. pneumoniae in the blood or cerebrospinal fluid between January, 1993, to April, 2002, were retrospectively reviewed.

RESULTS. RESULTS. 32 cases of pneumococcal meningitis were diagnosed in 29 patients. Median age was 24 months (range 1.8 m-9.8 y). 24 children were younger than 5 years old (75%). Male-female ratio was 1.2:1. None of the children had a previous immunological deficit. Thirteen patients (41%) were pre-treated with antibiotics. The most frequent signs on admission were fever (100%), vomiting (72%), headache and irritability (34%), othalgia (22%) and shock (16%). Neurological findings were lowered level of consciousness in 18 patients (52%), signs of meningismus in 24 patients (75%) and arreactive mydriasis in 3 patients (9%). The mean leukocyte counts in blood were 19164/mm3 and the mean C-reactive protein was 141mg/L. Cerebral spine fluid indices on admission were: white blood cell=2301 (50-9800) /mm3; protein=148 (43-396) mg/dl; and glucose= 38 (0-262) mg/dl. Main serogroups were: 18 (16%), 6 (13%), 4 (9%), 19 (6%), 23 (6%), 7 (3%), 14 (3%) and 9 (3%). Overall, 50% of the pneumococcal isolates were penicilin-nonsusceptible, 28% cefotaxim-nonsusceptible and 3% were vancomycin-nonsusceptible. An initial abnormal cranial computed tomography was found in 6 patients. The median duration of parenteral antibiotic therapy was 10 days. All patients were empirically treated initially with cefotaxime (associated to vancomycin in 22 of them). Twenty-six patients (81%) received dexamethasone. The administration of mannitol was necessary in 6 patients (19%) and anticonvulsants were administrated in 8 patients (25%). Only 8 patients (25%) needed inotropic support (no longer than 48 hours). Mechanical ventilation was required in 15 patients (47%) during a mean of 1.5 days (range 0-10). Acute complications were: metabolic acidosis (3/32), disseminated intravascular coagulopathy (6/32), seizures (7/32), SIADH (3/32) and diabetes insipidus (2/32). Twelve patients (37%) suffered deafness, three patients (3%) hemiparesia and four (12%) were exitus. The mean hospital stay was 18.5days and mean intensive care stay was 3.8days.

CONCLUSION. There is an increased prevalence of pneumococco with decreased susceptibility to penicillin and to cefotaxime. Deafness is one of the most common and serious sequelae of pneumococcal meningitis. Corticotherapy has reduced the incidence of hearing loss. The new, antipneumococcal conjugated vaccine will confer effective prevention from the age of two months and will reduce the incidence of this meningitis.

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SEDATION AND ANESTHESIA FOR MEDICAL PROCEDURES IN CHILDREN

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INTRODUCTION. Aims : to analize sedation/anesthesy methods used in our Hospital for painfull or unconfortable procedures in children in relation to : 1)patient confort, 2)sedation complications, 3)and efficacy of the procedure

METHODS. A prospective study was conducted from January to March 2002 in 154 disconfortable procedures in 154 children. Mean age was 40m ; their ASA score was 4 in 7%, 3 in 16%, 2 in 57%, and 1 in 20%. More frequent procedures were : 54 lumbar punctures (LP), 23 thoracentesis or drainages, 21 central catheters insertion, endoscopys 18. We identified 3 different groups in relation to methods of sedation/analgesy : 1- Procedures done in the emergency department with local anesthesia; 2- procedures done with administration of intravenous midazolan+ketamine; 3- procedures done with anesthesic support. We used the Ramsay scale to classify the degree of anesthesia and the Serna behavioral scale to classify the reaction to the procedure.

RESULTS. Group1(n=36):42%patients fighted against the procedure (serna scale 1) and in 25% of the patients, complications of the procedure were found to be related to inadequate sedation. Group2 (n=67): in 10%, sedation was considered inadequate – serna level 1 (n=1) and 2 (n=5)-and in 1 case there were complications of the procedure related to unsufficient sedation; there were 7 (10%)cases of minor complications sedation-related; Group3(n=51): patient confort and adequacy of the sedation were found in 100%, with 2 (4%) complications of the anesthesic method.

CONCLUSION. Sedation/anesthesia were needed for the confort of the patients; only minor complications of sedation/anesthesy were found ; efficacy of the procedure was best achieved with the anesthesic method.

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EARLY COMPLICATIONS ASSOCIATED WITH ENDOTRACHEAL INTUBATION IN PEDIATRIC EMERGENCIES

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INTRODUCTION. The goals of emergency airway management are to antecipate and recognize respiratory problems and support therapy. The endotracheal intubation (ET) is not a routine procedure and it requests planning and personnel qualified to reduce the complications associated to this technique [1] . The purpose of this study is to evaluate early complications associated with endotracheal intubation

METHODS. Data were collected prospectively from February 1995 to January 2000 in tertiary teaching hospital. The variables were obtained in four age groups: Group 1 (>1 month); group 2 (between 1 month to 11 months); group 3 (between 12 months to 144 months)and group 4 (>144 months). The data were collected as demographic data, reason for endotracheal (ET) intubation, sedation administered, local of ET, physician responsible for ET, complications associated with airway management. The major complications were defined as technical problems that resulted increased morbidity. Minor complications were incidents that should be avoided. The complications were compared between emergency or elective ET intubation. Statistical analysis by chi-square, Fisher exact test .

RESULTS. We evaluated 612 (45% female and 55% male) no consecutive patients. Indication for intubation were: Respiratory failure (31%), coma or depressed sensorium (7.5%), post-operative (45%) and shock (17%). Sedation and/or analgesic were used in 54% of patients and 3.5% did not receive a sedative or analgesic for ET intubation. A total 125 ET emergency intubation (42.6%) occurred in pediatric ICU. Complications were present in 353 patients. Complications were noted in 29 (8%, group1), 122 (34%, group 2), 186 (52%, group 3), 16 (4.5%, group 4) patients. Complications occurred in 51.3% (group1) of the patients in emergency ET intubation versus 28.1% in elective surgery (p=0.083; RR=1.83); in group 2 occurred 79.3 % complications in emergency versus 30.2% (p=0.000; RR=2.63); in group 3: 82.1% versus 52.9% (p=0.000;RR=1.55) and group 4:100% versus 37.5% (p=0.002;RR= 1.67). A total of 369 complications occurred in 293 emergency patients. A total of 99 events were classified as minor complications (size incorrect and cuffed tube in <6yrs old): 0.33 events/patients in all age group. A total of 369 major complications (airway trauma, bradycardia, hypoxemia, multiple attemps and prolonged procedure tracheal intubation >3 minutes) events occurred in all age group (1.25 events/patients).

CONCLUSION. Emergency airway management in children is very diffICUlt. Most complications could be avoided by improved education, appropriated training and a pre-learned plan of action. Special teams with increased education in pediatric emergency ET intubation are need to improve morbidity in critically ill children.

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RESPIRATORY SYNCITICAL VIRUS OUTBREAK IN A PAEDIATRIC INTENSIVE CARE UNIT

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INTRODUCTION. We report an outbreak due to RSV in a 20 bedded PICU with an annual admission rate of approximately 1000 patients, cardiac and medical patients accounting each for 40% of the population and 20% surgical.

METHODS. An outbreak is defined as an event in which minimally 2 patients develop bronchiolitis due to RSV following transmission via hands of carers within a limited period of 1 week.Nasopharyngeal aspirates were obtained from children with symptoms of lower airway infection, all samples were tested for RSV using the enzyme immuno assay, followed by tissue culture when the assay was negative. RSV positive children were isolated in cubicles and strict standards of hygiene were implemented.

RESULTS. During the 4 winter months November 2001 – February 2002 45 children were infected with RSV, 29 on admission and 19 acquired the virus on the PICU. Of those 19 children 11 were cardiac, 6 were medical and 2 were surgical; the median age being 112 days [IQR 38-681] and the median length of stay was 26 days [IQR 6 -35]. The outbreak commenced on 17 December 2001 reaching a peak of 4 nosocomial cases on 24 December 2001, declining to 0 cases on 14 January following rigorous re-enforcement of hygiene measures. The outbreak re-surged on 21 January 2002 with 2 nosocomial cases per week for the next 3 weeks.

CONCLUSION. During the previous two years only 4 cases of RSV were acquired on the PICU. Three main risk factors were identified; the ongoing admission of RSV positive patients requiring ventilation, failure to cubiclise all positive patients during the Christmas period, breaches of hygiene, cardiac surgery. In order to prevent this situation occurring again next season a strict program including appropriate bed management, high standards of hygiene and passive immunisation in high risk patients will be implemented.

Prognostic determinants – 434-447

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ICU PHYSICIANS SLEEP PATTERNS DURING THE NIGHT ON DUTY AND AT HOME. A BISPECTRAL INDEX STUDY

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INTRODUCTION. Sleep deprivation and sleep disorders may lead to day time fatigue and wrong decision making in humans. ICU physicians frequently suffer from sleep deprivation during the nights on duty and their sleep pattern has never been investigated. Bispectral Index analysis (BIS) is an accurate method for sedation assessment and it was recently suggested as a simple method to measure the depth of sleep. BIS values below 60 were consistent with deep sleep.

METHODS. The sleep pattern of 8 ICU physicians was investigated with BIS during three consecutive nights on duty in the ICU and compared with the sleep pattern of three consecutive nights at home. In each sleep chart of BIS we identified and measured the following parameters. 1. Total sleep time 2. The time to achieve a deep sleep pattern 3. The total deep sleep time and 4. The ratio of deep sleep to the total sleep time. Moreover, all the above mentioned physician's sleep parameters when on duty were correlated with 1.The number of patients in the ICU 2. The mean APACHE score of the patients hospitalized, and 3.The physician's subjective appreciation of the severity of patients illness on a scale of 0-10. Paired t-test and correlation's were used for statistical analysis.

RESULTS. Total sleep time and total deep sleep time were significantly different during the nights on duty compared with this at home (286 vs 414 min and 91 vs 145 min respectivelly, $p<0.01$) The time to achieve a deep sleep pattern and the ratio of deep sleep time to the total sleep time were not significantly different (25 vs 34 min and 0.32 vs 0.34, respectivelly). Furthermore no correlation was found between all above mentioned sleep parameters and the number of patients hospitalized, their APACHE score, or the subjective appreciation of severity.

CONCLUSION. Physicians in the ICU – when they are able to sleep – maintain the same sleep pattern as at home (ratio of deep sleep to the total sleep time). Nevertheless the total sleep time and the total deep sleep time are significantly shorter.

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PROGNOSTIC VALUE OF TRANSFUSION AFTER INTRODUCTION OF RESTRICTIVE TRANSFUSION GUIDELINE

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INTRODUCTION. Hebert and col (1) showed recently that restrictive strategy of red-cell transfusion could be at least as effective as and possibly superior to a liberal transfusion strategy in critically ill patients. The aim of this study was to assess the impact of local transfusion guidelines emphasizing restrictive strategy on patients undergoing heart surgery and the prognostic value of transfusion following those restrictive criteria.
METHODS. Two groups of 100 heart surgery patients were compared before and after the introduction of local transfusion guidelines. These guidelines involved general information on blood transfusion risks and obligation for the physician to respect predetermined transfusion criteria (Hb <7g/dl or >7 g/dl associated to systolic arterial pressure <90 mmHg or age over 70yrs or HR >100/min or CI <2.2 l/mim/m² or other associated disease). Study was performed in a 48 bed ICU in a teaching hospital. Student's test and Fisher's exact test were used for statistical analysis.
RESULTS. RESULTS are shown in the following table. $ between transfused patients* before and after guidelines

	Before Total	Guidelines Transfused Pts	After Total	Guidelines Transfused Pts	p$
N	100	64*	100	36*	0.04
Red cell units transfused		103*		45*	<0.05
Pre-transfusion Hb g/dl		8.3∂0.9*		7.9∂1*	0.04
Mechanical ventilation (h)	34∂7	39.7∂86.5*	30∂130	84∂245*	<0.05
Pulmonary complications (%)	11	12*	13	31*	<0.05
Cardiac complications (%)	33	39*	27	61*	<0.05
Renal complications (%)	33	36*	27	58*	<0.05
ICU lenght of stay (d)	5.5∂5.2	6∂6.4*	5.6∂5.6	8.5∂9.9*	<0.05
Mortality (%)	4	6*	6	19*	<0.05

CONCLUSION. Introduction of local restrictive transfusion guidelines was associated to a significant reduction in red cell transfusion during the postoperative period of heart surgery. The global morbidity and mortality rates in the whole group of patients were not affected. However patients who required blood transfusion following the restrictive strategy had a worse outcome. Transfusion was probably more the consequence than the cause of this worse prognosis. If transfusion was the cause of the worse prognosis, then morbidity and mortality rates would have been higher among patients requiring transfusion during liberal period than in the whole group of patient.
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ARE PROTEIN S-100 B AND NSE PROGNOSTIC MARKERS OF THE OUTCOME OF PATIENTS WITH SEVERE HEAD INJURY?

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INTRODUCTION. Introduction.The objective of the study was to investigate the validity of outcome prediction after severe head injury using serum levels of protein S-100 B and of neuron specific enolase NSE.

METHODS. Methods.Fifteen patients with severe head injury were included in this prospective study (9 men and 6 women) mean age 38 yrs (18-69). None of the above patients had spinal cord injury or any other neurological disease. Venous blood samples were taken on admission and consecutively the 1, 2, 3, 4, and 5 day. Immunoluminometric assay was used for the specimens. We tried to correlate the S-100 B and NSE serum concentrations with the CT scan intacerebral pathology as well with the age, gender and outcome.

RESULTS. Results. All patients had elevated S-100 B and NSE serum concentrations, with a gradual reduction towards the 5th day of ICU stay. The mean values of day 1, for S-100 B were 2.4 ig/L and for NSE were 32.5 ig/L. Of day 5, they were for S-100 B 0.57ig/L and for NSE 14.9 ig/L. Patients who died had the first day mean values of S-100 B 4.2ig/L and NSE 47.2 ig/L, whereas the survivors had mean values of S-100 B1.32 ig/L and of NSE 27.4 ig/L (P <0.05). There was no strong correlation between the CT scan findings, the initial serum S-100 B and NSE values and the GCS, on admission.

CONCLUSION. Conclusion. The protein S-100 B and NSE are biochemical markers that seems to be elevated during the first days of injury, in patients with severe head trauma and could be used as markers of he severity of the injury. If protein S-100 B and NSE could be used as a prognostic factor of the patient outcome, needs more investigation. Our study is continued.

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SCORING SYSTEMS IN CANCER PATIENTS ADMITTED IN ICU FOR MEDICAL COMPLICATIONS

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INTRODUCTION. Several scoring systems intend to estimate the probability of dying to assess the severity of illness. They need prospective validation studies for application in a partICUlar setting. The objective of our study was to validate and compare eight severity scoring systems and to determine their prognostic value in a specific population of cancer patients admitted to ICU for an acute medical complication.

METHODS. Prospective cohort study in a multidisciplinary ICU of a university tertiary hospital. 250 consecutive cancer patients admitted to ICU for an acute medical complication in a 66 months period. Variables included into the APACHE II & III, MPM II, SAPS II, LODS, MODS, SOFA and the model developed by Groeger, as well as cancer characteristics, were collected on admission, during the first 24 hrs, and along the ICU stay. Performance of the scoring systems was analysed using the goodness-of-fit Hosmer-Lemeshow test and their discrimination was calculated with the area under the receiver operating characteristic (ROC) curve. Hospital and in-ICU mortalities, overall survival, and survival after day 30 were measured.

RESULTS. Observed hospital and ICU mortalities were 58% and 38%. One-yr. survival rate was 15%. The mean predicted risk of death was 54.3% with APACHE II, 57.4% with SAPS II, 40.2% with MPM II, 48.6% with LODS and 72% with Groeger's model. All scoring systems showed good calibration for mortality at hospital discharge, with the exception of MPM at admission (MPM0).Discrimination between survivors and non-survivors was better with total maximum SOFA (TMS) and total maximum MODS (TMM), that are derived parameters measured along ICU stay. Discrimination of the other scoring systems was good (area under ROC curve greater than 0.75), with the exception of MPM and those models calculated at admission (SOFA 0, MODS 0, MPM 0).

CONCLUSION. There is no major difference between the performance of the assessed scoring systems, except for MPM that presented worse calibration and discrimination. They should not be used to make decisions about therapy prolongation. A combination of factors must be taken into account to estimate a critically ill cancer patient's prognosis in the ICU.

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A COMPREHENSIVE APPROACH TO OUTCOME IN MECHANICALLY VENTILATED ICU PATIENTS

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INTRODUCTION. Estimates such as 28-day survival may be grossly misleading for assessment of intensive care utility. Late mortality and morbidity may severely affect overall outcome. We studied 100-day survival rate in addition to survivors´ general health evaluation and prevalence of signs indicating post-traumatic stress disorder (PTSD).
METHODS. The setting is a university general intensive care unit. During the study period all adult patients who had been intubated and mechanically ventilated for at least 48 hours were included (patients who died before 48 hours are excluded). Three to six months after their critical illness, survival data were retrieved from hospital and national registers. All patients surviving at this time were sent a health survey questionnaire (SF-36) and the Post-Traumatic Stress Syndrome 10-Questions Inventory (PTSS-10).
RESULTS. 153 patients fulfilled the inclusion criteria. The mean age was 69 years, 40% were women. Health questionnaires were returned by 36 (58 %) of the 62 survivors at follow-up time. 28-day survival rate was 58 %, at 100 days survival rate had fallen to 46%. Among the 36 responding survivors the frequency of a response pattern compatible with PTSD was 28%. Survivors without signs of PTSD had SF-36 mean scores more than 1 standard deviation (SD) below the Swedish norm in the domains of Physical Functioning, Role-Physical and Social Functioning. Survivors with signs of PTSD scored below non-PTSD survivors in every domain, and were more than 3 SD below the Swedish norm in the domains of Social Functioning, Role-emotional and Mental Health. In total, there were only five persons (14 % of respondents) who scored at or above the Swedish norm for both the Physical and the Mental Health Summary Scales. Assuming the same outcome in non-respondents this figure would correspond to about 6% of all the 153 included patients.
CONCLUSION. In this cohort of severely ill patients 28-day mortality was in the expected range but much mortality (another 12 %) occurs in the following 10 weeks, indicating a number of patients who have been subjected to long-lasting care with very meagre benefits. At 3-6 months following onset of their disease, survivors show considerably reduced subjective rating of their general health and life quality. As much as 28 % of the survivors show signs compatible with PTSD. It could be estimated that about 6 % of all patients included will both survive and within 3 –6 months reach a level of general health comparable to that of the general population.
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OUTCOME IN CRITICALLY ILL HEMATOLOGIC CANCER PATIENTS: IMPACT OF BACTERIAL INFECTION

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INTRODUCTION. Bacterial infection is one of the most frequent and most feared complications in patients with a hematologic malignancy (PHM). In a retrospective study, we found that bacteremia precipitating ICU admission in PHM was associated with a better outcome [1]. However, it remained unclear whether this finding could be extrapolated to all bacterial infections. The aim of this prospective study was to evaluate whether bacterial pneumonia (BP) and bacterial sepsis or other bacterial infections (BS) had a better outcome compared to non-bacterial or non-infectious complications (NBC) in critically ill PHM.

METHODS. 106 consecutive PHM admitted to the ICU over a 2 year period were categorized into BP (n=32), BS (n=24) or NBC (n=50) according to strict diagnostic criteria by an independent panel of physicians who were blinded for the outcome. The impact of BP and BS on the in-hospital mortality was assessed by logistic regression after adjustment for severity of critical and underlying hematologic illness, duration of hospitalization before ICU admission and other potentially important prognostic factors. Two models were tested, the first using a classical severity of illness score (Apache III) and the second using a score system especially designed for cancer patients (Groeger score)[2].

RESULTS. In hospital and 6 month mortality rates in BP, BS and NBC were 50%, 29.2% and 68% (p=0.006) and 55.2%, 41.7% and 76.1% respectively (p=0.01). In the first model, the Apache III score (OR 1.41; 95% CI 1.02-1.06) and hospitalisation > 48 hrs before ICU admission (OR 5.1; 95%CI 1.9-14) were associated with poor outcome, whereas BP (OR 0.21; 95% CI 0.07-0.67) as well as BS (OR 0.08; 95% CI 0.02-0.31) were associated with a better outcome. In the second model, BP (OR 0.25; 95% CI 0.08-0.76) as well as BS (OR 0.01; 95% CI 0.08-0.76) remained independent predictors of favourable outcome regardless of the severity of critical or underlying hematologic illness (Groeger score: OR 1.04; 95%CI 1.02-1.06). Of the 42 PHM with a expected survival of < 5 % according to the Groeger score, 8 (19%) survived, 6 of them had a bacterial infection. Five of these 6 patients were still alive at 6 months. Bacterial infection precipitating ICU admission was more beneficial in the hospital-acquired setting (mortality 14/28(50 %) in patients with BP or PS vs. 22/26 (84.6%) in patients with NBC, p=0.01) compared to the community-acquired setting (9/28 (32.1%) vs. 12/24 (50%), respectively, p=0.26).

CONCLUSION. Bacterial infection is one of the more favourable complications precipitating ICU admission in PHM and is associated with comparable mortality rates as in general ICU patients. Therefore, reluctance to admit PHM to the ICU for advance support is unjustified, especially when a bacterial infection is suspected to be the cause of deterioration.

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THE COMBINATION OF PRE AND POSTOPERATIVE RISK SCORE IMPROVES PREDICTABILITY IN CARDIAC SURGERY

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INTRODUCTION. For about 20 years, several risk scores try to predict outcome of cardiothoracic patients, collecting preoperative data.(1,2) The Cleveland Clinic score is the only one, to compile intraoperative data until the timepoint of ICU admission.(3,4) We wanted to find out, whether the combination of pre and postoperative score, in alliance with additional parameters, improves the predictability of outcome.

METHODS. From 1995 until 1999, 4859 adult cardiothoracic patients were examined. Logistic regression was used for analyzing those variables, dealing with mortality. The selection of significant factors is based on a stepwise forward procedure(p<0,05). The accuracy of multivariate analysis is shown as ROC(receiver-operator characteristic) curve.

RESULTS. 21 variables, pre as well as intraoperative parameters proved to be statistically significant in the analysis, 9 in the multivariate analysis: both scores, operation and aoX time, preop AT III, assessment of intraop course, Hb at ICU admission, blood loss 24h<1155ml and rethoracotomy for bleeding. The pre and the postoperative Cleveland Clinic risk score were both statistically significant in the uni and multivariate analysis, but their combination improved ROC. Additional parameters had only little further impact.

	AUC
preop score	0.722
postop score	0.739
both scores	0.864
all variables	0.895

ROC

CONCLUSION. Pre and postoperative Cleveland Clinic score are reliable in predicting the risk of cardiothoracic patients. Adding further intra and postoperative data, risk stratification becomes more precise. The appearance of unexpected intraoperative difficulties was highly significant for adverse outcome. The collection of data should be continued on the ICU and therapy should be reevaluated and modified any time.

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COMPARISON OF THE PERFORMANCE OF FOUR SCORING SYSTEMS IN AN INDIAN INTENSIVE CARE UNIT

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INTRODUCTION. Severity scoring systems have an increasing role to play in the current critical care setting as they help to assess quality of care of individual units. This is an aspect not studied extensively in India[1]. We undertook this study to evaluate the performance of APACHE II, SAPS II, SOFA[2] and TISS* in our 30 bedded multi disciplinary intensive care unit.

METHODS. Data was collected prospectively from all patients admitted to the ICU between May 1999 and March 2002. The APACHE II, SAPS II, SOFA and TISS scores were obtained within the first 24 hours of admission. In case of multiple admissions, the last admission was taken into consideration. The outcome measure analyzed was ICU mortality. Calibration was assessed by the Hosmer-Lemeshow Goodness-of-Fit test and discrimination by calculating the area under the receiver operator characteristic curve (AUC).

RESULTS. There were 5497 admissions to the ICU which included medical, surgical (post operative cases and polytrauma) and neurology (ICH, stroke) cases with 813 deaths giving a crude mortality rate of 14.78%. 4510 patients were included in this study and the rest (987) were excluded due to incomplete data. The overall mean scores obtained were APACHE II – 11.8, SAPS II – 33.9, SOFA – 3.4 and TISS – 15.5. Calibration was poor with both APACHE II and SAPS II. Discrimination was best with TISS (AUC – 0.620) and was poorer with APACHE II (AUC – 0.564), SAPS II (AUC – 0.558) and SOFA (AUC – 0.535).

CONCLUSION. The available scoring systems show overall poor calibration and discrimination in the Indian setting which may be because of the different case mix (infectious diseases, envenomation and suicidal organophosphate poisoning topping the list). Thus further customization is required before these scoring systems can be applied to the Indian population.

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IS ICU PATIENTS OUTCOME DEPENDING ON GENDER?

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INTRODUCTION. The aim of this study is to probe that critically ill patients gender is not associated with differences in severity of illness and related mortality. We had tested the premise in front of a controversial evidence offered by several years of our ICU activity.

METHODS. Observational study. Retrospective analysis using data prospectively collected in a medical-surgical ICU of 15 beds, in a teaching reference hospital, from November 1997 to July 2001. We analyzed 3152 consecutive admissions considering reason for admission, age, ICU length of stay, severity of illness (MPM0, MPM24, SAPS II and Spanish version of APACHE III) and related risk of death. Cases were analyzed according to gender and age decades. Therapeutic effort was analyzed according NEMS system. Standarized mortality ratio (SMR) and its 95% CI was determined.

RESULTS. One thousand and twelve cases out of 3152 were women. Mean age (sd) was 60 (17) years. Significative differences were founded in MPM0 prognostic values (0.243±0.249 for men and 0.267±0.264 for women, p 0.003). The rest of epidemiological data do not offer significant differences. SMR for men was 0.96, and for women 1.21, but 95% CI overlapped 0.86-1.07 vs. 1.04 – 1.41, p NS. The same differences were found when different age intervals were analyzed. Only 3 admission diagnostic (ischemic cardiopathy, post cardiopulmonar arrest and multiple trauma with no head trauma) showed greater mortality rates in women, but these differences disappeared when age intervals were considered.

CONCLUSION. In spite of certain confusing data about greater mortality ratios in women admitted to our ICU, accurate analysis does not show significant differences in severity of illness, associated prognosis and mortality, and therapeutic effort between male and female.

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USEFULNESS OF PRE-ARREST MORBIDITY SCORES IN PREDICTING OUTCOME AFTER IN-HOSPITAL CARDIAC ARREST

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INTRODUCTION. Outcome prediction in cardiac arrest is diffICUlt. To predict unsuccessful resuscitation, pre-arrest morbidity scores are available. We retrospectively collected these scores in patients who initially survived to cardiac arrest, to evaluate their capability to predict the post-arrest mortality as well. APACHE II score, based on patient's conditions after cardiac arrest, was also calculated and compared with pre-arrest scores.

METHODS. The study included 98 cardiac arrest patients (62 men and 36 women, mean age 66,4±16,10 years) treated at Gemelli University Hospital (1400 beds) during 40 months. Resuscitation data were collected in real time using the Utstein template. PAM (Pre-Arrest-Morbidity), MPI (Modified PAM Index) and PAR (Prognosis After Resuscitation) scores have been calculated in all patients survived to cardiac arrest. In the patients who survived more than 24 hours, the APACHE II score has been calculated.

RESULTS. Causes of the arrest were: respiratory failure (36%), lethal arrhythmias (19%), AMI (11%), metabolic (10%), hypothension (15%), massive pulmonary embolism (2%), others (2%) and unknown (14%). Return of spontaneous circulation (ROSC) occurred in 85% of patients. In 7.3% of cases ROSC lasted for less than 20 minutes, in 30% between 20 minutes and 24 hours, in 62% more than 24 hours. Survival rate at discharge was 22%. No patient with PAM score greater than 7 or MPI score greater than 6 survived to discharge. All patients except two with a PAR score greater than 8 died. Using these values as cut-off to predict death before the discharge, the specificity was 100% for PAM and MPI scores and 90% for PAR, while the sensitivity was 22% for PAM, 39% for PAR and 27%for MPI. We found all the three scores above the cut-off in 11/76 patients with a sensitivity of 14%, whereas one or more score were above the cut off in 33/76 patients with a 43% sensitivity. All the patients with an APACHE II score more than 29 died before the discharge, while all the patients with a score less than 10 were discharged alive. Combining APACHE II with the other three scores, the sensitivity rises to 82% when one or more of the four scores were above the cut-off.

CONCLUSION. PAM, MPI and PAR can identify those patients who will not survive at discharge after cardiac arrest with specificity close to 100% but they have a low sensitivity (22%, 27% and 39% respectively), which can be increased to 43% by associating the three scores. In the patients who survived more than 24 hours to cardiac arrest the combination of the pre-arrest morbidity scores with APACHE II, based on post-arrest variables, increased the overall sensitivity to 82%.

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TISS-28 & SAPS II ARE ASSOCIATED WITH DEATH ON THE WARD AFTER ICU DISCHARGE IN MEDICAL ICU PATIENTS

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INTRODUCTION. A subset of patients discharged from the ICU subsequently die on the ward without prior classification to withhold or withdraw therapy. Aim of this study was to analyse this subset of patients with regard to differences during the course of the ICU stay and at the time of discharge in order to identify common characteristics predicting adverse outcome shortly after ICU discharge.

METHODS. Demographic data, SAPS II on admission, and SOFA with total maximum score [TMS] of all consecutive patients staying longer than 24 h in the ICU were prospectively assessed. Furthermore in a subset of 641 consecutively admitted patients TISS-28 was recorded daily. None of the patients has been classified as ultimately fatal or fatal with respect to their expected outcome and no withhold or withdrawal of therapy occurred. Risk ratios [RR] with 95% confidence intervals [CI] for death on the ward were calculated employing uni- and multivariate regression analysis.

RESULTS. During a two year period 1677 patients were admitted to the ICU out of which 182 (11%) died during their ICU stay. The remaining 1495 patients comprised the study population out of which 79 patients [NS] (5%) died after discharge to the ward. NS were older (71±12 vs 63±14, p<.001), had higher SAPS II on admission (36±12 vs 24±11, p<.001), and had a higher SOFA TMS (5.4±4.5 vs 2.6±3.1, p<.001) compared to patients surviving hospital discharge. TISS-28 of NS did not differ on day 1, but was significantly higher on the day of discharge [TISS-28dx] (25±10 vs 20±6, p<.001). Applying univariate regression analysis the risk of death increased by 7.4% per SAPS II point (CI 1.056-1.094), 9% per TISS-28dx point (CI 1.045-1.136), and 18.6% per TMS point (CI 1.129-1.245). Multivariate analysis revealed an independently increased RR for death for both, SAPS II (RR 5.5%, CI 1.026-1.085) and TISS-28dx (RR 6.3%, CI 1.017-1.111).

CONCLUSION. Death after ICU discharge is common in ICU patients. In our cohort 30% of the patients died subsequently on the ward. Risk of death increased independently with higher TISS-28 on the day of discharge and admission SAPS II. Hence, factors leading to death after ICU discharge eventually could have been anticipated during ICU stay. Whether increased length of ICU stay or TISS-28 as a discharge trigger decrease death after ICU discharged needs to be prospectively studied.

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BODY MASS INDEX (BMI), PREDICTOR OF POOR OUTCOME IN INTENSIVE CARE?

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INTRODUCTION. In sex-specific proportional hazards analyses, risk of mortality was increased for men and women at the high and low extremes of BMI. There are a few data that focus specifically on the relationship of weight and mortality in patients who need intensive care.

METHODS. This was a prospective monocentric study. During a 10 month period, all ventilated patients were included. Weight and height at admission, SAPS II, diabetes, ventilator days (VD), length of stay (LS) and final outcome were recorded. BMI was calculated. The patients were grouped according to BMI (BMI <18.4, 18,5<BMI<24, 25<BMI<29, BMI>30). Data were analyzed by multivariate analysis after adjusted on SAPS II.

RESULTS. Complete data were available for 503 patients. There 284 (56.5%) men and 219 (43.5%)women. Data are presented as mean ± SD

	BMI<18.4	18,5<BMI <24	25 <BMI<29	BMI>30	p
number	26	219	145	113	-
SAPS II	39.1 ± 22.8	42.3 ± 20.2	43.3 ± 18.2	43.2 ± 20.2	0.774
Death OR versus 18,5<BMI<24	1.08 [0.32; 3.68]	-	1.10 [0.63; 1.93]	1.07 [0.58; 1.98]	NS
Ventilated Days	4.53	6.45	5.1	6.66	0.104
Length of stay (days)	7.0	9.9	9.1	8.0	0.085

OR: Odd Ratio

CONCLUSION. In this study BMI was not a risk factor of poor outcome in critically ill ventilated.

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PREDICTION OF MORTALITY USING PLASMA LIPOPROTEIN PATTERN AT THE ADMISSION TO THE INTENSIVE CARE UNIT

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INTRODUCTION. The accurate prediction of patient outcome has become a major objective of intensivits. Our aim was to assess the discriminating value on the outcome of critically ill patients of plasma levels of lipoproteins at the admission to the intensive care unit (ICU)comparing with existing scales (APACHE II and SOFA score).

METHODS. One-hundred and twenty one consecutive critically ill patients were enrolled in this prospective study. Exclusion criteria were pregnancy, acute pancreatitis, sedation with propofol, cirrhosis, and end-stage renal disease. The Acute Physiology and Chronic Health Evaluation (APACHE) II score and Sequential Organ Failure Assessment (SOFA) scale were calculated considering the worst punctuation of the first 24 hours in the ICU. Mortality predicted by APACHE II was also calculated. Within the first 24 hours of admission to the ICU and always before starting nutritional support, a blood sample was obtained for plasma lipid and lipoprotein determinations:total cholesterol, triglycerides, cHDL (high-density lipoprotein), cLDL (low-density lipoprotein), phospholipids, apoprotein A, apoprotein B. As nutritional markers, albumin, prealbumin and transferrin were also measured.Univariate and multivariate análisis were performed using chi-square test, T-test, U-Mann Whitney test and logistic regression models, using a <0,05

RESULTS. In-hospital mortality was 31.4% (38 patients). None of the biochemical variable was significantly different in survivors and non-survivors except for transferrin (122.4± 54.6 in non-survivors vs. 153.7± 57.2 in survivors; p=0.006). In contrast, APACHE II score, SIRS and SOFA scores were significantly higher in non-survivors. In the multivariate analysis, APACHE II (OR 8.9, 95% CI 1.2-14.3; p=0.003), SOFA (OR 4.7, 95% CI 1.-14.1p=0.03) were independent predictors of in-hospital mortality.

CONCLUSION. We fail to demonstrate that plasma lipoprotein profile is a superior discriminator of patient outcome than the APACHE II and SOFA scores.

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COMPARING PROGNOSTIC MODELS FOR PREDICTION OF ICU MORTALITY OF PATIENTS WITH LIVER CIRRHOSIS

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INTRODUCTION. Cirrhosis is one of the major causes of mortality among the nonmalignant digestive diseases. Intensive care unit mortality of cirrhosis is very high as much as 40–90 %. Several prognostic models have been proposed but few have been validated. Aim of this study to validate prognostic models and to identify independent factors of mortality among the patients with cirrhosis admitted to our medical intensive care unit (MICU)

METHODS. Patients with cirrhosis admitted to MICU from January 1997 to December 2001. All patients had histologically proven cirrhosis. Each admission has been accepted as one case. Demographics of the patients, etiology of cirrhosis, physical examination findings, laboratory data, pulmonary variables, hematological variables, gastrointestinal variables, renal variables, infectious variables, and APACHE II, APACHE III, SAPS II and Child-Pugh scores of the patients were recorded. Logistic regression analysis was performed for identification of independent predictors of ICU mortality. ROC analysis was performed to identify sensitivity and specificity of scoring systems.

RESULTS. Mean age of the patients were 55±12,7 and 80 of the patients were male and 55 were female with a total of 140 admissions. MICU mortality rate was 45 % (63). Etiologies of cirrhosis were as follows: alcohol 6 patients, Wilson disease in 1 patient, primary biliary cirrhosis in 1 patient, hepatitis B in 69 patients, hepatitis C in 31 patients, hepatitis B and C in 12 patients, hepatitis B and D in 5 patients, hepatitis B and C and D in 2 patients and 12 patients with unknown etiology. The one and only factor that predicts mortality was Glasgow Coma Scale (Odds ratio [OR], 0,64; CI 0,15 to 0,81; p<0.0001). When we accepted 25 points of score as a cut-off point for APACHE II sensitivity and specificity for ICU mortality was 73 % and 72 % respectively (OR, 6.76; CI 3.21 to 14.23 p<0.001). Sensitivity and specificity of APACHE III score for mortality was 70 % and 74 % if cut-off point is 80 (OR, 7.06; CI 3.35 to 14.92, p<0.001). Sensitivity and specificity of SAPS II score was 70% and 77% respectively for cut-off point of 43 (OR, 7.59; CI 3.57 to 16.12, p<0.001). Sensitivity and specificity of Child-Pugh score was 75% and 66% respectively for cut-off point of 9.5 (OR, 5.76; CI 2.75 to 12.05, p<0.001).

CONCLUSION. APACHE II, APACHE III, SAPS II and Child-Pugh scoring systems are equally effective for prediction of ICU mortality of patients with liver cirrhosis. Either one of these prognostic models can be used for this specific group of patients. The one and only independent factor for mortality of these patients is Glasgow Coma Scale.

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RELATIONSHIP BETWEEN BACTEREMIC MICROORGANISMS AND ORIGIN OF INFECTION IN INTENSIVE CARE PATIENTS

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INTRODUCTION. Frequently bacteremic episodes in intensive care unit are empirically treated after the identification of the probable focus of infection. In order to choose appropriate empirical antibiotic treatment of bacteremia we realized a local study to know the relation between the focus of origin of bacteremia and the most frequently microorganisms isolated.

METHODS. Study of 141 monomicrobial bacteremias in a 12-bed intensive care unit in a teaching hospital, from 1995 to 2000. Analysis of the microorganisms causing of infection, clinical outcomes and focus of bacteremia. For the identification of the origin of the bacteremias both local signs of infection and simultaneous culture of the bacteremic organism at that site were required. We defined catheter as the source of infection if an appropriate organisms was cultured from the catheter after it was removed by the method of Maki et al (1997).

RESULTS. One hundred monomicrobial bacteremias were caused by five microorganisms: Coagulase-negative Staphylococci (28%), Acinetobacter baumannii (25%), Escherichia coli (18%), Staphylococcus aureus (15%) and Pseudomonas aeruginosa (14%). Eigthy-one percent of bacteremias were hospital-acquired. Men/women ratio was 1.6/1. The global mortality was 50% and the related mortality 23%. The focus of origin were: respiratory (23%), catheter (15%), urinary (10%), abdominal (7%), endocarditic (3%) and unknown (42%). The most frequently organisms isolated according the focus of infection were: Respiratory: *A. baumannii* (40%), *S. pneumoniae* (12.5%), *P.aeruginosa* (12.5%); catheter: *A. baumannii* (33%), CNS (22.2%), *P. aeruginosa* (16.6%); urinary: *E. coli* (77%), *Enteroccoccus faecalis* (23%); abdominal *E. coli* (42%), *P. aeruginosa* (15%); unknown: CNS (36%), *S. aureus* (9%), *P. aeruginosa* (6%).

CONCLUSION. Marked differences in the etiology of bacteremias were found according with the source of infection. To avoid inadequate empirical antibiotic treatment it should be considered that high resistant microorganisms are most frequently isolated in respiratory, catheter and not identified focus of bacteremic episodes.

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SEPTIC SHOCK IN CARDIAC SURGICAL PATIENTS

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INTRODUCTION. To describe the incidence of septic shock and its characteristics in the cardiac surgical setting.

METHODS. Between January 1, 2000 and April 10, 2002, we prospectively collected data in patients with complicated postoperative course requiring ICU stay > 4 days. Septic shock was defined according to ACCP/SCCM criteria.

RESULTS. Among 1605 adult cardiac surgical patients, 140 (8.7%) fulfilled the above mentioned criteria of complicated surgery and septic shock developed in 24 (16.9%) of them. In all but one of these 24 patients, septic shock developed during ICU stay and low output syndrome had been present in 20 (83,3%) of them. In hospital mortality in septic patients was 37.5%, in 116 non septic 6.7% (p<0.05) and mean (±SD), median ICU stay was 21.8 (±10.7), 20 days and 8.9 (±7.1, p<0.05), 7, respectively. In septic patients a pathogen was identified in 58.3%: Gram negative in 7 cases, Gram positive in 3 and mixed infections in 4. Most Gram negative infections were caused by Enterobacteriacee (7) and Ps. Aeruginosa (4). Among Gram positive infections, St. aureus (3) and St. epidermidis (3) were the most frequent.

CONCLUSION. In our population, septic shock superimposed on postoperative complications was associated with prolonged ICU stay and high mortality. In this series, Gram negative pathogens were more frequent than Gram positive, possibly due to intestinal bacterial translocation. Albeit septic shock is an uncommon complication, it has a major impact on the use of ICU resources.

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CENTRAL VENOUS CATHETER USE AND CATHETER- RELATED INFECTIONS IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Central venous catheters (CVCs)are used with increasing frequency in the ICU.Infections continue to be frequent complications of their use,and a major source of sepsis in the ICU.Catheter-related infections(CRI)are associated with increased morbidity,mortality,length of stay and related medical costs.

METHODS. One-year observational,prospective study (01/01/00 to 01/01/01).Consecutive patients admitted in a 8-bed mixed medical/surgical ICU in a university-affiliated hospital who required CVC during >24hs.To determine the incidence of different CRI (CDC definitions): a) Colonized catheter (CC): growth of 15^3or more CFU in a semi quantitative culture,or 103^3or more CFU in a quantitative culture from a proximal o distal catheter segment in absence of accompanying clinical symptoms; b) Exit-site infection (ESI): erythema,tenderness,induration,or purulence within 2 cm at the exit skin site of the catheter; c) Catheter-Related bloodstream infection (CR-BSI): isolation of the same organism (identical species and antibiogram) from a semiquantitative or quantitative culture of a catheter segment and from the blood drawn from a peripheral vein of a patient with accompanying clinical symptoms of BSI and no other apparent source of infection. All catheters were replaced by placing a new one at another site. No routine or scheduled replacement of CVC was used. Catheters changes were performed if there was suspicion of infection, malfunctioning or end of need,but in all cases tip catheters were cultured and blood cultures were drawn.All catheters were made of polyurethane material.

RESULTS. Of the 209 adult patients admitted to the ICU,only 80(38%) underwent central venous catheterization >24hs (268 catheters). Mean indwelling time of catheters was six days. 132 of 268 catheters(49%) were replaced o drawn due to clinical suspect of CR-BSI;19(7%) due to ESI. 117(44 %) were drawn for other reasons.However,CRI was present in 22 catheters (19%)of this last group: 2 CR-BSI and 20 CC.Our CR-BSI rate was 4.2 per 1000-catheter-days,and for femoral, yugular,and subclavian accesses: 3.1,1.2,and none per 1000-catheter-days,respectively. 70(26%)CC were found; 37(14%) yugular; 32(12%)femoral;and 1(0,4%) subclavian. 42(61%)of the CC were monomicrobian infections,mainly by Gram-negative species(n=26;17 Acinetobacter), followed by Gram-positive coccus (n=14.8 Coagulasa-negative Staphylococcus). Among polymicrobian infections, Gram-negative rods were also prevalent (n=25;12 Acinetobacter). There were 19(7%) cases of ESI: 14(74%), 3(16%),and 2(10%) for yugular,femoral and subclavian accesses, respectively. No CR-BSI had ESI.

CONCLUSION. 1) Our incidence of CRI was in accordance to most reported studies. 2) However,our prevalence of Gram-negatives infections is higher than the figures usually described, and 3) Our use of femoral accesses is higher than the generally advised. Despite this,CR-BSI showed an acceptable rate.

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BACTERMIAS IN A MEDICAL-SURGICAL INTENSIVE CARE UNIT

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INTRODUCTION. Objective: To describe the frequency, etiologies, forms of presentation, and foci of bacteremia identified in patients admitted to the ICU.

METHODS. Prospective epidemiological surveillance study carried out from April 1998 to March 2001. Bacteremia was defined as the isolation of a pathogenic microorganism in one or more blood samples. Bacteremias were classified into contaminating or true according to clinical manifestations. A descriptive analysis of variables including mean values, ranges, and standard deviations is presented.

RESULTS. A total of 332 episodes of bacteremia were identified, 228 of which were true bacteremias (27.8 episodes per 100 patients). The characteristics of patients with true bacteremia were as follows: mean (SD) age 64 (16.3) years; male sex 58.8%; mean APACHE II score on admission 14.9 (5.8); and mean length of previous hospitalization 22 (27) days. In 153 (67.1%) cases, bacteremias were acquired in the ICU and in 49 (21.5%) episodes were polymicrobial. A total of 289 pathogens were cultured. These included Gram-positive cocci in 173 (59.9%) cases, Gram-negative bacteria in 94 (32.5%), and fungi in 17 (5.9%). Initial presentation included severe sepsis in 36 (15.8%) cases and septic shock in 51 (22.4%). The most frequent origin of intra-ICU true bacteremias was unknown in 42.5% of cases (primary bacteremia) followed by catheter-related bacteremia. Crude mortality was 45.2% and bacteremia-related mortality 21.5%.

CONCLUSION. Primary bacteremia and catheter-related bacteremia were the most common. A total of 21.5% bacteremias were polymicrobial. Gram-positive cocci were the predominant causative pathogens.

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NOSOCOMIAL INFECTION-MAIN CAUSE OF SEPTIC COMPLICATIONS IN POSTOPERATIVE PATIENTS

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INTRODUCTION. Nosocomial infection remains a significant challenge for clinicians in ICU. Intensive care units are unique because they house seriously ill patients in confined environments where antibiotic use is extremely common. Since our last publication (1) there is a substantial rise in emergence of nosocomial infection namely Gram-positive as well as changes of pattern of emergence.

METHODS. To study the frequency of emergence of nosocomial infection (NCI) in intensive care unit (ICU) we studied retrospectively data from case records and flow sheets of 1451 postoperative patients in our ICU during 1999-2000 and compared data with last period.
RESULTS. Of 1451 patients in our ICU during two years, we include those 613 (42.2%) who stayed for more than 72 hours. According to results from cultures we divided them to three groups. Group one included 355 (57.9%) patients without bacterial growth. Group 2 included patients with proved nosocomial infections /NCI/. We obtained samples: 898 from urinary catheters (376 positive- 41.9%), 552 from tracheal tube (457 positive- 82.8%), 597 from blood (282 positive- 47.2%), 64 intradermal segments from central venous lines (34 positive-53.1%), and 17 from sputum (15 positive- 88.2%). The most common place for emergence of NCI in our ICU is respiratory tract. On 5-th ICU day the tract became infected in almost 56% of the patients. The major role among pathogens played *Acinetobacter spp*. (27.4%), Citrobacter spp. (20.3%), P.aeruginosa (12% and Serratia spp. (10%). The second place for emergence of NCI is "reserved" for blood-stream infections. Almost the half of the cultures (47.2%) showed bacterial growth. The isolated pathogens were the same: *Acinetobacter spp* (19%), *Serratia spp*. (16%), but there was substantial rise in frequency of emergence of *S. epidermidis* during the last years (see figure). Its frequency almost equalized that of *Acinetobacter spp*. The other two main sources for NCI were urine catheters and CV catheters. They remained on 3-rd and 4-th place. Group 3 included patients with endogenous surgical wound infections. In this group we obtained samples from surgical wounds and drainages. In 1999 25.6% of cultures showed bacterial growth. During next 2000 this figure rose nearly twice (48.3%). The leading role played the same *Acinetobacter spp., Citrobacter spp., P. aeruginosa, Enterococcus spp. and E. coli.* The role of *S. epidermidis* increased greatly during this period

CONCLUSION. There is a rise in frequency of nosocomial and secondary endogenous surgical infection in 1999-2000. The frequency of Gram-positive pathogens, namely Staphyllococcus epidermidis, nearly equalized that of Gram-negative flora as a cause of nosocomial infection. Nosocomial infection still remains the main cause of septic complications in postoperative ICU patients.

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PANCREATIC SURINFECTION AFTER SURGERY FOR ACUTE NECROTIZING PANCREATITIS

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INTRODUCTION. Intra abdominal infections frequently complicate the postoperative course of patients with acute necrotizing pancreatitis. The objective of this study was to analyze the incidence of pancreatic surinfection after surgery for acute necrotizing pancreatitis, describe its characteristics and identify associated risk factors.

METHODS. We retrospectively (1995-2001) analyzed 46 patients treated surgically for acute pancreatitis. Surgical treatment consisted of debridement and postoperative continuous lavage. We recorded demographic characteristics, incidence of organ failure, data on surgical and infectious complications, data on surgical and medical treatment and disease severity by Ranson and APACHE II score.

RESULTS. Surinfection of the pancreatic necrosis was present in 30 out of 46 patients (65%). The surinfection was polymicrobial in 17 patients. Most of the organisms were gram- negative (54%), the others were gram-positives (28%) or fungi (17%). Patients with surinfected necrosis were younger (50 y vs. 64, $p<0.01$), had surgical complications more often (70% vs. 26.7%, $p=0.01$), needed retroperitoneal lavage for a longer time (28 days vs. 9, $p<0.01$), and had a longer hospital stay (84 days vs. 29, $p<0.001$) than patients without surinfection. Multivariate analysis demonstrated that age (OR 0.90; 95% CI: 0.83-0.97, $p<0.01$) and the occurrence of a surgical complication OR 10; 95% CI 1.53-66.6, $p<0.01$) were independently associated with pancreatic surinfection. The mortality in patients with infected necrosis was higher (72% vs. 40%, $p=0.04$), although in multivariate analysis no association was found.

CONCLUSION. Pancreatic surinfection is high after debridement and retroperitoneal lavage, with mainly gram negative bacteria involved. Surgical complications and younger age are significant risk factors for surinfection.

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SEVERE ACUTE PANCREATITIS IN SPANISH ICU'S

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INTRODUCTION. The aim of this report is to describe the current status of SAP in Spanish ICU's

METHODS. SAP cases are identified in accordance with generally accepted criteria in each ICU, such as Ranson, Imrie, PCR and CT-dynamic criteria. SAP was selected from the data base of the National Study of Spanish Nosocomial Infection Monitoring (ENVIN). This study covered the period from 1997 to 2000. ENVIN is an observational, prospective and multicentre study. SAP patients hospitalized during more than 24 hours in all the participating ICU's have been included in the study. These patients were monitored until their discharge from the ICU or up to a maximum of 30-60 days. Secondary infections have also been monitored. Severity is measured by means of APACHE II. Infections, mortality, epidemiological data and antibiotics used as a means of prevention are described. The statistical analysis used the Chi X2 Test for the association of qualitative variables, the Student t for the comparison of averages and the 5% statistical significance level

RESULTS. 199 patients (1.18%) of the 16,927 patients monitored by ENVIN were found to have SAP. The average APACHE II was 14.9 and the average stay was 12.2 days. The base illness was medical (94.5%) and surgical (5%). 30.7% of the patients underwent emergency surgery. NI accumulated incidence was 48.7% and density incidence was 40/1000 hospitalization days. Crude mortality was 31% and NI-related mortality was 45%. 97 infections were detected: 27 of abdominal origin (27.8%), 17 ventilator-associated pneumonias (18.5%), 12 secondary bacteremias related to abdominal infection (12.4%), 12 catheter-associated urinary tract infections 12.4%; primary bacteremias (10.3%); 3 central venous catheter-associated bacteremia (1.5%). A total of 66 pathogens were isolated. BGN 58.5%, CGP 24.5% (MRSA 4.2%), Fungii 17% (principally Candidas), Enterococci 15% and anaerobes 3.7%. 85.4% of the SAP patients received antibiotic treatment. The antibiotic most frequently used in prophylaxis was Imipenem-cilastatine (70%) and Piperaciline-tazobactam (10%). The antibiotics most frequently used in absolute indication were Imipenem 70%, Piperaciline/tazobactam 19.4%, Metronidazol 14%, Vancomicina 13.5%, Ciprofloxacino13%, Amikacina in 13% and Fluconazol 7.6%

CONCLUSION. SAP cases in Spanish ICU's account for little more than 1% of all hospital cases, but they result in high levels of severity, morbidity and mortality. Crude mortality and SAP septic complication-related mortality in Spanish ICU's are much higher than the average indicated in the literature (29.7% and 14.9%). Imipenem is the antibiotic most frequently used in prophlaxis. The irruption of Candidas has been detected.

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INCIDENCE AND SIGNIFICANCE OF CATHETER-RELATED INFECTION FOLLOWING OPEN HEART SURGERY

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INTRODUCTION. The aim of this study was to evaluate the impact of catheter related infections in the outcome of patients undergoing cardiac surgery.

METHODS. 161 (17.26%) of 933 consecutive cardiac surgery patients operated at Onassis Cardiac Surgery Center, from January 1st to June 30th 2001, developed T>38.5 C and leucocytosis, without evidence of specific site of infection. Those patients were examined for possible catheter related infection, by removing central and arterial catheters and sending them along with blood specimens for culture. Infections within the first postoperative 48h were defined as early, whereas those developed after the first 48h were defined as late. We examined the relation between the incidence of catheter related infection and the type of microorganism isolated, the type of operation performed, the ICU stay and the hospital mortality.

RESULTS. 610 coronary artery bypass grafting(CABG), 202 valve or ascending aorta replacement(VR), 86 combined(CABG+VR), 13 acute dissecting aneurysm(ADA) and 22 other operations were carried out. Positive blood or catheter cultures were found in 36 patients (3.85%). Staphylococcus epidermidis was cultured from all patients with early(n=6) and 83% of those with late(n=30) infection, while candida was found in 30% of those with late infection. ICU stay and hospital mortality was ten times higher in patients with positive blood or catheter cultures compared to the general ICU population (21.4 vs 2.1 days and 27.7% vs 2.36%, respectively). Finally, mortality was higher in patients with late compared to those with early infection(30% vs 17%).

	Blood Culture	Central Venous Catheter	Arterial Catheter
CABG, n (%)	3 (0.49%)	18 (2.95%)	1 (0.16%)
VR, n(%)	5 (2.48%)	10 (4.95%)	2 (0.99%)
CABG+VR, n (%)	1 (1.16%)	2 (2.33%)	2 (2.33%)
ADA, n (%)	3 (23%)	2 (15.4%)	1 (7.69%)
Others, n (%)	0 (0%)	0 (0%)	0 (0%)

Positive blood / catheter cultures in cardiac surgery patients

CONCLUSION. Positive blood or central venous catheter cultures are associated with a dramatic increase in ICU stay and hospital mortality of cardiac surgery patients. Staphylococci are isolated in the majority of patients, while fungal infections are responsible for a significant number of late infections. Blood and catheter cultures are very important for the management of ICU patients with fever and leucocytosis.

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SEVERE PERITONITIS IN ICU PATIENTS

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INTRODUCTION. The aim of this clinical trial is to clarify the predictive factors of mortality in ICU patients (pts) with severe peritonitis.

METHODS. We studied retrospectively 77 ICU pts, 69 male (89.6%) and 8 female (10.4%), with a severe peritonitis. All of them were mechanically ventilated. Mean age: 56.9±21.7 years. The episodes of peritonitis were distinguished as: Community-acquired (CAP) : 18 (23.4%), hospital-acquired (HAP) : 32 (41.55%) and ICU-acquired (ICUAP) : 27(35.1%). Pts with pancreatitis were excluded. Mean stay in ICU: 22.9±11.2 days. We studied several factors and their influence on prognosis: Age, duration of mechanical ventilation (DMV), length of stay (LS), relaparotomy, development of sepsis and MODS and mortality (M) rates.

RESULTS. Our observations are listed in the following table (number of cases per group in parenthesis):

	Age years	DMV days	LS days	Relaparotomy number	Sepsis %	MOD %	M %
CAP (18)	62.1±19.2	12.4±8.1	16.3±7.9	0.8±0.5	22.2	16.7	16.7
HAP (32)	67.2±16.4	21.3±6.7	25.9±7.4	1.8±0.5	43.7	37.5	34.4
ICUAP (27)	41.4±18.9	20.6±5.9	23.8±7.1	2.2±0.6	37.0	33.3	25.9

CONCLUSION. Statistical analysis showed: 1) Non-survivors were older ($p<0.05$). 2) Pts with HAP ($p<0.01$) and ICUAP ($p<0.5$) had poorer prognosis than pts with CAP. 3) Upper gastrointestinal tract perforation had similar prognosis as other etiologies. 4) In ICUAP multiple trauma pts, rupture of liver, more than other abdominal injury was associated to severe sepsis, MODS and high M rates. 5) In non-survivors the incidence of sepsis and MODS was more frequent ($p<0.05$). 6) DMV and LS were greater in HAP and ICUAP pts than in CAP pts ($p<0.05$). 7) The ratio of relaparotomies for residual sepsis was higher in non-survivors ($p<0.01$). 8) In cultures of peritoneal fluid were isolated the common ICU pathogens: Ps. Aeruginosa, Ac. Baumanii and St. Aureus

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INFECTION COMPLICATING CRITICALLY ILL PATIENTS WITH TRAUMATIC BRAIN INJURY

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INTRODUCTION. The purpose of this of this study was to investigate the occurrence of infection (INF) complicating ICU patients (pts) who had suffered traumatic brain injury (TBI) as well as the immune response of these pts.

METHODS. Pts with moderate to severe TBI (GCS =<11) and age >17 were enrolled under the presupposition they remained on mechanical ventilation (MV) >4 days. A total of 35 TBI pts were followed-up; infected pts were identified and associated factors were studied. In addition, serum immunoglobulin (sIg) levels and soluble interleukin-2 receptors (sIL-2R) were measured in infected pts.

RESULTS. A total of 35 TBI pts (mean age=37.4±19.14, GCS:8.1±1.8, APACHE II score:13.7±4.8, ISS: 38.8±12) had a mean ICU stay of 22.8±11.5 days and MV support for 19.3±10.2 days. Pts were mainly fed enterally. The overall mortality was 14.2%. Nineteen TBI pts (54.2%) experienced a kind of infection over the study period. The most common sources were lung and blood (30 episodes of pneumonia (P) and 11 blood borne (BI) infections were recorded over the 770 patient-days). P was an early- onset event in TBI pts (probably due to aspiration) with 12 pts (34.2%) infected in the first 5 days; BI occurred later and was the main infection in the 3rd and 4th week (5 and 3 respectively). INFs peaked in the second week of ICU stay (P:14, BI:3). Pts who eventually experienced an infection were older (42.9±19.2 vs 29.5±16.5, p=0.050), had a higher APACHE II score (14.9±4.2 vs 11.3±4.9, p=0.016) and lower GCS (7.8±2.0 vs 9.7±1.8, p=0.055) – both scores estimated at the first trauma day – in comparison to non-infected pts. They also needed longer ICU stay (27.3±12.3 vs 16.6±8.2, p=0.008), longer MV treatment (22.6±10.3 vs 14.2±6.5, p=0.027) and were given propofol for more days than non infected pts (10.3±4.6 vs 7.3±3.4, p=0.062). The main pathogens responsible for INF were Ac. Baumanii, Ps. aeruginosa and Staph aureus. Mortality was 15.7%. Concerning sIg levels, while Ig classes were within the normal range (±2se) in the 1st week, in the 3rd week IgM levels averaged 150 % (256±32 mg/dl) and IgA 146% (414±53 mg/dl) of the mean of the controls in the infected pts. IgG increased later than IgM and IgA to 136%. The average weekly levels of sIL-2R, gradually increased, ranged from 724±247 for the first week to 1878±374 for the fourth week supporting an ongoing immune activation.

CONCLUSION. TBI predisposes to INF. The severity of the brain injury, the APACHE II score and the older age seem to be associated with the prevalence of INF which is related with the time since the injury; pneumonia is an early onset event and INFs peak during the 2nd week. Although, infected TBI pts seem to amount sufficient humoral immune response and ongoing immune activation and finally control their infections, they suffer augmented morbidity.

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HOTLINE FLUID WARMERS – A POTENTIAL SOURCE OF NOSOCOMIAL INFECTION

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INTRODUCTION. Fluid /blood warmers help to prevent hypothermia by raising the temperature of intravenously administered fluids & blood. The HL-90 Hotline fluid warmer is the model used in our hospital. It consists of disposable tubing set with a central channel through which the fluid is infused and outer tubing through which heated water circulates. The water is contained in a reservoir, which is heated by an electric element. The manufacturer's instructions recommend changing the water in the reservoir every 30 days. This water is a potential source of infection and we therefore sampled the water in the reservoir for microbiological contamination.

METHODS. This study was conducted at Royal London Hospital during the month of December 2001.There are 10 fluid warmers, all Hotline in our Operating Theatres. Samples of water were taken from each of the reservoirs at the end of the working day. Using aseptic techniques 20 ml of water were added to a labeled blood culture bottle. Each sample was cultured for 48 hours. After one week we repeated procedure

RESULTS. After 48 hours of incubation, Pseudomonas sp. grown in 7 out of 10 culture bottles. The results from the second sets also grew Pseudomonas Sp. in the same 7 out of 10 water reservoirs.

CONCLUSION. The water in the reservoir is heated to 41-42 degree Celsius. This temperature does not inhibit the growth of Pseudomonas. Each time the disposable tube is disconnected from the reservoir approximately 5 ml of water is spilled potentially spreading microorganisms. In addition there are case reports of cracks/splits in the inner tubing of the disposable tubing potentially exposing infused fluid or blood to heated water from the reservoir (1).

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CANDIDEMIA IN ICU PATIENTS: CANDIDA SPECIES AND ANTIFUNGAL SUSCEPTIBILITY

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INTRODUCTION. Candida blood stream infections are increasingly reported among ICU patients and are associated with high mortality. Although *Candida albicans* is the commonest species, the relative incidence of non-*C.albicans* species have increased. We studied the distribution of *C.* species and antifungal susceptibility of isolates in an 26 bed general ICU.

METHODS. Between March 2000 and April 2002 all episodes of candidemia occurring in ICU patients were recorded. BACTEC-NR 9240 system was used for blood cultures according to standard recommendations. The in vitro activity of 5-flurocytosine (5FC), amphotericin B (AB), ketoconazole (KETO), fluconazole (FLU) and intraconazole (ITR) against Candida bloodstream isolates was tested by determination of Minimum Inhibitory Concentration (MIC).

RESULTS. Twenty eight episodes of candidemia were detected in 26 patients out of 953 ICU patients (incidence 2.1%). The percentage of isolation of different species of *Candida* from blood was the following: *C. albicans* 57%, *C. tropicalis* 16%, *C. glabrata* 10%, *C. parapsilosis* 7%, *C. krusei* 7% and *C.psedotropicalis* 3%. All *C. albicans* were susceptible to 5FC and AB(MIC=0.5-2mg/ml). FLU, KETO and ITR were active against *C. albicans* isolates and moderate active against non-*C. albicans* strains. The overall mortality of candidemic ICU patients was 57%. No difference in mortality was found between patients with fungemia involving *C. albicans* and non-*C. albicans* species.

CONCLUSION. Candidemia in ICU patients is associated with a high mortality rate. *C. albicans* was the most common yeast isolated from blood. Non-*C. albicans* species have a frequent occurence among candidemic ICU patients. The moderate susceptibility of azoles against non-*C. albicans* species indicates the usefulness of susceptibility testing for antifungal treatment.

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EPIDEMIOLOGY OF CANDIDURIA IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Objective: To determine the frequency of different Candida spp. in urine samples of critically ill patients admitted to Services of Intensive Care Medicine (ICUs).

METHODS. Prospective, cohort, observational, and multicenter study. Urine cultures were performed once a week to all patients admitted to the ICU. Samples were processed at the different clinical microbiology laboratories of the participating hospital using specific culture medium (Sabouraud) and the BACTEC technique and the A20C (Biomerieux) system for the identification of species. Candiduria was defined as < 104 CFU of *Candida spp.* in the urine. Frequencies are expressed as cumulative incidence (%) and incidence density (episodes per 1000 days of urinary catheter).

RESULTS. RESULTS. A total of 1765 patients admitted >7 days to the 70 participating ICUs between May 1998 to January 1999 were included in the study. Of these patients, 1730 (98%) had a urinary catheter inserted, with 40,273 urinary catheter days. One or more Candida spp. in the urine were detected in 389 patients. The rate of candiduria was 22 per 100 patients/ICU and the incidence density 9.5 per 1000 days of urinary catheter. In 23 cases, Candida spp. in association with different bacteria (5.9%) were found, mostly Gram-negative pathogens (13 cases), in partICUlar *P. aeruginosa* (n=5) and *E. coli* (n=3), and Gram-positive pathogens (10 cases) especially *enterococcos* (n=7). In respect to *Candida spp*., *C. albicans* predominated (68.4%) followed by *C. glabrata* (8.2%), *C. tropicalis* (3.6%), *C. parapsilosis* (2.3%), and *C. krusei* (1.3%), independently of the week in which isolation of pathogens was made.

CONCLUSION. Conclusions: Candiduria was diagnosed in 22% of critically ill patients admitted for more than 7 days in the ICU. *Candida albicans* was the pathogen most frequently recovered (68.4%), although *C. non-albicans* was isolated in one out of each three cases.

REFERENCES. EPCAN Group

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FUNGAL INFECTION IN ICU

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INTRODUCTION. Incidence of yeast infections is increasing constantly, especially in most diffICUlt patients in Intensive Care Unit. The most common causative agent is Candida sp.(1) Patients with greatest risk of yeast infection are: premature neonates, patients with chronic diseases, patients after transplantation, with immunodeficiency, mechanically ventilated patients, patients with parenteral nutrition, patients that require invasive diagnostic and therapeutic interventions (I.V. catheter, endotrachel tube, central venous catheter, etc.), as well as patients that receive wide-spectrum antibiotics.(2,3,4)

METHODS. A retrospective study was done over the last year that included 19 neonatal patients admitted at the Intensive Care Unit. All patients had congenital anomalies (6 patients with gastroschisis (31.5%), 3 patients with esophageal atresia (15.7%), and others with intestinal obstruction, duodenal atresia and malrotation). 90.9% of the patients were on total parenteral nutrition and mechanical ventilation. The average stay in the ICU was 9.6 days. *Candida albicans* was checked for in swabs of wound, in blood-culture, stool-culture, urine-culture, tracheal aspirate, gastric asp

RESULTS Candida albicans was identified in 11 patients (57.8%). It usually appeared 3-4 days after the introduction of the antibiotic therapy. It was most commonly found in gastric aspirate (63.6%), stool-culture (36.3%) etc. It would first appear in gastrointestinal tract (stool-culture and gastric aspirate after 8 days). In respiratory and urinary tract Candida was identified after 12 days, and in blood-culture after 18 days. 54.5% of the patients received Cephtriaxon or Ampicillin, and 36.3% Amikacin or Gentamycin and Metronidazol.

CONCLUSION. Morbidity in patients with yeast infection is very high. The most common causative agent is Candida, and the predilection organ is digestive tract. Risk factors are: prematurity, mechanical ventilation, total parenteral nutrition, longer hospital stay and wide-spectrum antibiotics. Due to unspecific clinical picture early diagnosis is usually made according to the results of taken cultures. There are still many dilemmas regarding systemic antimycotic profilaxys.

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