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**P3 Comparison of closed with open tracheal aspiration system**

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The aim of the study was to compare colonization rates of the ventilator tubings, frequency of ventilator associated pneumonia (VAP) and mortality in the intensive care unit (ICU) in mechanically ventilated patients for whom closed or open tracheal aspiration systems were used in a randomized fashion.

The study was started in 1 April 2000 and patients who received mechanical ventilation (MV) for at least 48 hours were included.

The results (mean ± SE or *n* [%]) of the analysis of the first 7 months are presented in the Table.

In conclusion, in the preliminary analysis of this study the rate of colonization tended to be increased in the closed aspiration system group when compared with the open aspiration system group. However, there was no difference between the groups in terms of the development of VAP and mortality in the ICU.

	Open ( <i>n</i> = 24)	Close ( <i>n</i> = 20)	<i>P</i>
Age	64.7 ± 3.9	63.6 ± 3.0	0.83
Male gender	9 (37.5%)	12 (60%)	0.22
APACHE II	23.6 ± 1.4	27.4 ± 1.6	0.08
Duration of MV	6.6 ± 0.9	8.7 ± 1.2	0.16
Rate of colonization*	11 (57.9%)	14 (82.4%)	0.16
Development of VAP	6 (25%)	7 (35%)	0.52
Length of stay in the ICU	10.1 ± 1.5	12.2 ± 1.7	0.36
Mortality in the ICU	18 (75%)	16 (80%)	0.73

\* *n* = 19 in the open aspiration system group and *n* = 17 in the closed aspiration system group.

**P4 A laboratory assessment of the learning and retention of skills required to use the Combitube and Laryngeal Mask Airway by non-anaesthetists**

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Both the Combitube and Laryngeal Mask Airway (LMA) have been successfully used by non-anaesthetists during resuscitation [1–5]. However, only one study (using the Combitube) has assessed how well these skills are retained after the initial training period. Here, nine of 11 paramedics demonstrated inadequate skill retention in the follow-up study at 15 months [6].

**Study purpose:** To assess and compare the ability of non-anaesthetists to learn and retain the skills necessary to use the Combitube and Laryngeal Mask Airways.

**Method:** With no prior warning, 10 non-anaesthetists (3 student nurses, 2 qualified nurses and 5 trainee operating department practitioners) took part in a study morning covering theoretical aspects of Combitube and LMA insertion and use, and a practical demonstration and practice session. This was followed by a written examination of 30 yes/no questions and a practical assessment for each airway device. Eight weeks later, again with no prior warning, the same 10 people retook the same written examinations and practical assessments.

**Results:** The mean decrease in score between the first and second visits was -1.3 (95% confidence limits, -0.13 to -2.47; *P* < 0.05) for the Combitube, and -0.5 (95% confidence limits, 0.63 to -1.63; *P* < 0.5) for the LMA.

**Conclusion:** This study suggests that the practical use of the Combitube is an easier skill to acquire than the LMA. Not surprisingly retention of theoretical and practical skills for both the Combitube and LMA deteriorated over a short time span (although not reaching statistical significance for theoretical LMA scores). Therefore, whatever airway device non-anaesthetists are taught to use, regular refresher courses will be needed.

However, larger numbers need to be studied to corroborate these findings.

**Table 1**

**Results of written examinations (means quoted)**

	First visit		Second visit	
Combitube	83.3%	25/30	79%	23.7/30
LMA	91.3%	27.4/30	89.7%	26.9/30

**Table 2**

**Results of practical assessments**

	Combitube ( <i>n</i> = 10)		LMA ( <i>n</i> = 10)	
	First visit	Second visit	First visit	Second visit
Successful insertions	10	10	10	9
Successful insertions within 60 seconds	10	8	8	7
Required number of insertion attempts before success				
1	10	8	5	7
2		2	4	2
3			1	
Number using correct cuff volumes	10	10	10	8 ( <i>n</i> = 9)
Number showing evidence of ventilation	10	10	10	9 ( <i>n</i> = 9)



**P7 Comparison of two percutaneous tracheostomy techniques**

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**Introduction:** Since the first report of dilatational percutaneous tracheostomy (PDT) many favorable reports have been published which accepted this technique as a safe alternative to surgical tracheostomy. In this study we want to evaluate two different kinds of techniques' advantages and complications.

**Methods:** We evaluated 90 patients who tracheostomized with PDT, 45 of them with dilating forceps technique (DFT) (SIMS Portex Kent, UK) and 45 of them with multi dilatational technique (MDT) (Cook Critical Care Systems Bloomington, USA). Indications were prolonged ventilator dependence, facilitation of weaning from mechanical ventilation, and prolonged coma. Prior to clinical application, informed consent from the patient or next of kin was obtained in all cases. The PDT procedure was chosen randomly. All patients were in routine ICU monitoring (ECG, SpO<sub>2</sub>, invasive

arterial monitoring). Two techniques were performed as previously described [1,2].

**Results:** We observed one tracheoeseophageal fistula, but it did not necessitate surgical repair, besides one peristomal infection, cuff rupture and late bleeding (in 5th day) in DFT group. Stomal fistula seen after decanulation in MDT group, peristomal infection and bleeding were also observed. Other demographic data are in the Table.

**Conclusion:** We have not seen any mortality due to PT in our cases and there were no differences in complication rates and other data except duration of PT. Tracheoeseophageal fistula is seen in DFT, however we need larger patient series to decide exactly which technique will be safer.

**Table**

Age (years)		APACHE II		Day of performing PT		ICU stay (days)		Duration of PT (minutes)		Complication rate	
DFT	MDT	DFT	MDT	DFT	MDT	DFT	MDT	DFT	MDT	DFT	MDT
52 ± 20.2	46.6 ± 21.8	14.8 ± 7.6	13.1 ± 5	10.9 ± 6.4	8.5 ± 6.8	45.4 ± 30.8	39.6 ± 24.1	4.5 ± 2.5	7.2 ± 3.5	12%	10.3%
<i>P</i> = 0.16		<i>P</i> = 0.15		<i>P</i> = 0.08		<i>P</i> = 0.20		<i>P</i> = 0.001			

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**P8 Percutaneous tracheostomy in patients with ARDS on HFOV**

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**Introduction:** High Frequency Oscillator Ventilation (HFOV) is a novel lung protective strategy in the treatment of patient with acute respiratory distress syndrome (ARDS). Percutaneous tracheostomy (PCT) has become the preferred mode of achieving long-term airway in ventilated patients, to facilitate weaning and airway toileting.

**Aim:** To demonstrate the safety and practicability of performing a percutaneous tracheostomy on patients with ARDS whilst on a high frequency oscillator ventilator (HFOV).

Patient no.	1	2	3	4	5
Age/sex	56/M	79/M	50/F	69/M	39/F
Days intubated pre-PCT	5	4	9	4	3
Days on HFOV	6	5	13	6	8
Total days ventilated	8	9	40	8	8
Complication of PCT	None	None	None	None	None
PCT technique	Serial	Serial	CBR	CBR	CBR
Mean airway pressure pre/post PCT	19/18	27/28	18/16	19/18	20/21
Amplitude ( $\Delta P$ ) pre/post PCT	60/55	61/70	56/61	55/56	62/65
PaO <sub>2</sub> /FiO <sub>2</sub> ratio pre/post PCT	210/215	177/202	200/205	240/268	220/200



**Conclusions:** Reconstruction of tracheobronchial stenosis by combination stenting was a very useful modality for end stage lung patients with severe central airway stenosis for the purpose of

improving pulmonary functions and quality of life. Selection of stents should be done after careful consideration of the characteristics of stents and tracheobronchial stenosis.

#### P11 **Ulcerative laryngitis in children admitted to intensive care**

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**Background:** Severe ulcerative laryngitis is rarely documented in children.

**Objective:** To present our experience of ulcerative laryngitis over a 5 year period.

**Setting:** Paediatric Intensive Care Unit (PICU) of a university hospital.

**Methods:** Retrospective case note review of 263 children admitted to PICU with severe upper airway obstruction and a clinical diagnosis of croup. Data are presented as median (range) and analysed by the Fisher's Exact test.

**Results:** One hundred and forty-eight children (56%) underwent microlaryngoscopy (Storz 3.0 rigid telescope), usually at the time of airway intervention for failed medical treatment of severe croup ( $n = 147$ ). Laryngeal ulceration, with or without exudation, oedema and erythema, was documented in 15 of these children (10%), median age 14 months (10–36) and median weight 10 kg (6–12). Twenty-seven of the children who underwent microlaryngoscopy (18%) also had ulcerative gingivostomatitis consistent

with Herpes simplex virus. Ulcerative laryngitis was documented in 9 of 27 (33%) children with, and in 6 of 121 (5%) children without, co-existent ulcerative gingivostomatitis ( $P < 0.002$ ). The presence of oral ulcers predicted ulcerative laryngitis with sensitivity and specificity of 80% and 86%, and positive and negative predictive values of 33% and 95%. Viral culture was available in 6 of the 15 children with ulcerative laryngitis, confirming Herpes simplex ( $n = 3$ ) and cytomegalovirus ( $n = 1$ ). All children with oral or laryngeal ulceration received acyclovir therapy.

One of the 15 children did not require airway intervention. Nine children required nasotracheal intubation for a median of 4 days (3–11) and median ICU stay of 6 days (4–14). Five children required tracheostomy *ab initio*, with a median ICU stay of 30 days (20–36), and duration of tracheostomy *in situ* for a median of 19 days (15–253). All 15 children survived.

**Conclusion:** Ulcerative laryngitis is more common in our patient population than the few reports suggest. Early microlaryngoscopy is recommended in children with severe croup who follow an atypical course.

#### P12 **Bronchial asthma in intensive care department: the factors influencing on exacerbation severity**

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The high frequency of severe exacerbation of bronchial asthma (BA) is still one of the main problems for pulmonologists in Ukraine.

Ninety-eight of 620 asthmatics, surveyed in the diagnostic center 'Pulmis' in Dniepropetrovsk during 10 months of 2000, were referred to the intensive care department because of severe exacerbation of disease.

The aim of present research was to study and to estimate the reasons for patients with BA hospitalizations in the intensive care department.

Ninety-eight patients of intensive care department (63 men, mean age  $45.5 \pm 3.2$  years, mean duration of disease  $8.3 \pm 1.7$  years) with severe BA (according to GINA classification) were enrolled into the study.

We evaluate patients' educational level, their medication and compliance. According to the results of our research, 34 patients (34.7%) did not receive any antiinflammatory medicine, 17 (17.3%) used only systemic corticosteroids.

Medication of 38 (38.8%) patients consist of short-acting  $\beta_2$ -agonists only.

Eighty-three (84.7%) patients have never applied long-acting  $\beta_2$ -agonists. Thirteen (13.2%) of them visited 'Asthma-school', 4 (4.1%) patients monitor their peak expiratory flow every day, 12 (12.2%) used additional methods of drug delivery (spasers, etc.).

The results show that inadequate anti-inflammatory and bronchodilator therapy, low educational level of the patients, absence of compliance have significant importance in the development of BA severe exacerbation.

#### P13 **Severe BOOP**

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**Background:** A subgroup of BOOP has recently emerged as an important cause of severe respiratory disease which is often progressive and is associated with a significant morbidity and mortality.

**Methods:** Retrospective and prospective study of ten patients with respiratory failure due to histopathologically confirmed BOOP. End points included determination of markers for severe BOOP,



breaths/min or more, active contraction of the accessory respiratory muscles or abdominal paradox, a ratio  $\text{PaO}_2/\text{FiO}_2 < 200$  and radiologic lesions on the chest radiograph. They were randomly assigned to receive either conventional therapy or conventional therapy and noninvasive positive pressure ventilation (NPPV) through a nasal mask. NPPV was provided with the BiPAP® Vision Ventilator System (Respironics Inc., Murrysville, PA, USA). The primary end point of the study was 'need for endotracheal intubation'. Secondary endpoints included: in-hospital mortality, the length of stay in the ICU, length of stay in the hospital, and the need for fiberoptic bronchoscopy. An interim analysis was designed at the middle of the study.

**Results:** Over this 16 month period, 912 patients were admitted to the Intensive Care Unit. Forty-eight patients were enrolled.

**Conclusion:** Because endotracheal intubation is the most important predisposing factor for ventilator associated pneumonia, bronchial stump disruption and bronchopleural fistula, postoperative re-intubation must be avoided. This is the first prospective, randomized study which demonstrates an improvement in survival and in avoiding endotracheal intubation in the postoperative care of patients undergoing lung resection surgery.

**P16 Noninvasive positive pressure ventilation in patients with blunt chest trauma and acute respiratory failure**

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**Background and objective:** Noninvasive positive pressure ventilation (NPPV) has been reported to be beneficial in the treatment of acute exacerbation of chronic obstructive pulmonary disease (COPD), and to facilitate weaning. In this trial we assessed the possible benefit of early NPPV in patients with blunt chest trauma and acute respiratory failure.

**Methods and design:** Eighteen patients admitted to ICU were enrolled in this prospective randomized study. Inclusion criteria were isolated blunt chest trauma with respiratory failure and ICU stay more than 7 days. Exclusion criteria were history of COPD and conditions when NPPV was contraindicated. The patients were randomized into two groups. Group 1 ( $n = 9$ ) received standard therapy (oxygen, regional analgesia, fluid and nutritional support, pulmonary physiotherapy/rehabilitation) including tracheal intubation and mechanical ventilation when indicated. Group 2 ( $n = 9$ ) received standard therapy along with NPPV. In Group 2 we used NPPV with face mask and Pressure Support (7–21

$\text{cmH}_2\text{O}$ )/CPAP (3–10  $\text{cmH}_2\text{O}$ ) ventilation. The need for tracheal intubation was assessed and the number of intubated patient in both groups was recorded on the 12, 24, 48, 96th hour and 7th day. The effect of the therapy was assessed on the 1, 6 and 12th hour using  $\text{PO}_2/\text{FiO}_2$  index, frequency/tidal volume index ( $f/V_t$ ), dispnea score, hemodynamics and the tolerance to pulmonary physiotherapy/rehabilitation.

**Results and discussion:** The main results suggest the possible beneficial effect of NPPV in decreasing the need for tracheal intubation and mechanical ventilation (Group 1 – intubated 7 [78%], Group 2 – intubated 3 [34%]). We found a significant statistical difference with improvement in all parameters ( $\text{PO}_2/\text{FiO}_2$  index, frequency/tidal volume index ( $f/V_t$ ), dispnea score, hemodynamics and the tolerance to pulmonary physiotherapy/rehabilitation) in the NPPV group. The results show that NPPV should be considered as systemic approach in management of all patients with blunt chest trauma and acute respiratory failure.

**P17 Helium–oxygen (He–O<sub>2</sub>) enhances oxygenation and increases carbon dioxide clearance in mechanically ventilated patients**

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**Introduction:** Helium is eight times less dense than nitrogen and only 10% more viscous. As a result of these physical properties it produces significantly higher gas flows for the same differential pressure gradient. This coupled with the fact that as a carrier gas He facilitates faster diffusion makes it a potentially useful adjunct in the ventilatory support of patients with acute respiratory failure. Substituting He for nitrogen has been shown to be of considerable benefit in the management of acute upper airway obstruction from a wide variety of causes. There is also a growing body of evidence for its use in acute severe asthma and decompensated COPD. We previously conducted a pilot study of He–O<sub>2</sub> in patients with acute respiratory distress syndrome (ARDS) and found that it led to a significant improvement in gas exchange in the majority of subjects. Having resolved a number of technical problem regarding the use of He–O<sub>2</sub> we have gone on to perform a larger cross over study in a wider variety of patients and present our preliminary findings here.

**Methods:** All patients who were mechanically ventilated on our unit were eligible. Exclusion criteria included haemodynamic instability, active weaning of respiratory support and imminent deterioration. All patients were ventilated in a pressure control mode. Patients were observed for a 15 min period on their established ventilatory regime of N<sub>2</sub>–O<sub>2</sub>. They were then switched to He–O<sub>2</sub>

and observations repeated after 15 and 60 min and then every 60 min for a maximum of 360 min. The trial was terminated when no further change in the partial pressures of arterial oxygen ( $\text{PaO}_2$ ) and carbon dioxide ( $\text{PaCO}_2$ ) were seen. Patients were then re-established on N<sub>2</sub>–O<sub>2</sub> and observed for a further 60–120 min. No alterations in ventilatory parameters were made unless warranted by changes in arterial blood gases. Ventilatory and haemodynamic parameters were continuously monitored throughout. The ventilator flowmeter was calibrated for use with He–O<sub>2</sub> as previously described.

**Results:** Six out of eight patients showed a significant improvement in  $\text{PaO}_2$  and  $\text{PaCO}_2$  within 15 min. Most of those studied showed further improvements at the successive observation time points. There were small improvements in respiratory mechanics, but these were insufficient to explain the improvements in gas exchange. There were no significant haemodynamic changes seen. The worse the derangement of gas exchange at study outset, the greater the magnitude of improvement seen on He–O<sub>2</sub>.

**Conclusions:** This study adds to the growing body of evidence that He–O<sub>2</sub> may be a useful adjunct to mechanical ventilation, especially in the most severe cases of respiratory failure.



oxygenation. The mean time to achieve  $FI_{O_2} \leq 0.6$  was  $5.2 \pm 0.9$  hours. Four of 38 patients developed a pneumothorax although none developed hypotension; one had bilateral pneumothoraces. All four patients evidenced decreased  $CO_2$  clearance and decreased release phase volumes as their only manifestation of a pneumothorax. 97% of patients on APRV with a  $Phigh \geq 20$   $cmH_2O$  pressure who were transported out of the ICU using bag-valve ventilation developed hypoxemia within 5 min. 100% of patients with a  $Phigh \leq 20$   $cmH_2O$  pressure were safely hand ventilated during transport without developing hypoxemia.

**Conclusion:** APRV is a safe rescue mode of ventilation for hypoxic or hypercarbic respiratory failure and requires a lower minute ventilation than does conventional modes. Decreasing release phase volumes and a rising  $pCO_2$  are excellent clues of a pneumothorax in a patient on APRV. Thus, routine end-tidal  $CO_2$  monitoring is recommended for patients on APRV. Preparations for safe intra-hospital transport may be keyed to the  $Phigh$  required for adequate ventilation and oxygenation.

**P20 Patient controlled pressure support ventilation**

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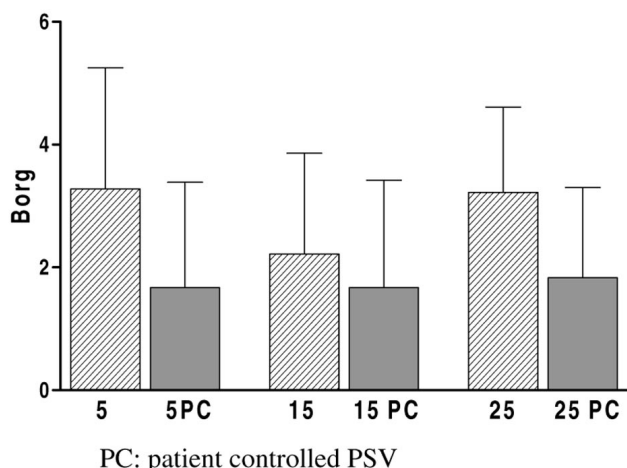
**Introduction:** Pressure support ventilation is mostly used in weaning from mechanical ventilation in acute respiratory failure. There are no data regarding the optimal level of assistance for each patient in different clinical conditions. We approach a new method that allows patients to set their own PSV level by a remote control connected to the ventilator.

(WOB J/min, estimated from a modified Campbell diagram [1]) and the dyspnea sensation using the Borg visual scale [2]. Patients were studied at three fixed levels of PSV (5–15–25  $cmH_2O$ ). At the end of each step we gave the patient the possibility to change the level of PSV using the remote control. Patients were previously instructed by attendant physician about the use of the remote control.

**Materials and methods:** In 9 awake intubated patients (age  $57 \pm 17$  years, BMI  $24 \pm 3$   $kg/m^2$ ,  $PaO_2/FIO_2$   $283 \pm 51$ , Ramsey  $1.9 \pm 0.4$ ) we measured the breathing pattern ( $V_T$ , RR), the work of breathing

**Results:** See Table and Figure. It appears that increasing the pressure support level, the patient work of breathing decreases while the Borg dyspnea scale shows no significant differences.

**Figure**



The dyspnea sensation when patient is allowed to set the pressure support level.

**Table**

	PSV 5	PSV 15	PSV 25
$V_T$ (ml)	$331 \pm 150^*$	$524 \pm 222$	$884 \pm 362$
RR (bpm)	$25 \pm 1^*$	$19 \pm 6^+$	$13 \pm 6$
WOB (J/min)	$8.2 \pm 0.3^*$	$2.2 \pm 2.2$	$1.8 \pm 2$
Borg (cm)	$3.3 \pm 2$	$2 \pm 1.6$	$3 \pm 1.4$

One way RM Anova \*  $P < 0.05$  vs others;  $^+ P < 0.05$  vs PSV 25.

**Conclusions:** Patient controlled PSV could be a useful technique in ventilatory management of critically ill awake patients.

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**P21 Impact of weaning failure in the evolution of patients under mechanical ventilation**

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**Introduction:** Weaning period is critical in the evolution of patients with acute respiratory failure (ARF) and mechanical ventilation (MV). Weaning failure has been associated with increased morbidity and mortality. We evaluated the impact of weaning failure on mortality, and MV and ICU length of stay.

**Methods:** Patients who were admitted to our 8-bed surgical-ICU and stayed more than 24 hours on MV were prospectively evaluated from June 1999 to June 2000. Demographics, ARF etiology, APACHE II and gas exchange and mechanical parameters were assessed. Weaning failure was defined as reintubation within 48



ventilation with a PEEP of 15 cmH<sub>2</sub>O was instituted to prevent derecruitment. Peak pressures were maintained at ≤ 35 cmH<sub>2</sub>O. Outcome measures were oxygenation index, PaO<sub>2</sub>/FiO<sub>2</sub> ratio and alveolar-arterial oxygen difference.

**Results:** The oxygenation index decreased from a median of 31 cmH<sub>2</sub>O to 14 cmH<sub>2</sub>O/mmHg immediately post recruitment and to 11 cmH<sub>2</sub>O/mmHg (*P* < 0.0001) 24 hours later. The A-aDO<sub>2</sub> improved from 454 mmHg to 128 mmHg (*P* < 0.0001) and the

PaO<sub>2</sub>/FiO<sub>2</sub> ratio from 75 to 218 (*P* < 0.0001) 24 hours later. 25% of patients had PaO<sub>2</sub>/FiO<sub>2</sub> ratio of 300 mmHg at 24 hours. Mean airway pressure increased by 3 cmH<sub>2</sub>O initially, from 23 cmH<sub>2</sub>O to 26 cmH<sub>2</sub>O (NS) as a consequence of the increase of PEEP but his had decreased to 25 cmH<sub>2</sub>O after 24 hours. There were no significant complications.

**Conclusion:** Rapid reductions in FiO<sub>2</sub> can be achieved safely by the implementation of a relatively simple recruitment technique.

**P24 The effects of recruitment maneuver on oxygenation in primary and secondary adult respiratory distress syndrome**

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**Introduction:** Recruitment maneuvers (RM), as an adjunct to mechanical ventilation, have been shown to be capable of reopening collapsed alveolar units in ARDS, providing better ventilatory parameters and improvement in oxygenation. The aim of our study is to investigate and to compare the response of patients with pulmonary and extrapulmonary ARDS to recruitment maneuver.

**Methods:** We studied 18 patients with severe ARDS of varying etiology admitted to the intensive care unit of Istanbul University, Istanbul Medical Faculty. The diagnosis of ARDS was based on the criteria proposed by the American-European Consensus Conference on ARDS. The patients who demonstrated impaired oxygenation, during pressure regulated volume-controlled ventilation with 10 ml/kg tidal volume and 12/min frequency comprised our study population. The patients were presented to four members of the ICU team individually and assigned to primary (ARDS<sub>p</sub>) and secondary (ARDS<sub>s</sub>) ARDS groups according to the patient's history and clinical presentation, along with the results of microbiological tests. During the recruitment maneuver, we applied sustained inflation (SI), which consisted of 40 cmH<sub>2</sub>O CPAP. After 30 s we returned to the previous tidal volume with 20 cmH<sub>2</sub>O PEEP levels. Keeping peak airway pressure below 45 cmH<sub>2</sub>O, we adjusted the optimal PEEP level, between 10–20 cmH<sub>2</sub>O, by matching the saturation on pulse oximeter with the lowest PEEP. Following the setting of PEEP level, we recorded arterial blood gas values, ventilatory parameters and hemodynamic measurements at 15 min, 1st, 4th and 6th hours of post-RM period.

**Results:** The clinical defining scores of patients are summarized in Table 1. Over 6-hour period of time following RM, there was no statistically significant change in both hemodynamic and ventilatory measurements, except PaO<sub>2</sub>/FiO<sub>2</sub> ratios (Table 2). Mean values of PEEP before and after RM were 10 ± 3.4 cmH<sub>2</sub>O and 14.6 ± 2.8 cmH<sub>2</sub>O in ARDS<sub>p</sub> (*P* = 0.04), 12 ± 5 and 17 ± 2.8 in ARDS<sub>s</sub> (*P* = 0.01). The mean values of PaO<sub>2</sub>/FiO<sub>2</sub> ratio difference between the baseline and the value at the end of the study were 41 ± 30 % in ARDS<sub>p</sub>, and 89 ± 111% in ARDS<sub>s</sub> (*P* = 0.6). PaO<sub>2</sub>/FiO<sub>2</sub> ratios started to increase significantly mainly 15 min following RM in ARDS<sub>s</sub>, and 4 hours after RM in ARDS<sub>p</sub>.

**Conclusion:** The response of patients with secondary ARDS to RM was observed earlier than the response of patients with primary ARDS.

**Table 1**

	ARDS <sub>p</sub>	ARDS <sub>s</sub>	P
APACHE II	14.5 ± 6.2	16.8 ± 9.5	0.7
Marshall MODS	4.8 ± 3.4	6.2 ± 2.3	0.06
Murray Score	11 ± 1.8	11 ± 1.5	0.8

**Table 2**

		Before RM	15 min	1st hour	4th hour	6th hour	ANOVA P
PaCO <sub>2</sub> (mmHg)	ARDS <sub>p</sub>	47 ± 10	51 ± 12	49 ± 10	47 ± 11	50 ± 7	0.7
	ARDS <sub>s</sub>	48 ± 10	47 ± 11	43 ± 17	47 ± 13	46 ± 12	0.9
PaO <sub>2</sub> /FiO <sub>2</sub>	ARDS <sub>p</sub>	117 ± 24	144 ± 37	134 ± 28	155 ± 34 *	162 ± 38 *	0.006
	ARDS <sub>s</sub>	111 ± 44	181 ± 116 *	193 ± 91**	191 ± 95 **	190 ± 99 **	0.01

\* *P* < 0.05 when compared to the values before RM. \*\* *P* < 0.01 when compared to the values before RM.

**P25 Comparison of the P/V curve obtained by the supersyringe and the optoelectronic plethysmography**

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The pressure volume (P–V) curve of the total respiratory system is drawn assuming the changes of chest wall ( $\Delta V_{cw}$ ) equal to the volume displaced from the syringe ( $\Delta V_{gas}$ ). We compared  $\Delta V_{gas}$

and  $\Delta V_{cw}$  during P–V curves obtained by supersyringe and optoelectronic plethysmography [1]. Eight sedated paralysed intubated ALI/ARDS patients (5 M/3 F, age 70 ± 13 years, BMI 25.6 ± 3



**Table**

Group	A	B	C	D
	PEEP 0	PEEP 5	PEEP 10	PEEP 15
Paw (cmH <sub>2</sub> O)	32 ± 5	35 ± 1	37 ± 3	40 ± 4
MAP (mmHg)	90 ± 15	92 ± 16	95 ± 17	93 ± 18
CVP (mmHg)	6 ± 3	5 ± 4	5 ± 3	6 ± 4
IOP (od) (mmHg)	13.4 ± 3.4	14.1 ± 4.1	13.4 ± 3.4	12.5 ± 3.0
IOP (os) (mmHg)	13.7 ± 3.3	14.5 ± 3.7	14.2 ± 3.4	12.8 ± 3.1
SaO <sub>2</sub> (%)	98 ± 2	98 ± 2	98 ± 2	98 ± 1

**Conclusion:** Mechanical ventilation with PEEP values of ≤ 15 cmH<sub>2</sub>O do not cause an increase in intraocular pressure in patients with intracranial pathology.

**P28 Effects of lung recruitment and PEEP after CPB on pressure–absolute volume curves**

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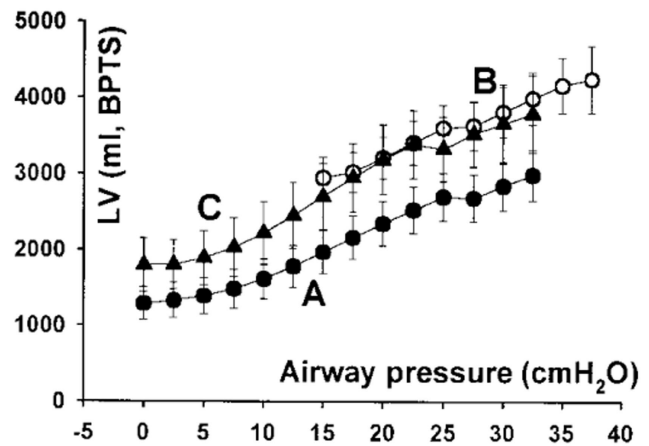
**Introduction:** Impaired lung function is common after cardiopulmonary bypass (CPB). We hypothesized that due to collapse tendency 1) the effect of a lung recruitment maneuver (LR) on a pressure–absolute lung volume (P–V) curve would be minimal, 2) but if LR is followed immediately by PEEP the curve would shift upwards and the slope would be steeper.

**Methods:** Sixteen patients (48–75 years) after CABG in CPB were studied postoperatively every 0.5 h during 3 h while mechanically ventilated (FiO<sub>2</sub> 1.0) with measurements of end-expiratory lung volume (EELV) and blood gases. Eight patients were randomized to LR (45 cmH<sub>2</sub>O airway pressure 2 x 20 s) after which PEEP was set 1 cmH<sub>2</sub>O > LIP obtained from a static P–V curve (PEEP group), while the 8 other were randomized to LR only (ZEEP group). Three inspiratory P–V (including EELV) curves were obtained in both groups. In the PEEP-group, the first curve (A ●) was obtained before LR and PEEP, the second (B ○) during PEEP (14 ± 3 cmH<sub>2</sub>O, mean ± SD) 2.5 h after LR, and the third (C ▲) 0.5 h after removal of PEEP, i.e. 3 h after LR. In the ZEEP group, P–V curves were obtained at similar times.

**Statistics:** ANOVA and Wilcoxon signed rank test.

**Results:** In the ZEEP group, no change in PaO<sub>2</sub>, lung volume or PV-relations occurred during the study. In the PEEP group, PaO<sub>2</sub> increased by 16 ± 15 kPa (*P* < 0.002) after LR and PEEP and was unchanged during the study. EELV increased by 1120 ± 235 ml (*P* < 0.0001) and remained stable until removal of PEEP. The 3 P–V curves are shown in the figure (A ≠ B or C, *P* < 0.03).

**Figure**



**Discussion:** In patients after CPB, LR without subsequent PEEP had no effect. However, when LR was followed by PEEP, EELV increased and the P–V curve became steeper and shifted upwards. Furthermore, the curve remained the same 0.5 h after PEEP-removal. This and the unchanged PaO<sub>2</sub> indicate that no new lung collapse occurred after removal of PEEP and suggest that PEEP might have a sustained stabilizing effect on lung structures in these patients.

**P29 The histopathological changes comparison in healthy rabbit lung ventilated with ZEEP, Sigh and PEEP**

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Our aim was to compare the effects of LV + ZEEP, LV + Sigh and LV + PEEP on histopathological changes with healthy rabbit lungs. Fifteen New Zeland rabbits were randomly divided into

three groups (*n* = 5). Animals were ventilated for 3 hours with F<sub>1</sub>O<sub>2</sub>:1.0, f:80/dk. Group 1: Low volume (5 ml/kg) + ZEEP, Group 2: Low volume (5 ml/kg) + 10 cmH<sub>2</sub>O PEEP, Group 3:



during the period studied and only reached significance 12 hours after proning ( $17.9 \pm 2.9$  v  $35.1 \pm 4.2$ ,  $P < 0.05$ ). Mean EVLW/ITBV did not change significantly.

At least 12 hours may be needed for maximal benefit with prone positioning. Changes in pulmonary vascular permeability in ARDS

do not appear to be an important mechanism to account for the improvement in gas exchange seen following prone positioning.

**Reference:**

1. Pallister I, Gosling P, Alpar K, Bradley S. *J Trauma* 1997, 42:1056–1061.

**P32 Prospective study to evaluate the kind of prone position concerning nursing, pulmonary outcome and material and personnel resources**

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**Introduction:** Acute Respiratory Distress Syndrome (ARDS) is one of the most common, potentially lethal disease processes encountered in critical care with extremely high mortality of about 60%. Researchers have found that a significant improvement in gas exchange often occurs when ARDS patients are turned from the supine to the prone position. But there are a lot of difficulties in nursing these patients in dependence of the kind of kinetic therapy. So the major goal is, to find out the best kind of kinetic therapy. The available study is designed by physicians and nurses. Besides the question of patients benefit concerning the gas exchange the handling, the acceptance of the nurses and economical consequences are proofed.

**Methods and materials:** Patients with ARDS, or those patients identified as requiring to be nursed in the prone position with a Horowitz-Quotient ( $\text{PaO}_2/\text{FiO}_2$ )  $< 250$  were treated by different kinds of kinetic therapy in order to compare the efficiency concerning clinical outcome, personnel and material resources and the incidence of complications. Patient were turned into face down

prone position, in near side prone position or they were treated in a Rotation bed. Gas analysis defined the clinical effect of the position on gas exchange. Also changes in skin integrity, skin status and clinical outcome of prone positioning were documented. Additionally number of nurses/physicians being involved in positioning the patient and the duration of time was documented.

**Results:** Ten patients were positioned in near side prone position (NSPP). Eight patients were positioned in 180°-position and 10 patients were treated in rotation bed. In handling, nursing and observing the NSPP is the preferred kind of kinetic therapy. The pulmonary outcome is comparable to the other forms of kinetic therapy but less need of personnel and material resources and the very small risk of complication (skin damages, oedema formation, lost of catheter or tube) are advantages of the NSPP. So at every point of time position changing can occur. Also the patients treated in rotation bed shows a similar clinical outcome concerning the gas exchange but the need of material resources is disproportionately high and the availability is to be estimated very low.

**P33 Effect of prone position on hepato-splanchnic hemodynamics in acute lung injury**

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**Objective:** Ventilation in prone position (PP) is a common method to improve gas exchange in patients with acute lung injury (ALI). Although no significant changes in systemic hemodynamics were observed [1], the question remains as to whether the PP may alter the hepato-splanchnic perfusion and oxygen exchange. Therefore, we studied the effects of PP on hepato-splanchnic hemodynamics in patients with ALI.

**Patients and methods:** Up to now five patients with ALI fulfilling criteria for PP ( $\text{PaO}_2/\text{FiO}_2 < 250$ ,  $\text{FiO}_2 > 0.55$ ,  $\text{PEEP} > 10$ ) were studied. In addition to systemic hemodynamics (radial and PA catheters) and gas exchange, hepatosplanchnic blood flow (HSBF, steady state indocyanine green technique) and hepatic venous

pressure (HVP) were measured using hepatic vein catheter. Gastric intramucosal-arterial  $\text{PCO}_2$  gap was determined using air tonometry (Tonocap) and intravascular pressure was recorded to monitor intra-abdominal pressure (IAP). Data collection was performed at the supine position (SP1), after 90 min of PP, and after 90 min of supine repositioning (SP2).

**Results:** Data are median and interquartile range (RM-ANOVA).

**Conclusion:** Our preliminary results suggest that the prone position, provided that IAP remains unaffected [2], compromises neither the perfusion of the hepato-splanchnic area nor the gut mucosal energy status in patients with ALI [3].

	SP1	PP	SP2	P value
MAP (mmHg)	91 (82–104)	90 (86–116)	92 (85–113)	0.52
CI (l/min/m <sup>2</sup> )	3.5 (2.9–4.0)	3.4 (3.1–4.0)	3.2 (2.7–3.5)	0.36
HSBF (l/min/m <sup>2</sup> )	1.17 (1.12–1.4)	1.26 (1.06–1.51)	1.22 (1.03–1.43)	0.95
HVP (mmHg)	14 (13.16)	15 (14–17)	14 (14–15)	0.95
$\text{PCO}_2$ gap (mmHg)	7.5 (5.3–10.9)	7.9 (5.3–8.3)	7.5 (6.9–9.8)	0.94
IAP (mmHg)	10 (9–13)	13 (10–16)	14 (11–14)	0.09



**Results:**

	NO 4 ppm	NO 10 ppm
Decrease of PAP (mmHg)	-0.7 ± 0.1 (n = 6)	-1.0 ± 0.1 <sup>†</sup> (n = 6)
Zaprinast (50 µg)	-1.9 ± 1.8* (n = 14)	-2.9 ± 1.3* (n = 4)
Sildenafil (10 ng)	-1.8 ± 1.1* (n = 6)	-2.4 ± 0.5* (n = 5)

<sup>†</sup>P < 0.05 vs NO ppm and \* P < 0.05 vs NO 4 ppm and NO 10 ppm, respectively; ANOVA.

**Conclusion:** These data demonstrate that specific inhibition of PDE type 5 improves responsiveness to inhaled nitric oxide in lungs obtained from endotoxin-challenged rats. In our model, decreased responsiveness to inhaled nitric oxide is at least in part attributable to increased pulmonary PDE type 5 activity.

**References:**

1. Weimann *et al: Anesthesiology* 2000, **92**:1702–1712.
2. Ichinose *et al: Anesthesiology* 1998, **88**:410–416.
3. Holzmann A *et al: Am J Physiol* 1996, **271**:L981–L986.

**P36 Partial liquid ventilation (PLV) vs conventional mechanical ventilation (CMV) with high PEEP and moderate tidal volume (Vt) in acute lung injury in piglets**

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**Objective:** To test the hypothesis that PLV combined with a high PEEP and a moderate Vt results in improved gas exchange and lung mechanics compared to CMV in acute lung injury in piglets. ALI was induced in 12 piglets weighing 9.0 ± 2.4 kg by repeated intravenous injections of oleic acid and repeated lung lavages. Thereafter the animals were randomly assigned either for PLV (n = 6) or CMV (n = 6) at a FiO<sub>2</sub> of 1.0, a PEEP of 1.2 kPa, a tidal volume < 10 ml/kg, a respiratory rate of 24 breaths/min, and an I:E ratio of 1:2. Perfluorocarbon liquid (30 ml/kg b.w.) was instilled into the endotracheal tube over 10 min followed by 5 ml/kg b.w./h.

Cardiorespiratory monitoring was done at baseline, after induction of ALI, and every 30 min up to 120 min. When compared with control animals, PLV resulted in significant better oxygenation, significant lower dead space ventilation, and significant better CO and DO<sub>2</sub>.

**Conclusions:** PLV combined with high PEEP and moderate tidal volume significantly improves oxygenation, dead space ventilation, cardiac output, and oxygen delivery in piglets with ALI, but has no significant influence on lung mechanics.

**Table 1**

**PA-aO<sub>2</sub> and DO<sub>2</sub> in 12 piglets with ALI during PLV or CMV**

Parameters	Group	Baseline	ALI	t-60	t-120
PA-aO <sub>2</sub> (kPa)	Control	5.8 ± 2.3 <sup>†</sup>	80.2 ± 2.9	72.7 ± 6.3*	71.9 ± 7.2*
	PLV	7.5 ± 4.1 <sup>†</sup>	80.5 ± 2.3	47.9 ± 20.0 <sup>†§</sup>	45.6 ± 21.3 <sup>†§</sup>
DO <sub>2</sub> (ml/min)	Control	18.7 ± 3.5 <sup>†</sup>	11.3 ± 2	11.7 ± 4.0	10.5 ± 2.6
	PLV	22.5 ± 4.1 <sup>†</sup>	15.3 ± 4.5	18.9 ± 6.9 <sup>‡</sup>	18.7 ± 7.2 <sup>‡</sup>

\* P < 0.05, <sup>†</sup> P < 0.01 vs ALI levels within the groups, <sup>‡</sup> P < 0.05, <sup>§</sup> P < 0.01 between groups.

**P37 Acute versus subacute haemorrhagic shock evaluated in an isolated perfused rat lung model**

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**Introduction:** Volume resuscitation of haemorrhagic shock (HS) may lead to delayed apparition of shock lung. We compared acute versus subacute grade IV HS with and without volume resuscitation in an isolated blood-perfused and ventilated lung rat model.

resuscitation in the rats submitted to the subacute but not to the acute HS. Ventilation parameters were maintained constant. The isolated lung circuit was primed and perfused with the blood of a donor rat.

**Methods:** Male Sprague Dawley rats were anaesthetised with isoflurane, fentanyl and pancuronium, tracheotomised and ventilated with a volume controlled ventilator. After 300 U/kg i.v. heparin, grade IV HS was induced by withdrawing 30 ml/kg blood with a roller pump in four groups of 10 rats (acute HS with and without volume resuscitation, subacute HS with and without volume resuscitation). A 5th group without HS served as control. Volume resuscitation consisted of infusion of Ringer Lactate (three times the volume of blood withdrawn) over 30 min, starting 60 min after initiation of HS. Mean arterial pressure (MAP) dropped from 75 mmHg to 10 mmHg in the acute HS, and from 75 to 25 mmHg in the subacute HS. MAP recovered initial values at the end of

**Results:** Acute HS with volume resuscitation was not associated with significant alterations in any of the measured variables of the perfused lung. In contrast, acute HS without volume resuscitation resulted in the most striking alterations in lung mechanics, haemodynamics, as well as weight changes. Subacute HS independently of volume resuscitation showed only moderate and non significant changes. See Figure 1 opposite.

**Conclusions:** Our results demonstrate that pulmonary injury following non resuscitated HS depends principally on the intensity and not on the volume of blood loss, and that during subacute HS even of grade IV, volume resuscitation is of minimal benefit.



**Materials and methods:** Forty-eight patients without pulmonary infiltrates and mechanically ventilated for < 24 hours entered the study. Gastric, oral and tracheal aspirates and rectal swabs were taken for semiquantitative analysis within 24 hours and in 3 days intervals thereafter up to 21 days of ICU stay. For aspirates, the amount of pathogens > 10<sup>5</sup>/ml was considered significant. Metoclopramide and sucralfate were used in all patients. Cyclic enteral nutrition was given into the stomach according to standard protocol.

**Statistics:** Chi-squared and Fisher exact tests were used, *P* < 0.05 was considered significant.

**Results:** Thirty-eight patients (15 lactulose – L and 23 placebo – P) stayed in the ICU > 4 days and were further analysed. L and P groups did not differ in age, APACHE II, ICU survival, LOS, ventilatory and antibiotic days. The frequency of stools was significantly higher in L group. On day 1 gastric aspirates were positive in 1 L and 2 P patients. On day 4 gastric colonisation increased to 4 (27%) and 7 (30%), respectively (NS). During further ICU stay the

colonisation remained in range 20–35% and did not differ between the groups. *Candida albicans* was the most often pathogen isolated. On day 1 tracheal aspirates were positive in 1 (L group) and 3 (P group) patients. Later on the frequency in both groups increased to and remained in the range of 40–75% (NS). VAS was diagnosed in 6 (40%) and 8 (35%) in L and P groups, respectively (NS). In 9 (L) and 12 (P) patients the pathogen was primarily isolated from oral cavity with *Pseudomonas aeruginosa* and coagulase negative Staphylococcus being the most often pathogens. The consecutive appearance of pathogen in stomach, oral cavity and trachea was clearly present in 2 patients. In further 5 patients the pathogens were isolated on the same day from all three sites.

**Conclusions:** Lactulose failed to prevent gastric colonisation in patients on mechanical ventilation. The most often source of pathogens in trachea and VAP in our conditions is the oral cavity.

This study was performed with support grant IGA 4072-3

**P40 Fiberoptic bronchoscopy and bronchoalveolar lavage in patients with a haematological malignancy with bilateral pulmonary infiltrates**

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**Introduction:** Pulmonary infiltrates in patients with a haematological malignancy presents a special challenge for both diagnostic approach and clinical management.

**Aim:** To analyse the utility and impact of Fiberoptic bronchoscopy (FOB) and bronchoalveolar lavage (BAL) in patients with haematological malignancy and bilateral pulmonary infiltrates.

**Method:** A FOB with BAL was performed using three 50 ml aliquot of 0.9% sterile saline solution and aspiration under continuous monitoring of the saturations, over a 24 month period.

**Results:** Data as median (range).

**Discussion:** We studied 35 patients with haematological malignancy with evolutive pneumonia despite treatment with appropriate empirical antimicrobial therapy. The overall diagnostic yield was 80%, which was identical in both neutropenic and non-neutropenic patients. This resulted in a change or rationalisation of antimicrobial therapy for both groups of patients.

<i>n</i> = 35	Neutropenic patients ( <i>n</i> = 10)	Non-neutropenic patients ( <i>n</i> = 25)
Baseline APACHE II scores	13.5 (9–33)	14 (9–27)
Positive results	8 (80%)	20 (80%)
Bacterial	8	11
Viral	5	5
Fungus/PCP	1	2/1
No growths	2 (20%)	5 (20%)

**Conclusion:** FOB with a BAL is a beneficial investigative tool in patients with haematological malignancy with an evolutive pneumonia as manifested by bilateral pulmonary infiltrates.

**Reference:**

Gruson D, Hilbert G, Valentino R, et al: **Utility of fiberoptic bronchoscopy in neutropenic patients admitted to the intensive care unit with bilateral pulmonary infiltrates.** *Crit Care Med* 2000, **28**:2224–2229.

**P41 Hospital-acquired respiratory infection in patients admitted in ICU**

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**Background:** Hospital-acquired respiratory infection is frequent in ICU patients, especially in those that are submitted to invasive procedures.

**Objectives:** To study comorbidities and risk factors for the development of hospital-acquired respiratory infection (HARI) and the microbiological profile.

**Methods:** Retrospective clinical study of 385 patients admitted to our ICU, from January to September 2000. **Respiratory infection** was defined by 'new' purulent bronchial secretions, with fever (>38.5°C, axilar) and leucocytosis (>10,000) with or without 'new' pulmonary infiltrate. Patients developing infection after 72

hours of hospitalisation were identified and studied for **comorbidities:** cancer, immunodepression, HIV positive, diabetes mellitus, pulmonary, cardiac, renal, hepatic and central nervous illnesses, alcohol and drug abuses and cigarette smoking; and **risk factors:** non-elective oro-tracheal intubation (OTE), re-intubation or tracheostomy, depression of conscience level (8 < ECG < 15), coma (8 ≤ ECG), intoxication, seizures, vomiting, documented tracheal aspiration and respiratory or cardiopulmonary arrest.

**Results:** During this period 78 (20.3%) patients had the diagnosis of HARI, with a mean age of 55.8 years. 62.8% had comorbidities. This group was compared with an equivalent group of 20 patients, without respiratory infection in the same period (mean age



	Number PN per 1000 MV-days	Number TB per 1000 MV-days	Number TC per 1000 MV-days	Number PN and TB per 1000 MV-days	Number PN, TB and TC per 1000 MV-days	Number Ex events per 1000 MV-days
BF	25.38	10.15	3.38	35.53	38.91	5.07
No BF	19.30	6.43	11.58	25.73	37.32	3.86
P	No S	No S	No S	No S	No S	No S

**Conclusions:** Bacterial filter in breathing circuits do not reduce the incidence of tracheal colonization, respiratory infections or exogenous events.

**Reference:**

1. van Saene HK, Damjanovic V, Murray AE, de la Cal MA: **How to classify infections in intensive care units—the carrier state, a criterion whose time has come?** *J Hosp Infect* 1996, **33**:1–12.

**P44 Risk factors for broncho-pulmonary nosocomial infection in medical intensive care unit**

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Broncho-pulmonary nosocomial infection (BPNI) has the highest incidence of nosocomial infection in intensive care unit (ICU) and is associated with substantial morbidity and mortality. The objective of this study is to determine the risk factors for BPNI and improve the prevention of this infection.

**Patients and methods:** Characteristics of all patients admitted in a 30-beds university medical ICU were prospectively collected from 03/93 to 09/99. The diagnosis criteria for nosocomial pneumonia and bronchitis were those published by the CDC. Patients

with first BPNI were compared to the others by univariate and multivariate analysis.

**Results:** We diagnosed 517 first BPNI representing: 12% of the 3681 patients hospitalised in our unit, 11.6 episodes/1000 days of hospitalization and 16 episodes/1000 days of ventilation. Microbiology studies were positives for 455 (88%) BPNI: *Acinetobacter* (28.1%), *P. aeruginosa* (23.1%), *Staphylococcus aureus* (12.6%). The 517 BPNI included 282 (54.5%) pneumonia and 235 (45.5%) bronchitis.

Patient characteristics	General population (n = 3681)	BPNI (n = 517)
Age (years)	58	62
Sex ratio (M/F)	1.84	2.54
Mortality (%)	35.9	53.5
Mechanical ventilation (%)	85.1	97
ICU stay (days)	12.2	32.6
Length of mechanical ventilation (days)	10.5	26.5
SAPS II	37.1	36.5 NS
Total Omega	245	347
Surgical patients (%)	15.3	20.3

Multivariate analysis	Odds ratio	IC (95%)
H2-blockers or omeprazole use	5.53	3.35–9.12
Sucralfate use	2.66	2.05–3.46
Previous corticosteroid treatment	1.93	1.46–2.56
Renal failure	1.52	1.10–2.10
Number of ATB	1.27	1.12–1.44
Length of mechanical ventilation	1.06	1.05–1.08
Stay in ICU	1.05	1.03–1.06

Univariate analysis identified the following risk factors ( $P < 0.05$ ): At admission: Male gender, age  $> 60$ , chronic lung disease antecedent, previous corticosteroid treatment, antibiotics (ATB) in the previous 2 weeks, surgery or trauma  $< 24$  hours, secondary hospitalization, broncho-pulmonary infection, sedatives use; respiratory, renal or digestive distress. During hospitalization: Mechanical ventilation, total omega score; ATB, omeprazole, ranitidine or sucralfate use.

**Conclusion:** Prevention of BPNI should consider all measures to decrease ICU stay, length of mechanical ventilation and the use of steroids, sedatives, H2-blockers, omeprazole, sucralfate and ATB therapy; especially in patients with renal failure.

**P45 Surveillance tracheal aspirate in ventilator associated pneumonia (VAP)**

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VAP is associated with increased ICU stay and mortality, particularly when treatment is delayed or inappropriate [1]. When a clinical suspicion of VAP is justified, specific diagnostic tests are usually conducted: bronchoalveolar lavage (BAL), protected specimen brushing (PSB), diagnostic tracheal aspirate (dTA), blood cultures

and pleural fluid. We evaluated the concordance between specific diagnostic tests and the surveillance tracheal aspirates (sTA).

**Methods:** In our ICU routine sTA are performed weekly. The sTA and the specific diagnostic tests were considered concordant if



**P48 ICU-acquired nosocomial infection: impact of delay in adequate antibiotic treatment**

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**Objective:** To evaluate the impact of the delay in adequate antibiotic treatment (AAT) on outcome in ICU patients with nosocomial pneumonia (NP) or bloodstream infection (NBSI).

**Design:** Retrospective cohort study.

**Setting:** A 6-bed medical ICU in a university hospital.

**Methods:** Patients with first NP (bronchoalveolar lavage culture  $\geq 10^4$  CFU/ml or protected specimen brush culture  $\geq 10^3$  CFU/ml) or first NBSI (CDC definition) were included between May 1998 and September 1999. The organ failure score (Fagon criteria) at the time of sampling (day 0) and the interval between sampling and the start of AAT were recorded. Antibiotic treatment was considered to be adequate when all etiologic organisms isolated from the culture specimen were found to be sensitive to the initial empiric antibiotics. Mortality was compared according to the time of AAT and the organ failure score on day 0.

**Results:** A total of 25 patients (mean SAPSII = 44) were included in the study. Seventeen of them presented with a first NP and eight with a first NBSI. The infection occurred  $6.5 \pm 4.6$  days after ICU admission, 23 patients were receiving mechanical ventilation on day 0. The ICU mortality was 48% (12/25) and was not different between NP patients and NBSI patients: 9/17 vs 3/8 ( $P=0.47$ ). Mortality increased with the duration without AAT ( $P=0.011$ ) and was reduced when AAT was started on day 0 ( $P=0.016$ ) or day 1 ( $P=0.036$ ). A subsequent change from inadequate to adequate antibiotic treatment had no impact on survival. Mortality was also associated with the number of organ failures on day 0 ( $P=0.017$ ).

**Conclusions:** The mortality rate in patients developing NP or NBSI can be reduced when AAT is started before day 2. When the results of the bronchoscopy specimen and blood cultures are obtained early, they can therefore be helpful to start AAT and influence survival.

**P49 Systemic inflammatory response during ventilator-associated pneumonia**

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**Introduction:** Diagnosis of ventilator-associated pneumonia (VAP) can be difficult which often a large associated infectious or inflammatory diseases. The aim of our study was to describe systemic inflammatory response to VAP with the help of procalcitonin (PCT), CRP and cytokines.

**Methods:** In a prospective study, we studied all patients in our ICU with VAP between January 2000 and September 2000. PCT, CRP and cytokines (TNF, IL-6, IL-8) were measured at admission (J0), on second day (J2) and on fourth and seventh day (J4, J7). Prog-

nostic indicators of severity were recorded on admission: Apache II, IGS II and SOFA score.

**Results:** Twenty-four consecutive patients (mean age  $52 \pm 17$  years, mean IGS II  $38 \pm 15$ , mean Apache II  $15 \pm 6$ ) were admitted in ICU. Mortality rate was 45% (11 patients).

**Discussion:** PCT seems to be a good marker of the intensity of inflammatory response to infection during VAP with PCT values often under 5 ng/ml. So higher PCT levels may be related to another sepsis and another aetiology must be researched.

	J0	J2	J4	J7	J14
PCT (ng/ml)	$5.27 \pm 14.14$	$6.01 \pm 12.65$	$10.79 \pm 26.26$	$10.52 \pm 26.52$	$2.99 \pm 8.44$
CRP (mg/ml)	$191 \pm 68$	$215 \pm 62$	$163 \pm 92$	$147 \pm 106$	$68 \pm 84$
TNF (pg/ml)	$10 \pm 9$	$8 \pm 8$	$10 \pm 9$	-	-
IL-6 (pg/ml)	$628 \pm 1491$	$611 \pm 1703$	$328 \pm 602$	-	-
IL-8 (pg/ml)	$111 \pm 248$	$78 \pm 183$	$66 \pm 129$	-	-

**P50 Procalcitonin (PCT) versus IL-6 levels in bronchoalveolar lavage (BAL) fluids of trauma victims with severe lung contusion**

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**Objective:** To examine whether measurement of procalcitonin (PCT) in comparison to Interleukin 6 (IL-6) is a reliable marker to score the extent of lung contusion in bronchoalveolar lavage (BAL) fluids in polytrauma patients.

**Design:** Prospective, non-randomized observational study.

**Setting:** Twelve-bed ICU in a 1100-bed primary care university hospital.

**Patients:**  $n = 14$  trauma victims presenting with severe lung contusion and acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) were enrolled in the study.



**P53 A new approach of endotoxic testing by using a monoclonal antibody against endotoxin (WN1-222/5) and flow cytometry**

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Serum-endotoxin was formerly measured by the limulus-amebocyte assay. A major step forward since this test assay was available was the introduction of chromogenic substrates which were convertible by LAL clotting enzymes. Further improvements could not prevent the results to be non-specific and in general unsatisfactory. An alternative approach of our group for the detection of endotoxin was the usage of a cross reactive monoclonal antibody against endotoxin (WN1-222/5) in combination with flow cytometry, measuring subsequent light emission of a second antibody directed against WN1-222-5 in peripheral mononuclear cells (MØs).

In our porcine endotoxin shock model we investigated 10 pigs under analgesedation receiving 250 ng/kg/hour endotoxin from *Salmonella friedeman*.

Separation of mononuclear cells every 4 h and determination of the concentration of endotoxin revealed the results shown in the Table.

In this preliminary study we could not find LPS at the cell surface *in vivo* but *in vitro* (unpublished data). The current results indicate that the process underlying LPS internalization are very complex. During the course of our endotoxin shock with continuous endo-

Time after LPS-infusion (h)	0	1	4
Amount of PMN endotoxin positive (%)	39.5	50.6	71.7
Amount of MØs endotoxin positive (%)	16.7	48.2	54.6
Amount of LYMPH endotoxin positive (%)	20.2	51.1	51.6
Mean fluorescence of PMN	23.7	49.8	37.9
Mean fluorescence of MØs	10.3	19.5	146.0
Mean fluorescence of LYMPH	1.9	26.1	91.1

toxin infusion endotoxin internalization increases gradually. Initially the PMNs show the highest activity and a small increase thereafter. In contrast the MØs revealed a more than 10 times higher activity after 4 hours of the experiment.

With our new specific endotoxin test protocol it might well be possible in the future to evaluate the different responses of LPS as it finds its way to different surface domains or intracellular components in different cell populations, respectively.

**P54 Increased concentrations of procollagen type III peptide in the evolution of septic phenomenon. An indicator of organ damage and fibrinogenesis? (Preliminary data results)**

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The systemic response to infection is defined as septic phenomenon. By its definition is a generalized inflammatory process and during its progression every organ and system can potentially be impaired. Its progression is associated with and mediated by the activation of a number of host defense mechanisms (cytokine networks, activation of leukocytes, etc) and is characterized by many organ damages mediated by this 'whole body inflammation'. Procollagen type III peptide (PIIIP), as marker of collagen type III biosynthesis and turnover, directly indicates collagen synthesis and seems to be a good marker of many fibrosing, destructive or healing processes. However, serum concentrations of PIIIP have never been systematically measured in patients with graded sepsis We hypothesized that procollagen type III peptide serum levels might be also of value in estimating the 'whole body inflammation and damage' appeared in sepsis. This study was undertaken to test the aforementioned hypothesis. We measured, by a commercially available radioimmunoassay (ELISA) technique, the serum procollagen

type III peptide levels of 51 septic patients (pts) (22 pts with sepsis [group G1], 12 severe sepsis pts [group G2], 17 pts with septic shock [group G3]) and we compared them with the findings of 12 healthy controls (group H). The definition of the stages of sepsis followed the criteria established by the ACCP/SCCM consensus conference (August 1992). We use one-way ANOVA to compare the results from sepsis, severe sepsis and septic shock patients with the ones from healthy controls. Procollagen type III peptide serum levels was markedly increased during the septic process: group H  $3.7 \pm 0.2 \mu\text{g/ml}$ , group G1  $10.1 \pm 1 \mu\text{g/ml}$ , group G2  $30 \pm 6.2 \mu\text{g/ml}$ , group G3  $34 \pm 8.1 \mu\text{g/ml}$  ( $P < 0.005$  – one-way ANOVA), and was to be of statistically significant value when group H and group G1 compared with group G3 ( $P < 0.05$  and  $P < 0.005$  respectively) (Scheffe test for the *post hoc* comparisons of means). We conclude that PIIIP serum levels increased in parallel with the increasing severity of septic process, probably being a good indicator of tissue inflammation, damage, and fibrogenesis.

**P55 Endotoxemia induced MCP-1 expression in the intestinal muscularis causes leucocyte infiltration that mediates smooth muscle dysfunction**

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**Background:** Endotoxemia causes a molecular and leukocytic inflammatory response with the intestinal muscularis, which is associated with an inhibition of gastrointestinal motility. The network of resident macrophages seems to play a major role as an initiator of this cascade. We hypothesize that these resident cells evoke the extravasation of immunocompetent leucocytes in the

intestinal muscularis through the release of chemotactic cytokines (eg MCP-1).

**Methods:** Endotoxemia was induced in ACI rats by a single intraperitoneal injection of lipopolysaccharide (LPS: 15 mg/kg). Animals were treated with LPS, LPS + non-specific antibody or LPS + MCP-1 anti-



age of Th2 cells did not show significant change in all patients. The significant reduction of Th1 cells and monocytic HLA-DR expression in ICU patients except for acute interstitial pneumonia (AIP)

indicates that major stress results in immunoparalysis. Two AIP patients who revealed more than 40% of Th1 cells were tried to immunomodulation by methylprednisolone administration.

**P58 Differential diagnosis of Th1/Th2-response by T-cell and monocyte function between sepsis and non-infectious SIRS via flowcytometry**

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**Objective:** Under systemic inflammatory response syndrome (SIRS), a change in Th1/Th2-response by T-cell and a defect in monocyte function is observed, which may lead a derangement of immunological homeostasis, associated with immunosuppression and susceptibility to sepsis. We have recently developed an immune-inflammatory monitoring system, that can detect a constitutional change in Th1/Th2-population of T-cell subsets and monokine production by monocyte, via multi-parameter flowcytometry. The aim of this study was to investigate whether these tests were useful in establishing the difference between septic SIRS and non-septic SIRS.

**Patients and methods:** In the septic SIRS group, 11 patients with sepsis followed by organ dysfunction were studied on admission to ICU in our hospital. In the non-septic SIRS group, 10 patients who underwent major elective surgery were studied on the first and third day after operation. We investigated the cytokine expression of T-cells after activation by ionomycin and PMA, and the expression of monokine and HLA-DR antigen by monocytes after being stimulated with LPS and/or IFN-gamma, using whole blood culture (6 hours). After stain for cell-surface phenotypes, the cells were fixed and permeabilized, then fluoro-immunostained for intracellular

IFN-gamma, IL-4 in T-cells, and TNF, IL-6, and IL-12 in monocytes. The frequencies of these cytokines-producing cells were estimated with multicolor flowcytometric analysis.

**Results:** 1) The number of IL-4 producing cells (Th2) in T-cells increased significantly both in CD4+ and CD8+ subsets in patients with sepsis, but not in patients with non-septic SIRS. While the IFN-gamma producing cells (Th1) increased slightly in patients with sepsis and non-septic SIRS. 2) The production of IL-6, TNF, IL-12 by monocytes from patients with sepsis and non-septic SIRS was significantly decreased, together with a reduction of HLA-DR expression. Afterwards, the defect of TNF and IL-12 production in monocytes from non-septic SIRS patients recovered by the third postoperative day.

**Conclusion:** These findings show a significant shift of Th2 response in T-cell subsets and a prolonged reduction of TNF and IL-12 production with a reduced HLA-DR expression by monocyte in sepsis, compared with those in non-septic SIRS. These tests may be available for the differentiation of immunosuppression subsequent to sepsis from the SIRS with a dominant pro-inflammatory state.

**Table**

		CD4+		CD8+		CD14+	Mo	TNF	IL-12
		IFN	IL-4	IFN	IL-4	HLA-DR	IL-6		
Control		9.7 ± 1.5	2.7 ± 0.6	25.4 ± 4.6	1.6 ± 0.3	96.1 ± 0.4	76.7 ± 4.7	71.6 ± 3.7	18.8 ± 1.6
Sepsis		13.8 ± 1.7	8.2 ± 1.5*	37.1 ± 6.6	7.3 ± 1.2*	35.8 ± 5.6*	31.5 ± 7.4*	17.7 ± 5.6*	9.3 ± 1.4*
Non-septic	D + 1	10.9 ± 2.1	3.2 ± 0.8	36.4 ± 6.4	3.4 ± 1.0	42.9 ± 5.1*	39.2 ± 5.5*	29.5 ± 3.7*	10.0 ± 1.5*
SIRS	D + 3	13.0 ± 2.6	3.5 ± 1.1	32.7 ± 6.3	4.6 ± 0.9	56.3 ± 7.5	53.1 ± 9.6	32.9 ± 7.6*	21.1 ± 3.6

\* P < 0.01 vs healthy control by one-factor ANOVA.

**P59 T-cell-subpopulations in septic patients**

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**Introduction:** The dysfunction of the immune system is a main problem during the systemic inflammation. T-Lymphocytes are responsible for the different detection of antigens and the correct answer related to pathogens. Different T-cell function was described in the TH1/TH2 concept in these patients with changes in the cytokine pattern of the subpopulation of CD4+-T-cells during sepsis. These results have shown the important part of CD4+ cells during the development of immune dysfunction and paralysis. A second subpopulation of T-cells are the cytotoxic (CD8+) cells. To determine the changes in CD4+/CD8+ subpopulation, the present study investigated the relationship between these T-cells in septic patients.

**Methods:** Ten patients with sepsis of an Internal Intensive Care Unit, University hospital, were included and compared to 10 healthy controls. The severity of the disease was assessed at the APACHE II and SOFA-score. Also were measured the serum concentration of the C-reactive protein, procalcitonin, TNF-alpha and interleucin-6. Levels of CD4 and CD8-expression were analysed flow cytometrically *ex vivo* and after stimulation with PMA at day 1, day 7 and day 14 in culture (proliferation index).

**Results:** There was a significant difference in the CD4/CD8-ratio between septic patients and healthy controls (P < 0.05) *ex vivo*



MAP levels of group 2 and group 4 were higher than group 1 and group 3 at 120th and 180th minutes ( $P < 0.05$ ). HR levels of group 2 were lower than the other groups at 120th and 180th minutes ( $P < 0.05$ ). PaO<sub>2</sub> levels of group 1 were higher than the other groups at 180th minute ( $P < 0.001$ ). There was no significant difference between four groups regarding PaCO<sub>2</sub>, pH.

In conclusion, IT and IV lidocaine (2 mg/kg) given after 5 min of HCl application had a beneficial effect on the haemodynamic and arterial blood gas values in acute lung injury in rabbits model.

**P62 Heparin nebulization attenuates acute lung injury with sepsis after smoke inhalation in sheep**

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**Introduction:** Fibrin formation in the airway is a common occurrence with acute lung injury. Mucous plugging in the airway prevents alveoli expansion and may increase shunt blood flow. The aim of this study was to investigate the effect of heparin nebulization in acute lung injury (ALI) with sepsis or burn after smoke inhalation in sheep.

scored from 0 (non) to 4 (severe) and total score was calculated (full score = 16).

**Results:** In sepsis study, the drop in PaO<sub>2</sub>/FIO<sub>2</sub> was significantly attenuated by a heparin while it was not in burn study. The lung histology score was also attenuated by heparin in sepsis but not in burn.

**Method:** Female sheep ( $n = 20$ ) were used. The animals were divided into two groups. One is an ALI model induced by a combination injury with smoke inhalation and severe pneumonia ( $n = 10$ ). The other is an ALI model induced by a combination injury with smoke inhalation and 3rd degree 40% body surface area flame burn ( $n = 10$ ). The preceding groups received 48 breaths of cotton smoke ( $< 40^{\circ}\text{C}$ ). The sham control animals were not injured, *Ps. aeruginosa* ( $5 \times 10^{11}$  CFU) was inoculated into the airway using a bronchoscope. All the animals were mechanically ventilated after the injury. Burned animals were resuscitated with lactate Ringer's solution following the Parkland formula. Both groups were divided into two. One was treated with heparin nebulization ( $n = 5$ ; 10,000 U 1 h after the injury and every 4 hours) and the other were treated with the same dose of 0.9% NaCl as a control. Lung histology was scored by a pathologist who was blinded for the animal grouping. Congestion, edema, inflammation, and hemorrhage were

**Histology score**

Treatment	Burn & smoke	Smoke & pneumonia
Sham control	2.60 ± 0.60	2.70 ± 0.49
Saline nebulization	6.62 ± 1.00	9.46 ± 2.33*
Heparin nebulization	6.95 ± 1.67	5.82 ± 0.90†

\*  $P < 0.05$  vs sham. †  $P < 0.05$  vs Saline-treated.

**Discussion and conclusion:** Heparin nebulization was effective in reducing acute lung injury induced by severe pneumonia and smoke inhalation but not in burn and smoke inhalation. Since heparin does not inhibit thrombin without antithrombin, the result suggests that antithrombin level in the alveolar space, which is exuded from a bronchial blood flow, may be different.

**P63 Reduced release of superoxide from isolated human neutrophils in response to high extracellular glucose**

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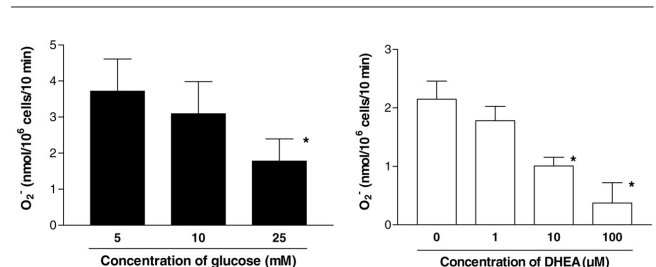
**Background:** Superoxide (O<sub>2</sub><sup>-</sup>) – a key anti-microbial agent in phagocytes – is produced by the activity of NADPH oxidase. High concentrations of glucose may reduce O<sub>2</sub><sup>-</sup> production through inhibition of glucose-6-phosphate dehydrogenase (G6PD) [1], which catalyzes the formation of NADPH.

**Aims:** To measure the acute effects of high glucose or the G6PD inhibitor, dehydroepiandrosterone (DHEA), on release of O<sub>2</sub><sup>-</sup> from isolated human neutrophils.

**Methods:** Neutrophils were isolated from peripheral blood of healthy subjects by gradient centrifugation and incubated for 1 hour in Krebs-Ringer buffer containing 5, 10 or 25 mM glucose, 5 mM glucose with 0, 5 or 20 mM mannitol or 5 mM glucose with 1, 10 or 100 μM DHEA at 37°C. *N*-Formyl-methionyl-leucyl-phenylalanine (fMLP)-induced O<sub>2</sub><sup>-</sup> release was measured by superoxide dismutase-inhibitable reduction of cytochrome *c* or luminol-enhanced luminescence. Scavenging of O<sub>2</sub><sup>-</sup> by glucose or DHEA was assessed by the pyrogallol assay [2].

**Results:** Incubation with glucose or DHEA, but not glucose/mannitol, dose-dependently reduced fMLP-induced release of O<sub>2</sub><sup>-</sup> as

**Figure 1**



Superoxide release from fMLP-activated neutrophils – effect of high glucose or DHEA. Note: Mean (± SEM;  $n = 6$ ) O<sub>2</sub><sup>-</sup> release. \*  $P < 0.01$  compared with 5 mM glucose or absence of DHEA (paired *t*-test).

detected by either method. In a cell free system, neither glucose nor DHEA scavenged O<sub>2</sub><sup>-</sup>.

**Conclusions:** Inhibition of G6PD may be the cause of acutely reduced O<sub>2</sub><sup>-</sup> release from activated neutrophils in response to high



**Methods:** Ten anaesthetised, and multi-catheterised pigs (20.6 ± 1.3 kg) were investigated over a period of 8 h. Sepsis was induced by fecal peritonitis. Animals were infused using 6% hydroxyethyl starch 200/0.5 to maintain a CVP of 12 mmHg. In kidneys biopsies TCC deposition was detected immunohistologically. Plasma levels of TCC were measured in a double antibody EIA using the neopeptide-specific MoAb aE11 as catching antibody. Albumin escape rate (AER; tc 99m-labeled albumin), serum protein (S-Protein), and hematocrit (Hct) were determined. After verifying normal data distribution (skewness < 1.5) Student's *t*-test was performed by rank-ordered stepwise testing. Data are mean ± SD.

**Results:** Septic animals showed marked renal deposition of TCC. Other results, see Table.

**Conclusion:** Although plasma levels of TCC declined over study period, in septic animals marked renal depositions of TCC indicated complement activation. Since AER increased and serum protein levels decreased, capillary loss of TCC into organ tissue may explain our findings in part. We conclude that in septic shock with substantial CLS plasma levels of TCC may not reflect degree of complement activation.

**Reference:**

1. Nuijens JH *et al: Blood* 1988, **72**:1841–1848.

**Table**

	Baseline		4 h		8 h	
	Sepsis	Control	Sepsis	Control	Sepsis	Control
TCC (%)	104 ± 40	118 ± 37	22 ± 29*	58 ± 11*	16 ± 31*	20 ± 22*
S-Protein (g/l)	43 ± 4	42 ± 2	13 ± 2**	26 ± 9*	9 ± 1**	22 ± 4
AER (%)			39 ± 16*	5 ± 5	52 ± 26*	3 ± 10
Hct (%)	29 ± 1	29 ± 2	30 ± 5	25 ± 3*	29 ± 3*	26 ± 1

\* *P* < 0.05 compared with baseline. † *P* < 0.05 compared with control group.

**P67 Peaks in G-CSF serum concentrations are accompanied by an increase in phagocytotic activity in most patients with severe sepsis or septic shock**

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**Objectives:** To investigate the relationship between endogenous serum concentrations of granulocyte colony stimulating factor (G-CSF) and phagocytotic activity of granulocytes during septic shock in postoperative/post-traumatic patients.

**Methods:** Over a 6 month period 35 patients with proven infection and severe sepsis or septic shock for at least 3 days' duration were monitored on a daily basis during their stay in the intensive care unit (ICU) until discharge from the ICU or death. In 19 out of these 35 patients one or more peaks in G-CSF serum concentrations occurred. Eleven of these 19 patients survived, eight patients died. A longitudinal analysis of G-CSF serum concentrations, phagocytotic activity of granulocytes and surface expression of monomeric Fc receptor type I (CD64, FcγRI) on granulocytes was performed by ELISA technique (R&D Systems, Minneapolis, MN, USA) and flow cytometry (Phagotest™; Orpegen, Heidelberg, Germany) and CD64 (clone 22; Immunotech, Krefeld, Germany), respectively on a daily basis.

**Results:** A G-CSF peak was defined as an increase of at least 30% from one day to the other, followed by a decrease of at least 15% on the next day. The following results are expressed as median (min – max) values. In seven episodes there was a parallel course of the G-CSF peak and phagocytosis with an increase in phagocytosis by 37% (6–50%). In 11 episodes, phagocytosis continuously increased and remained on a higher level after the increase of 10% (1–164%) from day 1 up to day 2. In 10 episodes, there was a decrease by 40% (17–76%) at the day of the G-CSF peak, followed by an increase by 58% (6–322%) on the next day. In 12 episodes, there was no increase (*n* = 4) or even a decrease (*n* = 8) by 24% (3–46%) over all days.

**Conclusions:** A peak in G-CSF serum concentration was followed by a continuous increase in phagocytosis at the same day in 7, and a delayed increase in 21 out of 40 episodes, but no increase or even a decrease in 12 out of 40 episodes. Thus, phagocytotic activity is increased when G-CSF peaks endogenously, in most patients with severe sepsis or septic shock.

**P68 Influence of GM-CSF supplementation on PaO<sub>2</sub>/FiO<sub>2</sub> index in septic patients**

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**Introduction:** Granulocyte-Macrophage Colony-Stimulating Factor (rHuGM-CSF) is used in leucopenic febrile patients to enhance leukocyte production. It can prime resting monocytes and augment

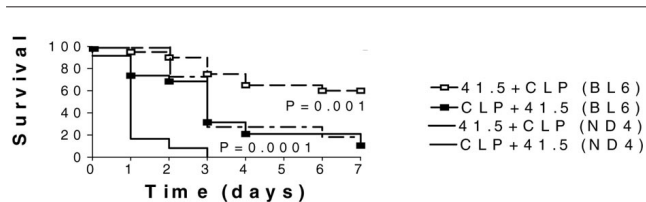
their inflammatory response [1]. It strongly up-regulates HLA-DR expression, LPS induced TNF-α monocyte secretion and down-regulates anti-inflammatory cytokines release [1].



In pilot studies to calibrate the murine HSR, 20–25 g ND4 mice were anesthetized and immersed in a water bath for a total of 20 min to raise core body temperature to 37, 40 or 41.5°C ( $n = 3$  per group). Livers were harvested 24 hours later. Western blot analyses for Heat Shock Protein-72 (HSP-72, a widely-accepted marker of HSR) showed the expression of HSP-72 at 41.5°C for 20 min but not at or below 40°C. This pattern is strain independent.

Next, the effect of HSR prior to or subsequent to cecal ligation and puncture via halothane anesthetic (CLP) upon survival was tested. 20–25 g male inbred C57-BL6 mice were randomized to one of six groups ( $n = 15–20$  per group) and heated for 20 min to either 37 or 41.5°C alone or in combination with CLP. Survival was 70% and 15% for HSR induction prior, or subsequent, to CLP respectively ( $P = 0.001$ ). To exclude the possibility that the order-dependent response was strain specific, the study was repeated with outbred ND4 mice ( $n = 11–13$  per group). In the ND4 mice, survival for HSR induction prior to CLP was 25% but following CLP was nil ( $P = 0.0001$ , Fig. 1).

Figure 1



Though beneficial and somehow protective when induced prior to insult, the heat shock response paradoxically increases mortality when activated after severe stress. This paradoxical potentiation of injury also appears independent of the specific strain. The susceptibility of infected animals to devastating HSR at 41.5 degrees may explain, at least in part, why human fevers are generally self-limited to 40 degrees or less.

P71 The influence of endotoxin on the expression of the ORL-1 receptor

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**Objective:** The ORL-1 receptor (Orphan opioid receptor) has been discovered recently and is involved in pain perception and immune function [1–3]. The regulation of the ORL-1 receptor in patients with systemic inflammation has not been elucidated yet. This study investigates the influence of different doses of LPS on ORL-1 expression in peripheral blood cells *ex vivo*.

**Methods:** Human whole blood from healthy volunteers was cultured at 37°C and 5% CO<sub>2</sub> without LPS or LPS 0.1 ng, 10 ng and 100 ng/ml for 3, 6, 12 and 24 hours. Reverse transcriptase polymerase chain reaction (rt-PCR) using specific primers was performed and RNA contents was estimated by semiquantitative analysis employing a housekeeping gene as internal standard. Southern blot analysis and hybridisation to a specific DIG-labeled probe confirmed the identity of the ORL-1 transcripts.

**Statistics:** Mean ± SEM, repeated measures ANOVA.

**Results:** ORL-1 receptor was expressed constitutively in human peripheral blood cells. Mean baseline expression resulted in a ratio of ORL/GAPDH of 1.0 ± 0.07. Semiquantitative rt-PCR revealed a dose and time dependent down regulation of ORL-1 expression ( $P < 0.05$ ). Incubation with LPS 0.1 ng/ml decreased the ratio ORL/GAPDH from 0.95 ± 0.06 at 3 hours to 0.19 ± 0.02 at 24 hours. In contrast, incubation with LPS 100 ng/ml already suppressed the ORL-1 message after 3 hours of incubation. Southern blot analysis and hybridisation proved the specificity of the amplified PCR products for ORL-1 transcripts.

**Conclusions:** Endotoxin decreased ORL-1 expression in human peripheral blood cells. The results suggest that the ORL-1 receptor is involved in immune response to infection.

References:

1. *J Neuroimmunol* 1998, **81**:184.
2. *BJA* 1998, **80**:577.
3. *Mol Brain Res* 1995, **32**:342.

P72 Influence of endotoxin adsorption to immunity

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The influence of direct hemoperfusion using polymyxin B immobilized fiber (PMX) to immunity was studied in severe septic patients with organ dysfunction. Thirty-four cases whose mean age and APACHE II were 59 years and 23 were treated by the PMX in 50 times. They were divided into the detectable ( $\geq 10$  pg/ml,  $n = 27$ ) and non-detectable ( $n = 23$ ) endotoxin group, analyzed before PMX by colorimetric limulus test with chromogenic substrate (Toxicolor). After PMX, mean arterial pressure and systemic vascular resistance index were significantly increased in both groups. Endotoxin, neutrophils and monocytes were significantly decreased from 76.4 ± 19.5 to 64.8 ± 17.8 pg/ml ( $P = 0.0158$ ), from 14810 ± 2020 to

9990 ± 1660/mm<sup>3</sup> ( $P = 0.0002$ ), and from 688 ± 103 to 512 ± 99/mm<sup>3</sup> ( $P = 0.0087$ ) respectively in the D group, while lymphocytes were decreased not significantly in both groups. Furthermore IL-6 was significantly decreased from 958 ± 437 to 722 ± 296 pg/ml ( $n = 37$ ,  $P = 0.0495$ ), IL-8 and CD4 were significantly increased from 162 ± 80 to 195 ± 114 pg/ml ( $n = 31$ ,  $P = 0.0456$ ) and from 31 ± 4 to 34 ± 3% ( $n = 14$ ,  $P = 0.0091$ ) respectively, but TNF $\alpha$  and IL-1 $\beta$  did not change significantly. These results indicated that the therapy with PMX in severe sepsis could be going to end the response of innate immunity and induce the adaptive immunity, so that it would be helpful for hemodynamic stability.



**P75 Dexamethasone effect on sFas/sFas ligand following cardiopulmonary bypass**

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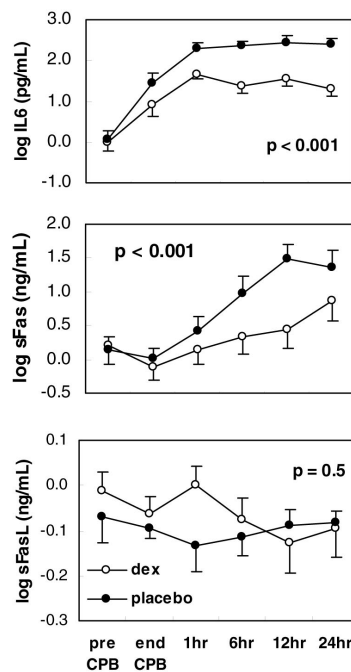
**Introduction:** Steroids decrease systemic inflammation following cardiopulmonary bypass (CPB). Membrane bound Fas is a receptor found on many cells, which stimulates apoptosis when cleaved by Fas ligand (FasL). FasL also has a proinflammatory role and is released following ischaemia-reperfusion. We wished to investigate the time course of release of the soluble forms of Fas and FasL (sFas, sFasL) post CPB, and whether steroid pre-treatment altered the response.

**Method:** Twenty-seven children with congenital heart disease were studied, median (IQ) age 7 (0.4–10) months. Patients were given 0.25 mg/kg dexamethasone (DEX) ( $n = 13$ ) or no DEX ( $n = 14$ ) at induction of anaesthesia. Groups were well matched in terms of age, type of operation, length of CPB, cross clamp, and circulatory arrest (all  $P > 0.15$ ). sFas, sFasL and interleukin (IL) 6 (a marker of cytokine response) were measured over 24 hours by double sandwich ELISA.

**Results:** DEX significantly blunted the release of IL6 and sFas, but not sFasL. The DEX group exhibited a decreased clinical inflammatory response post CPB as evidenced by a lower temperature, less colloid requirement, chest drain loss, acidosis, hyperlactataemia and coagulopathy (all  $P < 0.05$ ).

**Conclusion:** DEX blunts IL6 and sFas but not sFasL release following CPB, attenuating clinical inflammatory response. The significance of the sFas response is unclear; this may be a passive marker of a decreased inflammatory response but decreased levels may also negatively influence apoptosis/inflammation by being less able to 'mop-up' excess membrane and soluble FasL.

**Figure**



**P76 Moderate hypothermia during cardiac surgery provides hepatic protection by modifying the balance between gene expression of TNF $\alpha$  and IL10**

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**Aims:** To investigate the effect of moderate hypothermia during CPB on intrahepatic gene expression of TNF $\alpha$ , IL10, apoptosis regulatory proteins (Fas, Bak and Bcl-xL) and hepatic cell death during and after cardiac surgery.

**Methods:** Pigs were assigned to a temperature ( $T^{\circ}$ ) group during standardized cardiopulmonary bypass (CPB): normothermia ( $T^{\circ}$ , 37°C;  $n = 8$ ) and moderate hypothermia ( $T^{\circ}$ , 28°C;  $n = 8$ ). Liver probes were taken before and 6 hours after CPB for standard and immunohistological examinations. Apoptotic cells were detected by TUNEL-staining. Intrahepatic gene expression of TNF $\alpha$ , IL10 and of apoptosis regulating proteins were examined by competitive RT-PCR.

**Results:** Gene expression of cytokine and apoptosis regulating proteins was not detected before but 6 hours after CPB. Pigs operated on under 28°C showed lower TNF $\alpha$ -mRNA and higher IL10-mRNA than those operated on under 37°C ( $P < 0.05$ ). While expression of apoptosis regulatory proteins and percentage of apoptotic hepatocytes were similar in both groups, percentage of necrotic hepatocytes was lower in 28°C than in 37°C group ( $P < 0.05$ ). TNF $\alpha$ -mRNA after CPB was correlated with the percentage of necrotic hepatocytes ( $P < 0.05$ ).

**Conclusions:** Moderate hypothermia during CPB provides hepatic protection by increasing IL10- and decreasing intrahepatic TNF $\alpha$ -gene expression without affecting gene expression of apoptosis regulatory proteins.



used an overcoated double luminal drain. The tube consisted of an outer big with many side pores containing an inner small drain and the tip of the inner drain was kept its site never extended the tip of the outer drain. We aspirate this overcoated drain with maximum negative high pressure of central aspirating system. Mucinous infectious fluid was aspirated with air. We evaluate the clinical course of the patients, condition of the infectious space, volume of aspirate, the number of dressing change.

**Results and discussion:** Fourteen patients were examined. We could (1) keep infectious spaces, (2) keep the skin around infec-

tious space intact resulting in good and rapid healing, (3) exactly evaluate the volume of aspirated fluid, that made it easy to evaluate the healing course, (4) save the number of dressing change resulting in saving the cost.

**Conclusions:** Overcoated double luminal drainage is useful for aspirating mucinous infectious fluid effectively, for keeping the infectious space dry, for reducing the infectious space, and consequently for preventing abdominal sepsis.

**P80 Catheter-related infections (CRI) after guidewire exchange of subclavian catheters compared to CRI after direct placement of the catheter**

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**Objective:** To compare CRI rate after guidewire exchange of subclavian catheters for suspected CRI with the rate observed after direct placement.

**Study design:** Prospective controlled study.

**Patients and methods:** All subclavian catheters placed consecutively in 202 adult ICU patients, from Oct 1999 to Nov 2000, were included. Maximum barrier precautions were used during insertion. Catheter placement, and catheter site care were made according to the recommendations for the prevention of nosocomial intravascular device-related infections. All catheters were left in place until no longer needed or until there was evidence of phlebitis, malfunction or if CRI was suspected. If a new central catheter was still needed, the catheter was exchanged over a guidewire (GWE catheter), unless there was evidence of phlebitis, inflammation at the catheter insertion point or if the previous catheter changed over a guidewire was colonized, in which case a new anatomical site was used (NSI catheter). After removal of the catheter, the tips were processed according to the Maki semiquantitative method.

Catheter colonization, exit-site infection, catheter related blood stream infection (CR-BSI) were defined according to the guidelines for prevention of intravascular device-related infections.

**Results:** We analysed 423 subclavian catheters (258 NSI and 165 GWE) from a total of 530 inserted (333 NSI and 197GWE). Hundred and seven catheters (74 NSI and 33 GWE), were not included in the study. They were lost to further analysis because either the patient left the ICU with the catheter in place (90), or there were missing data (accidents at the time of removal 10, other 7). Duration of catheterisation was 7.5 ± 4 days for NSI vs 6 ± 4.4 days for GWE catheters (*P* < 0.05). There were 17 CR-BSI in the NSI catheters (8.8/1000 catheter-days) vs 14 in the GWE (14.1/1000 catheter days) (*P* > 0.1). Thirty-one NSI catheters were colonized vs 36 GWE (*P* < 0.05).

**Conclusions:** Exchange of the subclavian catheters over guidewire was not associated with higher CR-BSI compared to catheters placed directly. A higher rate of colonisation was however observed in the GWE catheters.

**P81 Low dose pentoxifylline (PTX) reduces mortality in an animal model of acute hepatic and multi-organ failure**

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**Introduction:** Pentoxifylline inhibits, release of TNF-α, platelet aggregation and adherence of leukocytes to endothelium. Previous studies report increased mortality following its use.

**Methods:** AHF is induced by two intraperitoneal (i.p.) injections (500 mg/kg 8 hours apart) of TAA. Four groups were studied (*n* = 5). Group 1 received TAA only. Groups 2, 3, & 4 followed the protocol for Group 1, however, Groups 2 and 3 were pre-treated for 5 days with once daily high dose PTX (300 mg/kg i.p.) and low dose

PTX (25 mg/kg i.p.), respectively. Whereas, Group 4, commenced PTX (25 mg/kg i.p.) post-TAA for 5 days. Mortality was determined at 96 hours in separate groups (*n* = 5).

**Results:** See Table.

**Conclusion:** Pre-treatment with low dose PTX reduces hepatic injury, multi-organ failure and mortality.

Hours	AST (iu/l)		PT (s)		Ammonia (µg/ml)		Lactate (mmol/l)		Mortality (%)
	24	72	24	72	24	72	24	72	96
G1-TAA	1553 ± 343	4512 ± 501	26 ± 3	121 ± 12	58 ± 8	134 ± 12	2.6 ± 1.2	6.3 ± 0.4	75
G2-PTX 300 mg/kg	2065 ± 330	5221 ± 528	>121*	>121	117 ± 34*	153 ± 13	3.9 ± 0.5	7.8 ± 0.6	100*
G3-PTX 25 mg/kg	1177 ± 177	2021 ± 43*	23 ± 4	101 ± 13	71.4 ± 9	70.2 ± 10*	3.5 ± 0.1	4.6 ± 0.2*	40*
G4-Post PTX 25 mg/kg	2161 ± 166	5014 ± 299	>121	>121	121 ± 8*	156 ± 12	4.7 ± 0.6*	7.4 ± 0.8	100*

\* *P* < 0.05, mean ± SD.



randomization, patients were stratified by the results of a rapid semiquantitative test (Septest) measuring serum IL-6 levels. A positive (+) Septest indicates elevated IL-6 levels. An aggregate MOD score  $\geq 9$  defines significant multiorgan dysfunction syndrome. Mean baseline score, percent patients with score  $\geq 9$ , and the strength of the agreement of each component of the aggregate MOD score were compared in the groups of patients Septest (+) and (-) at baseline. The difference (delta) between the percent of Septest (+) and (-) patients with the highest scores for each component of the MOD score was used to test the strength of agreement between IL-6 levels and each organ system component of the aggregate MOD score.

**Results:** A total of 2634 patients were enrolled. 998 (37.9%) had elevated IL-6 levels and 1636 (62.1%) did not. Baseline mean MOD score was higher in Septest (+) patients compared to Septest (-) patients, 8.77 vs 6.64 ( $P < 0.001$ ), respectively. Baseline aggregate MOD score  $\geq 9$  was found in 52% of Septest (+) versus 28% test (-) patients. The cardiovascular, neurologic and respiratory components of the MOD score appeared to show the best agreement with baseline IL-6 levels.

Organ systems components of MOD score	Septest (+) percent pts with highest score	Septest (-) percent pts with highest score	Delta
Cardiovascular	14.8	4.6	10.2
Neurologic	27.4	18.5	8.9
Respiratory	9.8	3.1	6.7
Renal	6.2	4.3	1.9
Hematologic	2.4	1.1	1.3
Hepatic	1.6	1.5	0.1

**Conclusion:** Despite lack of strong agreement between certain organ system components of the MOD score, the aggregate MOD score and Septest strongly agree at baseline. By inference, therefore, the results suggest that the Septest might also be a useful marker for ICU mortality.

**Reference:**

1. *Crit Care Med* 1995, 23:1638.

**P85 Baseline characteristics of patients with and without hypercoaguable sepsis and the effect of afelimomab on mortality: a post hoc analysis from the MONARCS trial**

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Tumor necrosis factor (TNF) $\alpha$  may modulate clot-promoting and inhibiting pathways, and have potentially important roles in disseminated intravascular coagulation (DIC).

**Purpose:** 1) To determine if differences in baseline characteristics exist between patients with and without hypercoaguable sepsis, and 2) to explore the effect of afelimomab (an anti-TNF $\alpha$  antibody) on mortality of hypercoaguable and non-hypercoaguable septic patients.

**Methods:** A post hoc analysis identified patients with a hypercoaguable state in the overall population enrolled in a large placebo-controlled sepsis trial investigating the safety and efficacy of afelimomab. A hypercoaguable state was defined by (1) platelet count below 140,000 per  $\mu$ l plus (2) D-dimer  $> 250$  ng/ml. Patients were randomized to receive placebo or afelimomab.

**Results:** A total of 2634 patients were enrolled, and 1313 (49.8%) had baseline determinations of both platelets and D-dimer. The table describes the baseline characteristics of the two patient groups. Compared to those without laboratory evidence of consumption coagulopathy, patients with a hypercoagulable state had higher organ dysfunction scores, higher interleukin-6 levels and higher frequencies of positive blood cultures. Among the patients with evidence of consumption coagulopathy, 283 were treated with placebo and 311 with afelimomab. Mortality at 28 days was 43.8% vs 38.6% in placebo and afelimomab patients, respectively. In patients not meeting the definition of hypercoaguability, 376 and 343 received placebo and afelimomab; mortality was 35.9% and 26.5%, respectively.

**Table**

	Hypercoaguable state (n = 594)	Absence of hypercoaguable state (n = 719)
Mean age (SD)	57.9 (17.0)	60.1 (17.0)
Gender (M/F)	58.6% / 41.4%	61.6% / 38.4%
Shock	399 (67.2%)	504 (70.1%)
MOD score	9.1	6.3
Median interleukin-6 (pg/ml)	1360	908
Mean platelet count $\times 1000$ (SD)	81.7 (35.6)	231.4 (141.7)
Positive blood culture (%)	278 (46.8%)	226 (31.4%)
G (+) bacteria only (%)	185 (31.1%)	207 (28.8%)
G (-) bacteria only (%)	169 (28.5%)	177 (24.6%)
Mixed G (+) and G (-) (%)	65 (10.9%)	102 (14.2%)
Other or unknown (%)	175 (29.5%)	233 (32.4%)

**Conclusions:** Septic patients with evidence of consumption coagulopathy had more organ dysfunction and a higher rate of positive blood cultures. Afelimomab appears to be beneficial in reducing the mortality of septic patients with a hypercoaguable state.



**Purpose:** The objectives of this study are to (1) establish the proportion and cost of cultures obtained in the first 24 hours after acute burn injury that yield positive microbiological cultures and (2) determine the utility of pan-culturing for temperatures greater than 38.5°C in the first 24 hours following burn injury.

**Design:** Retrospective, computer-assisted chart review.

**Setting:** University-based burn center.

**Methods:** The records all burn injuries evaluated at the Burn Center or in the Emergency Department between 1/1997 and 1/1998 were retrospectively identified by ICD-9 release codes. Patients presenting with evidence of infection and pediatric burn patients were excluded. Data evaluated included: extent of burn injury, length of stay (LOS), documentation of initial cultures, culture results, and intervention/treatment.

**Results:** A total of 713 patients were identified. 598 charts met the inclusion criteria. 447 patients had LOS < 1 day and were primarily treated in the ED and discharged home. Wound cultures

were obtained for 42 (10%) of these patients. Thirty cultures (71%) had no significant growth. Twelve cultures (29%) grew mixed, common skin flora. No patients in this group were pan-cultured. No patients in this group required antibiotic treatment on the basis of culture results. A total of 151 patients were admitted to the Burn Center with an average LOS of 3.9 days (range 2–125 days). In this group, 45 patients (30%) had wound cultures and 24 patients (16%) were pan-cultured in the first 24 hours of admission. One patient with a deep, open abdominal burn grew enterococcus species from the initial wound culture and was treated with antibiotics. No other patients had antibiotics ordered on the basis of cultures.

**Conclusion:** Clinical management of the acute burn is not altered by the results of routine wound cultures and pan-cultures obtained in the first 24 hours of admission. Management of patients with deep, abdominal wounds with potential contamination from bowel flora may prove an exception. The cost for a wound culture and gram stain at this hospital is \$58.00 (US). Omitting initial cultures would result in potential savings of \$16,686.00 (US) and would not compromise the quality of patient care.

## P89 The utility of routine wound surveillance cultures in the management of burn injury

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**Purpose:** The objectives of this study are to establish the proportion and cost of surveillance cultures that yield a positive microbiological culture and to determine the influence of surveillance cultures in the ordering of antimicrobials.

**Design:** Retrospective, computer-assisted chart review.

**Setting:** University-based burn center.

**Methods:** The records of all burn injuries admitted to the Burn Service between Jan 1997 and Jan 1998 were retrospectively identified by ICD-9 release codes. Patients with length of stay less than 1 day, or who had a bed assignment other than in the burn center were excluded. Patients with at least one surveillance culture were included. Surveillance cultures were defined as cultures obtained on Wednesdays and Saturdays per Burn Center protocol. Data collected included: length of stay, extent of burn injury, documentation of surveillance culture results, documentation of signs and/or symptoms of cellulitis and intervention and treatment. A *P* value < 0.05 was considered statistically significant.

**Results:** 151 patients were identified. Eighty patients met the inclusion criteria. A total of 179 surveillance cultures were col-

lected. 89% (71/80) of study patients received antimicrobials during their hospital course and 82% (58/71) had clinical signs of cellulitis. 91% (53/58) of patients with clinical signs of cellulitis were treated with antimicrobials. Most of these patients (86%) received empirical antimicrobials for cellulitis, based solely on clinical judgment not on culture results. In only three cases (1.6%) were orders for antimicrobials initiated or changed on the basis of wound surveillance cultures. Patients with surveillance culture were significantly more likely to receive antimicrobials than those who were not cultured (39.6% vs 1.7% *P*=0.001). However, among those patients with surveillance cultures (*n* = 179), there were significantly more patients who did not receive any antimicrobials (60.3% vs 39.7% *P* = 0.001). There was no significant relationship between a positive or negative surveillance culture and orders for antimicrobials (*P* = 0.097).

**Conclusion:** The clinical management of burn wounds is not significantly altered by the results of routine surveillance wound cultures. The diagnosis of cellulitis is based on clinical judgment and treatment is initiated empirically. Omitting twice-weekly routine surveillance cultures would result in potential savings of \$25,550.00 (US) and would not compromise the quality of patient care.

## P90 Attributable mortality in critically ill patients with bacteremia involving methicillin susceptible (MSSA) and methicillin resistant *Staphylococcus aureus* (MRSA)

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**Background:** *Staphylococcus aureus* bacteremia carry high fatality rates. Outcome comparisons between MRSA and MSSA bacteremic patients are difficult to perform because of important differences in severity of illness.

**Methods:** In a retrospective study (01/1992–12/1998), attributable mortality for MSSA and MRSA bacteremia was investigated

and compared in critically ill patients. Two independent case-control studies were performed. Matching (1:2-ratio) was based upon APACHE II-score and admission diagnosis. As expected mortality can be derived from these two variables, this matching procedure resulted in an equal expected mortality rate for cases and controls. Attributable mortality is determined by subtracting the in-hospital mortality rate of the controls from the in-hospital mortality rate of the cases.



germs were isolated: 48% and 45% gram negative, 45% and 45% gram positive, 7% and 10% fungi. Most frequently germs reported in first period were: 15% *S. Aureus*, 12% Enterococci and 11% *E. Coli*; and second period were: 19% Epidermidis Staphylococci, 9% *S. Aureus* and 9% *E. coli*. The differences we found with EPIC are shown in the Table.

**Conclusions:** The antibiotic therapy policy with a patient-to-patient rotation can be useful for the control of infectious mape in ICU.

**Reference:**

1. Vincent JL *et al*: **Results of the European Prevalence of infection in Intensive Care (EPIC) Study.** *JAMA* 1995, 274:639–644.

**P93 Cefepime in critically ill patients: continuous infusion versus intermittent regimen**

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**Background:** Beta-lactams have a time-dependent bactericidal activity and the time above MIC ( $T > MIC$ ) is the best predictive factor of efficacy. The aim of this study was to compare the pharmacokinetic and pharmacodynamic parameters and the clinical efficacy of a continuous infusion of cefepime versus an intermittent regimen in critically ill adults patients with gram negative bacilli infection.

**Methods:** The prospective cross-over study was carried out in 34 patients with severe pneumonia ( $n = 26$ ) or bacteriemia ( $n = 8$ ). There were randomized to receive Cefepim 4 g per day either as a continuous infusion (Group 1,  $n = 17$ ) or intermittent administration 2 g x 2 (Group 2,  $n = 17$ ) in combination with amikacin 15 mg/kg/day in the two groups. Patients were significantly comparable in terms of age, sex, initial infection disease, IGS II score and MIC of gram negative bacilli isolated. Clinical outcomes: mechanical ventilation, ICU stay durations and clinical recovery were assessed along with pharmacokinetic (24-hour AUC, 12-hour AUC) and pharmacodynamic ( $T > MIC$  and  $T > 5 MICs$ ) in both

groups and compared (chi-squared and Mann–Whitney *U*-tests). Results with  $P < 0.05$  were considered significant.

**Results:** Mechanical ventilation, clinical recovery (13 vs 11), bacteriologic eradication (12 vs 10) and duration of stay in ICU (35 vs 38 days) were better in Group 1 but did not significantly differ between the two group. Neither did 24-hour AUC (569 vs 414) nor 12-hour AUC (218 vs 202). However,  $T > MIC$  in Group 1 ( $23.8 \pm 0.2$ ) was significantly higher ( $P < 0.05$ ) than in Group 2 ( $20.4 \pm 3$ ).  $T > 5 MICs$  in Group 1 ( $23.6 \pm 0.6$ ) was also very significantly higher ( $P < 0.01$ ) than in Group 2 ( $16.7 \pm 6$ ).

**Conclusion:** Clinical outcome was similar but our results indicate that continuous infusion likely provides a better steady bactericidal effect with concentration above MIC than intermittent administration, especially if there is a high risk of cephalosporinase as with Enterobacter spp. Further studies including more patients are necessary to confirm the interest of continuous infusion and to assess the possibility of reducing the daily dosage.

**P94 Leptospirosis and acute respiratory failure: report of 34 cases**

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**Introduction:** Leptospirosis is generally found in tropical regions but it can occur in temperate regions. It is caused by all kinds of leptospiras and it is, in general, a self limited disease. However, reports of important complications as acute respiratory failure (ARF), associated or not with other organic dysfunction had increased in the last years and had been associated with a high mortality rate [1].

**Objective:** The goal from this paper is to evaluate the clinical characteristics and the morbimortality of severe leptospirosis associated with ARF in two general ICU from two general hospitals.

**Methods:** All cases with the diagnosis of leptospirosis, confirmed by blood macroagglutination test, associated with ARF and admitted from January 1990 to October 2000, in two general ICU from two general hospitals, were studied. There were analyzed the clinical and laboratory characteristics, the associated organic dysfunction and the mortality rate. Survivors were compared with non-survivors. The quantitative variables have been compared by unpaired *t*-test and the qualitative variables by a chi-squared test. The level of significance was  $P < 0.05$ .

**Results:** We described 34 adults patients,  $39 \pm 16$  years, 28 men and 6 women. The most frequent clinical manifestation were

dyspnea ( $n = 32$ ), fever ( $n = 31$ ), myalgias ( $n = 29$ ), jaundice ( $n = 28$ ), hemoptysis ( $n = 25$ ) and cough ( $n = 25$ ). All patients showed ARF needing for mechanical ventilation ( $PaO_2/FIO_2 = 169 \pm 73$ , with diffuse pulmonary infiltrates in all cases) as well as some level of other organic dysfunction as hepatic ( $n = 26$ ), renal ( $n = 25$ ), cardiovascular ( $n = 22$ ), hematological ( $n = 20$ ) and neurological ( $n = 11$ ). The mortality rate was 53% ( $n = 18$ ). The comparison between non-survivors and survivors showed they were older ( $P < 0.05$ ) and had: 1) higher number of organic dysfunction, principally higher incidence of renal, cardiovascular and neurological failures ( $P < 0.05$ ); 2) higher levels of acidosis ( $P < 0.05$ ); 3) higher use of invasive mechanical ventilation and positive end-expiratory pressure ( $P < 0.05$ ).

**Conclusions:** In endemic regions leptospirosis has to be considered as a cause of ARF as well as a cause of other associated organic dysfunction. Leptospirosis associated with ARF has a high mortality rate mainly when associated with other organic failures.

**Reference:**

1. Ko AI, Reis MG, Dourado CMR, Johnson Jr WD, Riley LW, and the Salvador Leptospirosis Study Group: **Urban epidemic of severe leptospirosis in Brazil.** *Lancet* 1999, 354:820–825.



**Conclusions:** The occurrence of acute renal failure in malaria is an ominous event even when it occurs on its own. ARDS is however a serious complication which carries a high mortality. The combination of ARF together with ARDS has an almost universally fatal outcome.

APACHE II score, SOFA score and WHO criteria correlate closely with outcome.

**P97 Malaria and the HIV virus: is there any interaction?**

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**Objectives:** The aim of the study is to see if HIV influences the severity and outcome of Plasmodium Falciparum Malaria.

**Results:** See Tables.

**Design and methods:** This is a retrospective analysis of ICU records of patients admitted to the ICU at the Chris Hani Baragwanath Hospital between 1990 and 1999 with a confirmed diagnosis of malaria. 70 of the 152 patients had their HIV status defined, those were reviewed.

**Conclusions:** There is no interaction between HIV seropositivity and severe Plasmodium Falciparum Malaria. HIV status does not impact on severity of malaria. The incidence and outcome of Multiple Organ Failure related to Malaria is not significantly different in HIV infected patients.

**Table 1**

**Characteristics**

	HIV positive (n = 20)		HIV negative (n = 50)		P value
Male/female ratio	12 M	8 F	26 M	24 F	0.454
ICU stay (median/range)	4.5 days	1-16	5 days	0.5-37	> 0.10
Parasitaemia (median/range)	14.5%	1-50%	1%	< 1-71%	> 0.10
WHO criteria (median/range)	5.5	0-11	5	1-12	> 0.10
APACHE II (median/range)	16	10-29	17.5	6-38	> 0.10
Incidence of ARDS	3/20	15%	14/50	28%	0.278
Incidence of ARF	12/20	60%	26/50	52%	0.454
Incidence of ARDS & ARF	3/20	15%	12/50	12%	0.372

**Table 2**

**Outcome**

	HIV positive		HIV negative		P value
Overall mortality	8/20	40%	15/50	30%	0.375
Mortality of ARDS	3/3	100%	11/14	78%	0.571
Mortality of ARF	8/12	66%	13/26	50%	0.410
Mortality of ARDS & ARF	3/3	100%	10/12	83%	0.600

**P98 Undiagnosed tuberculosis as the reason of failure in treatment of critical care patients**

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Intensive treatment sometimes becomes unsuccessful due to diagnostics mistakes. Tuberculosis – one of the most serious diseases in Russia – also leads to critical status of patients. But in some of such patients tuberculosis remains undiagnosed. Purpose of present study was to analyse why not recognition of pulmonary tuberculosis became the reason of failure in treatment of critical care patients. Thirty-eight cases of patients (28 men and 10 women) treated in emergency departments of general practice hospitals of Tatarstan Republic, Russia, were investigated. Age of patients was from 42 to 77 years. Clinical diagnosis of pneumonia was in 86.8% of them, pleuritis of obscure etiology in 10.5% and one patient had clottage of mesenteric

blood vessels. Patients status at entering the hospitals was estimated as serious. Complaints to tussis with a sputum were in 89.5% cases. Average value of ESR was 17.3 mm/h, leukocytosis –  $16.2 \times 10^9/l$ . All patients received a complex intensive care. Patient with the surgical pathology was operated. But despite treatment there were not improvement in patients status, and 1-5 days after entering hospitals all patients died. Postmortem examination found out that the reason of failure in complex treatment of patients was undiagnosed pulmonary tuberculosis. Infiltration tuberculosis was in 14 patients, fibro-cavernous in 13 patients and disseminated tuberculosis in 11 patients. Analysis of that cases showed that radiography was done only to 36.8%



induced IL-8 production in three *in vitro* cellular systems. Citrated whole blood, human umbilical vein endothelial cells (HUVECs) and mononuclear cells (MNCs) were stimulated with LPS for 4–6 hours in the presence and absence of 0–40 IU/ml AT. IL-8 was measured by ELISA. In all three systems, AT dose-dependently inhibited IL-8 production, with greatest inhibition ( $98.7 \pm 5.2\%$  at 40 IU/ml) observed for the whole blood system and the least inhibition seen with MNCs ( $8.7 \pm 21.7\%$  at 40 IU/ml). RNA extraction of time

course whole blood experiment followed by the detection of mRNA specific for IL-8 showed that in the absence of AT, mRNA for IL-8 was apparent after 30 min incubation with LPS. However, the level of IL-8 mRNA was found to decrease with increasing concentrations of AT. These results imply the inhibition of IL-8 antigen production by AT is due to the suppression of mRNA and indicated that the anti-inflammatory activity of AT also extends to the inhibition of IL-8, an important cytokine implicated in neutrophil migration.

## P102 Distinct antithrombin III preparations deactivate IL-8-induced neutrophil chemotaxis with different potency

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**Background:** Neutrophil activation is a crucial step in the pathogenesis of sepsis and subsequent development of multiple organ failure. Antithrombin III (ATIII) exerts direct effects on neutrophils by inhibiting chemokine-induced migration. The positive outcome of animals in models of severe sepsis treated with ATIII may be due to this neutrophil-dependent action. The aim of the present study was to determine the potency of different ATIII preparations in inhibiting neutrophil chemotaxis compared to monoclonal antibody-purified ATIII.

**Methods:** Human neutrophils were isolated using standard preparation methods. Cell migration was tested in modified Boyden microchemotaxis chambers bearing nitrocellulose filters in the leading front assay. Human neutrophils were incubated with seven different ATIII preparations at various concentrations (1  $\mu$ U/ml to 5 IU/ml) for 20 min. Immuno-purified ATIII served as positive control. After washing twice, neutrophils migrated toward interleukin-8 (1 nM) for 30 min in humidified atmosphere at 37°C. After staining of the cells, migration depth was measured microscopically.

**Results:** At concentrations below 10 mIU, neutrophil chemotaxis toward interleukin-8 was decreased by the ATIII preparations with different potencies, whereas at higher concentrations (1 IU and 5 IU) no significant differences could be observed. Deactivation of neutrophil chemotaxis was most pronounced by Kybernin®P (Aventis Behring, Marburg, Germany) at 100  $\mu$ U and was comparable in potency to homologous deactivation with IL-8. The purified ATIII inhibited interleukin-8-induced chemotaxis at all concentrations tested (1  $\mu$ U to 5 IU).

**Conclusion:** We suggest that anti-inflammatory activity of ATIII may be due to deactivation of chemokine-induced leukocyte migration. Commercially available ATIII-preparations at distinct concentrations show significant differences in their ability to deactivate neutrophil chemotaxis toward interleukin-8. This may suggest also different activities *in vivo* depending on the various preparation procedures.

## P103 Specific deactivation of monocyte and lymphocyte migration by antithrombin III

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**Background:** Antithrombin III exerts direct effects on neutrophils by inhibiting chemokine-induced migration [1]. Whether ATIII directly affects the migratory behaviour of other types of leukocytes is unknown.

**Methods:** We investigated the effect of ATIII on spontaneous and chemokine-triggered migration using RANTES and interleukin-8 as attractants of lymphocytes, and RANTES and monocyte chemoattractant peptide-3 as attractants of monocytes, in modified Boyden chamber micropore filter assays. Lymphocyte and monocyte populations from human peripheral blood were pure. Signaling of ATIII in migration of the leukocytes was studied by blocking signaling enzymes with staurosporine, GFX, wortmannin and rolipram. As AT III, the concentrate Kybernin®P and antibody purified AT III thereof were used.

**Results:** Pretreatment of lymphocytes with ATIII slightly augmented random locomotion, chemotaxis toward optimal concentrations of RANTES or IL-8 was significantly inhibited by pretreatment of the cells with ATIII followed by washing. Significant inhibition of chemotaxis was seen at ATIII concentrations as low as 10 nU/ml. Exposure of lymphocytes to gradients of ATIII stimulated migration in the absence of additional chemokines. Pretreatment of monocytes with

ATIII before triggering of directed migration revealed similar findings, with ATIII again being active at low concentrations. In the absence of chemokines, ATIII again activated monocytes' directed migration. This ATIII-induced augmentation of migration was used for investigating signaling events induced in the cells by preincubation with various enzyme blockers: in contrast to neutrophils, where ATIII effects are mediated by protein kinase C and cAMP, responses of monocytes were wortmannin- and rolipram-sensitive; lymphocytes were additionally affected by GFX.

**Conclusion:** ATIII directly affects monocyte and lymphocyte functions *in vitro*. ATIII inhibits chemokine-stimulated migration of the two peripheral blood mononuclear cell populations. Thus, cellular effects of ATIII may occur not only in neutrophils but also in other immune cell populations. Signal transduction may be cell type-dependent, as it differs between neutrophils, lymphocytes and monocytes. A specific pathway for direct cellular activation by ATIII is postulated.

### Reference:

1. Dunzendorfer *et al*: Cell-surface heparan sulfate proteoglycan mediated regulation of human neutrophil migration by the serpin antithrombin III. *Blood* (in press).



**P106 Efficacy of substitution therapy with PPSB concentrate in intensive care patients**

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**Introduction:** Substitution of clotting factors is one of the most costly therapies in ICU treatment. However, efficacy of such treatment in clinical practice is poorly investigated. In a multi-centre trial we evaluated if substitution of PPSB-concentrate is able to raise clotting parameters.

**Methods:** In a multi-centre observational trial in 27 Austrian Hospitals and following ethics committee approval 280 patients (median age 58 [6–93]) were included in the study. During the observation period all patients requiring substitution with PPSB concentrate were included. No trigger-levels and no prescribed dosage was defined but patients received a PPSB-concentrate containing the vitamin K dependent factors II, VII, IX, X and the vitamin-dependent inhibitors C and S (Prothromplex® Total S-TIM 4, Baxter) as

regarded clinically necessary by the physician concerned. Change in coagulation parameters, dosage applied, and adverse side-effects were registered. Statistical analysis based on the intention-to-treat principle while using the last value technique.

**Results:** Median dose applied was 21.4 IU/kg and led to a median rise in Quick test from 38 to 62%. No side effects were reported. The increase was clinically sufficient in all cases and no further substitution was required.

**Conclusion:** For the first time in a representative number of patients we showed that the substitution of 1 IU/kg bodyweight PPSB concentrate raised Quick test by about 1%. Use of PPSB concentrate is safe and no side effects, especially thrombosis were reported.

**P107 Assessment of rVIIa as a universal haemostatic agent in a model of haemodilution**

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Haemostatic failure, secondary to large volume fluid replacement, is a major component to the mortality and morbidity associated with blunt trauma. Progressive bleeding in multiply injured patients is due to both dilution effects and specific inhibitory effects on platelet function of the colloids used. Recombinant factor VIIa (rVIIa) is seen increasingly as a possible universal haemostatic agent that could act to reverse or prevent haemostatic failure associated with dilution and the direct effects of the colloids within the 'Golden' hour of haemorrhagic shock.

We have conducted a pilot preclinical study to evaluate the potential role of rVIIa as a universal haemostatic agent in a model of large volume fluid replacement using thrombelastography (TEG). TEG is a method of global haemostasis assessment, providing information on the rate of clot formation, clot strength and durability.

Whole blood samples from normal donors were tested undiluted (100%) or diluted (50% and 80%) with standard colloid replacement solutions (Haemacel, Albumin, Gelofusine, Hydroxyethyl starch) and N/Saline. Global haemostasis was assessed in the TEG,  $\pm$  90  $\mu$ g/kg rVIIa added. In undiluted blood (100%) there were no statistically significant changes in any TEG parameter when rVIIa was added. At dilutions of > 50% addition of rVIIa significantly improved the kinetics of clot formation and rate of platelet reactivity,  $P < 0.05$ , although time to the start of coagulation and final clot strength were not significantly different. The beneficial effects of addition of rVIIa did not differ between different fluid replacement solutions.

Addition of rVIIa therefore appears to improve markers of global haemostasis in this model of large volume fluid replacement. Further work is required to assess its potential value as a universal haemostatic agent in the setting of blunt trauma and large volume fluid replacement.

**P108 Measurement of serum transferrin receptor (sTfR) in critically ill patients**

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**Introduction:** Measurement of sTfR is an important new haematological parameter. Laboratory studies have indicated that sTfR values are elevated in anemias associated with enhanced erythropoiesis and tissue iron deficiency only. The aim of this study was to demonstrate whether iron deficiency, expressed through elevations of sTfR, constitutes an important etiologic component of ICU patients' anemia.

**Methods:** Twenty-seven patients were studied (10 male, 17 female), mean age  $65.4 \pm 4.0$  years and mean APACHE II score of  $16.5 \pm 1.0$ . Five patients had sepsis syndrome, 12 severe sepsis, 8 had septic shock and 2 patients suffered from multiple organ failure. Patients who presented with a bleeding episode were excluded from the study. We measured sTfR, hemoglobin, hematocrit, serum iron concentration and ferritin and calculated APACHE

II and sepsis score on day 1, 4 and 8 of ICU stay. For the measurement of sTfR, monoclonal antibodies were used.

**Results:** All critically ill patients had sTfR values at the lower level of the normal range ( $0.93 \pm 0.5$  mg/l, with normal values ranging between 0.94 and 1.28 mg/l). Though all sTfR values were found in the normal range, variations of transferrin receptors were correlated to sepsis score, hemoglobin and hematocrit on corresponding days. Statistical analysis revealed no significant difference.

**Conclusion:** Investigation of anemia in critically ill patients includes bone marrow examination for iron status determination. This invasive procedure can now be substituted by transferrin receptors' measurement, since ferritin levels are not reliable in septic patients, as it is the case with all acute phase proteins.



**P111 Regional release of tissue-type plasminogen activator in sepsis: effects of volume resuscitation**

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**Background:** Septic shock is characterised by increased systemic fibrinolytic activity. This study in endotoxemic pigs was designed to: 1) describe regional tPA (tissue-type plasminogen activator) activity; 2) assess changes in tPA activity following aggressive volume resuscitation.

**Materials and methods:** Anesthetised, mechanically ventilated pigs (24–29 kg) were instrumented to monitor cardiac output (CO), portal- ( $Q_{MES}$ ), hepatic- ( $Q_{HEP}$ ), and renal ( $Q_{REN}$ ) blood flow. Aortic arterial and renal, portal and hepatic venous blood samples were collected. Total tPA (ng/ml) in plasma was analysed by ELISA and together with blood flow data enabled the calculation of net flux of tPA across the pulmonary (PULM), mesenteric (MES), hepatic (HEP) and renal (REN) circulation. Following baseline sampling, endotoxin (*E. Coli* 0111:B4) was infused for 2 hours. Animals were then volume resuscitated with albumin and saline and observed another 3 hours. Statistical analyses were made by ANOVA and Fisher's PLSD. \*  $P < 0.05$ . Values are mean  $\pm$  SEM,  $n = 8$ .

**Results:** CO decreased from  $4.1 \pm 0.3$  l/min to  $2.7 \pm 0.1^*$  during sepsis and was restored to  $4.7 \pm 0.1$  by volume resuscitation. Parallel changes were observed in  $Q_{MES}$  (from  $0.9 \pm 0.1$  l/min to  $0.5 \pm 0.1^*$ , and back to  $1.1 \pm 0.2$ ) and  $Q_{REN}$  (from  $135 \pm 15$  ml/min, to  $62 \pm 20^*$ , and back to  $124 \pm 25$ ).  $Q_{HEP}$  was maintained at  $1.1 \pm 0.1$  to  $1.3 \pm 0.1$  l/min by an effective hepatic arterial buffer response. Net regional plasma fluxes of tPA are shown in the Table.

**Conclusions:** Fibrinolytic activity increases early in sepsis shown by a net pulmonary and mesenteric release of tPA. Increased net hepatic uptake would mask the pre-hepatic changes in tPA. Early volume resuscitation in sepsis is able to completely reverse all these changes. The findings demonstrate the dynamics of hemostasis during sepsis. Early interventions to restore hemodynamic stability are important to maintain normal fibrinolytic activity.

**Table**

	Baseline	2 hours	3 hours	4 hours	5 hours
Net PULM ( $\mu$ g/min)	$2.2 \pm 1.3$	$33 \pm 12^*$	$-1 \pm 6$	$1 \pm 1$	$0.1 \pm 1.6$
Net MES ( $\mu$ g/min)	$1.3 \pm 0.4$	$8.3 \pm 2.8^*$	$2.7 \pm 0.5$	$0.8 \pm 0.4$	$0.7 \pm 0.4$
Net HEP ( $\mu$ g/min)	$-1.9 \pm 0.4$	$-21 \pm 5^*$	$-6.9 \pm 0.8$	$-2.2 \pm 1.4$	$-2.4 \pm 1.1$
Net REN ( $\mu$ g/min)	$0.1 \pm 0.1$	$0.4 \pm 0.4$	$-0.07 \pm 0.2$	$-0.1 \pm 0.1$	$0.04 \pm 0.04$

**P112 The effect of the combined administration of colloids and Ringer's Lactate on the coagulation system – an *in vitro* study using thrombelastography (roTEG®)**

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**Introduction:** Gelatine and hydroxyethylstarch (HES) based colloids are given in clinical practice normally in combination with Ringer's Lactate (RL), but also dose dependent combinations of HES and gelatine are administered. Colloids impair the coagulation system in different ways: gelatine disturbs fibrin polymerisation and HES reduces F VIII and vWF in plasma in the first line. There are no data available, to which extent the combined administration of colloids and RL affects the coagulation system. Aim of our study was to investigate, if the combined administration handicaps the coagulation system differently than the use of single substances.

**Methods:** We diluted citrated blood from 10 healthy male volunteers to 20%, 40% and 60% with gelatine (Gelofusin®), 6% HES 130:0.4 (Voluven®), 6% HES 200:0.5 (Iso-Hes®) and RL, as well as with the combinations of these solutions in a ratio of 1:1 (gelatine/RL, 6% HES 130:0.4/RL, 6% HES 130:0.4/gelatine, 6% HES 200:0.5/RL, 6% HES 200:0.5/gelatine). Thereafter, blood was recalcified, the samples were activated with InTec® (thromboplastin, Nobis®) and analysed by modified thrombelastography

(roTEG®). A repeated measures ANOVA as applied for the analysis of the influence of dilution on thromboelastographic parameters, different colloid combinations were compared using an ANOVA after subtracting the 0% dilution value and Tukey's *post hoc* tests for individual intergroup comparisons.

**Results:** We could not detect any significant differences between the combination gelatine/RL and 6% HES 130:0.4/RL. The clot formation time (CFT) of 6% HES 200:0.5/RL was significant longer than gelatine/RL at 40% and 60% dilution. At 40% dilution, the CFT of 6% HES 130:0.4/RL and gelatine/RL was significant shorter and the maximal clot formation (MCF) significant higher than 6% HES 130:0.4 and 6% HES 200:0.5 alone.

**Conclusion:** Concerning to our data, 6% HES 200:0.5 and the combination of 6% HES 200:0.5/RL impair the coagulation system more than the combination of gelatine/RL or 6% HES 130:0.4/RL. Regarding its influence on the coagulation system, 6% HES 130:0.4 may be as safe as gelatine in patients with blood loss and huge volume substitution.



with a low degree of substitution (0.5) has been preferred. The present study investigated, whether a long-term, high-dose volume therapy with a newly developed 6% HES 130/0.4 (Voluven®) is safe in patients suffering from acute ischemic stroke. In particular, the effects on hemostaseology were examined.

**Patients and methods** In a randomized, double-blind, placebo-controlled study carried out in accordance with GCP and ICH guidelines, 40 patients suffering from acute ischemic stroke received either 6% HES 130/0.4 or crystalloid solution, after giving their informed consent. There were no differences between the treatment groups regarding demography and baseline characteristics. Each patient received a loading dose of 500 ml HES or crystalloid solution over 1 hour and subsequently 1500 ml HES or crystalloid solution per day over a period of 4 days for a total dose of 6500 ml. Hemostaseological parameters (platelets, prothrombin time, aPTT, fibronectin, Factor VIII:C, von Willebrand factor antigen, von Willebrand Ristocetin cofactor) were measured daily. Patients were followed-up until 90 days post treatment.

**Results:** A total of 390 g HES per patient was administered and well tolerated by all patients in the study group. Only one serious adverse event was noted in the crystalloid group, whereby a relation with the study medication was unlikely. The most frequent adverse event was itching, reported by two patients in the crystalloid group and three patients in the HES group.

At baseline all hemostatic parameters were within the normal range and no clinically relevant changes were observed with respect to any parameter between the two treatment groups.

**Conclusions:** Medium molecular weight HES 130 with a low degree of substitution (0.4) was well tolerated and can be administered in larger doses over longer periods of time without relevant effects on hemostaseology compared to a crystalloid group. In particular, there is no increased risk of bleeding in this clinical setting.

## P116 No evidence of excess mortality in patients receiving human albumin: a meta-analysis of randomized controlled trials

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A meta-analysis of randomized controlled trials was conducted to test the hypothesis that albumin administration is not associated with excess mortality. Candidate trials must have compared albumin administration with crystalloid, no albumin or a lower dosage of albumin. No restrictions were placed on clinical indication. Trials were identified by computer searches of bibliographic databases, the Cochrane Controlled Trials Register, the Cochrane Medical Editors Trial Amnesty and other Internet-resident resources; hand-searching of general medical journals; contacts with albumin suppliers; and consulting the reference lists of prior meta-analyses, review articles and other publications. A total of 55 trials with 525 deaths among 3504 randomized patients were included in the meta-analysis. Included trials involved six categories of clinical indications: surgery or trauma ( $n = 27$ ), burns ( $n = 4$ ), hypoalbuminemia ( $n = 5$ ), high-risk neonates ( $n = 6$ ), ascites ( $n = 5$ ) and other ( $n = 8$ ). The pooled relative risk of death and mortality risk difference were 1.11 (95% CI, 0.95–1.28) and 1.5% (95% CI, -0.7 to 3.8%), respectively, under a fixed-effects model ( $P = 0.66$  and  $P = 0.65$  for heterogeneity, respectively). Thus,

without the application of any exclusion criteria that might have biased the results, there was no evidence of significant excess mortality risk in albumin recipients. In addition, there was no significant excess risk within any of the six categories of clinical indications. For the seven trials incorporating some form of blinding the pooled relative risk was 0.73 (95% CI, 0.48–1.12). The pooled relative risk among the 17 trials with mortality as an endpoint was 1.00 (95% CI, 0.84–1.18). In the 35 trials without crossover of control group patients to the albumin group the pooled relative risk was 1.04 (95% CI, 0.89–1.22). For all trials there was evidence of significant small-trial bias (ie publication or other bias) favoring control ( $P = 0.03$  by Egger's test). The adjusted relative mortality risk taking into account small-trial bias was 0.83 (95% CI, 0.65–1.08) based on regression analysis. Thus, lack of blinding, absence of mortality as a study endpoint, crossover and small-trial bias all consistently biased pooled relative risk in favor of control. This meta-analysis furnished no evidence of excess albumin-associated mortality and strongly suggested that albumin may reduce mortality. These findings support the safety of albumin.

## P117 Evaluation of early and late histamine release by three standard volume substitutes

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**Introduction:** Following meta-analysis [1], the use of colloidal solutions in intensive care medicine is under discussion. Although polygeline [2] and human albumin are known to cause histamine release, other substances eg hydroxyethyl starch were thought to be without effect. Histamine release depends on the clinical scenario, concomitant drugs, infusion speed, duration and amount of infusion. However, there is no information about their effect regarding time periods longer than immediate reactions. This study investigated the histamine releasing effects of three plasma substitutes administered and observed over a longer period of time, simulating many of the clinical scenarios.

**Methods:** In a prospective, randomised, controlled clinical study 21 healthy, male volunteers were randomly allocated to three groups receiving i.v. 3.5% polygeline (Haemaccel,  $n = 9$ ), 5% human albumin ( $n = 6$ ) and 3% hydroxyethyl starch 200/0.5 (HAES-steril,  $n = 6$ ) for normovolaemic haemodilution over a period of 90 min, after calculated and adjusted blood withdrawal before infusion. H<sub>1</sub>-antagonist (dimetinden) and H<sub>2</sub>-antagonist (cimetidine) i.v. premedication was given to prevent histamine-related clinical signs. Blood samples for plasma histamine determination were drawn at defined time points and systemic (cardiovascular, skin reactions, etc) parameters documented over 240 min after start of infusion.



## P120 Some metabolic and hormonal aspects of enteral nutrition

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Enteral nutrition is popular in intensive care. Keeping the intestine in function by feeding stimulation helps to treat intensive care patients. We aimed to find metabolic and hormonal differences between enteral and parenteral feeding.

**Design:** Twenty cardiopulmonary stable patients hospitalised at the Metabolic Department of Teaching Hospital in Hradec Králové were monitored in a prospective study.

**Interventions:** The patients, who were fed more than 2 weeks parenterally without enteral feeding due to their disease (mostly uncomplicated intestinal fistula after surgical intervention with possibility to start enteral feeding), were studied after obtaining informed consent. The parenteral nutrition was fortified by 4200 kJ parenterally in days 0–2 and next enterally in the same contents (Nutrison 1000 ml) in days 7–14. The local Ethics committee approved this research project.

**Measurement and methods:** Comparisons between parenteral + parenteral period and parenteral + enteral period in several serologic and urine parameters were calculated. Wilcoxon's pair *t*-test was used for statistical analysis.

**Results:** HDL cholesterol (0.61 vs 0.72 mmol/l), apoprotein A (0.63 vs 0.71 g/l) and insulin like growth factor (IGF-1) (291.7 vs 321.4 ng/ml) were significantly higher in enteral period ( $P < 0.05$ ). The urinary output of urea (551 vs 489 mmol/day), P (31 vs 24 mmol/day), Na (418 vs 220 mmol/day) were significantly lower during enteral period ( $P < 0.05$ ).

**Conclusion:** Enteral nutrition application is associated also with some anabolic effects in comparison to application of parenteral nutrition alone. The higher level of IGF-1 is main anabolic marker of enteral nutrition in our study. The decline of urea output means an enhanced proteosynthesis (probably most in intestine mass). Higher level of HDL cholesterol and apo A during enteral feeding we explain by the enhanced synthesis of cholesterol in the intestine. The metabolic function of intestine may be important for intensive care patients. Because tolerance of enteral feeding is changing quickly during the critical situation, we prefer combination of parenteral and enteral nutrition in unstable intensive care patients.

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## P121 Endoscopically placed naso-jejunal feeding tubes in ICU patients: a retrospective review

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**Introduction:** The preferred method of nutritional support in intensive care patients is via the enteral feeding route due to its favourable trophic effects on the intestinal mucosa, reduced rate of complications and lower costs when compared with parenteral nutrition. Impaired gastric emptying can be a limiting factor in providing enteral nutrition, commonly affected by critical illness, and naso-jejunal tube feeding can be useful in patients who fail to tolerate naso-gastric tube feeding. Endoscopic placement of naso-jejunal tubes can be performed at the bedside, is highly successful, 85–90% success rate can be expected and enteral feeding can start immediately following the procedure.

**Method:** This retrospective review evaluated the use of feeding tubes (8 fr, 240 cm: Wilson-Cook Medical Inc.) endoscopically placed in ICU patients over a 15 month period.

**Results:** A total of 27 patients had 36 naso-jejunal feeding tubes placed endoscopically (five patients had more than one placement). The patients were typically male admitted to the ICU following an emergency procedure. All were placed successfully and used for a mean 5.7 days/tube (range 1–27 days). Avoidable complications such as blockages or accidental misplacement of the tube occurred in 28% of the tubes.

A review of these results suggests that the majority of patients would have benefited from placement of an enteral feeding tube during theatre, and that the success of naso-jejunal feeding could be improved by attention to the care of the feeding tubes once placed.

**Conclusion:** Following this review, new standards and guidelines have been produced within the Critical Care Directorate for the multidisciplinary team members caring for patients who have naso-jejunal feeding tubes.

## P122 A novel technique for nasoduodenal feeding tube placement in critically ill patients

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**Introduction:** Although enteral nutrition is considered superior to parenteral nutrition in critically ill patients, it is frequently delayed or prevented by gastroparesis. A variety of approaches have been developed to bypass the stomach, but none has proved entirely satisfactory. The Cathlocator™ is a novel device that permits real time localization of the end of feeding tubes by detection of a magnetic field generated by a small electric current in a coil in the tip of the tube. It is portable, can be used at the bedside and uses no ionizing radiation.

**Study objective:** To evaluate placement of tubes for (i) nasoduodenal feeding, and (ii) nasogastric drainage in critically ill patients using the Cathlocator™.

**Methods:** Ten nasoduodenal tube placements were attempted in nine critically ill patients. The Cathlocator™ was used to guide positioning of the tube beyond the pylorus and also to determine whether a separate nasogastric tube was placed correctly. Tube tip position was confirmed by plain abdominal X-ray. Data are median and range.



**Method:** Nineteen children were enrolled within 48 hours of ICU admission. Exclusion criteria included: liver disease, gastrointestinal abnormalities and use of prokinetic agents. All patients were N.P.O., and maintained on a *ivi* glucose (5–8 mg/kg/min). Gastric emptying (GE) was assessed clinically by feed intolerance and using a paracetamol absorption technique (PTA). Feed intolerance was defined as a residual gastric volume > 0.25 ml/kg after 4 hours of a bolus 2 ml/kg test milk feed. At this point (T0), a single 15 mg/kg dose of paracetamol was administered nasogastrically, and serial blood samples taken for paracetamol assay at 0, 15, 30, 60, 120, 240 and 360 min.

GE was calculated using the gastric emptying ratio (GER) which is the time to reach peak paracetamol level divided by its peak concentration, with high values reflecting delayed gastric emptying [3]. Blood amylin and insulin sample were taken at T0 and T360 with the mean of these two values used to reflect the average level over the study period. Amylin was measured by radioimmunoassay. Data were assumed non-parametric, thus Spearman's correlation coefficient and Mann–Whitney tests were used. Data are shown as median (interquartile range).

**Results:** Nineteen patients were enrolled with a median age 6 years (1.7–8.5), and weight 20 kg (11.5–31.5). Diagnoses included sepsis ( $n = 8$ ), respiratory ( $n = 5$ ), head injury ( $n = 2$ ), neurology ( $n = 2$ ) and other ( $n = 2$ ). Four patients did not tolerate enteral feeds (median residual volume 4.4 ml/kg). Factors associated with impaired gastric emptying were not different between the two groups, in particular opiate infusions (4/4 vs 14/15  $P = 0.6$ ) and dopamine use (0/4 vs 2/15  $P = 0.4$ ). Amylin levels (pmol/l) were higher in patients ( $n = 4$ ) with feed intolerance 44.1 (37.0–50.8) vs 22.7 (13.6–26.7),  $P = 0.009$ . This coincided with higher GER values 4.29 (2.75–5.25) vs 1.54 (0.69–2.25),  $P = 0.08$ . Overall, amylin levels correlated with GER  $r = 0.49$  (95% CI 0.03–0.78),  $P = 0.03$ , and with insulin  $r = 0.51$ , (95% CI 0.08–0.78),  $P = 0.02$ , which is consistent with co-secretion.

**Conclusion:** Failure to establish enteral feeds in critically ill children may be due to raised amylin levels.

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**P126 The effect of lactulose on tolerance of gastric feeding in long term ICU patients**

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**Introduction:** Lactulose was reported to inhibit gastric tone and motility in healthy volunteers [1]. Double blind placebo controlled study using lactulose four times 15 ml daily (ie 40 g) or saline for prevention of ventilator associated pneumonia was performed in our ICU during 1999–2000. In this report the impact on gastric feeding tolerance of lactulose given into stomach is evaluated.

**Materials and methods:** Forty-eight patients without pneumonia and mechanically ventilated for < 24 hours entered the study. From day 2 EN was given by a standardised protocol into the stomach. Daily amount of enteral nutrition (EN) was recorded. Failure was defined as EN interruption > 24 hours because of large residuals. Metoclopramide was used in all patients.

**Statistics:** Chi-square and Mann–Whitney *U*-tests when appropriate. Data presented as means  $\pm$  SD.  $P < 0.05$  was considered significant.

**Results:** Thirty-eight patients in whom EN was not contraindicated and stayed in the ICU > 3 days were analysed. Fifteen patients received lactulose (L) and 23 were given placebo (P). L and P

groups did not differ in age ( $50.3 \pm 18.2$  and  $52.7 \pm 16.3$ ; NS), APACHE II on admission ( $24.7 \pm 8.7$  and  $26.0 \pm 7.3$ ; NS). There also was no difference in L and P groups in mortality (6 ICU survivors and 9 non-survivors in lactulose group and 13 non-survivors and 10 survivors in placebo group; NS), length of ICU stay (LOS) ( $13.5 \pm 7.4$  and  $15.2 \pm 11.0$ ; NS) and ventilatory days ( $12.5 \pm 6.8$  and  $12.0 \pm 7.8$ ; NS). Patients receiving L did not differ from P in daily tolerance of gastric feeding ( $604 \pm 438$  and  $425 \pm 264$  ml/day;  $P = 0.16$ ) and number of EN intolerances per hospitalisation ( $0.51 \pm 0.26$  and  $0.50 \pm 0.35$  intolerances/LOS; NS). This was also true when ICU survivors were analysed separately.

**Conclusions:** Lactulose administered into the stomach has no impact on poor tolerance of gastric feeding in mechanically ventilated long term ICU patients.

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**Reference:**

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**P127 Investigation of insulin clearance in septic patients with glucose intolerance: analysis under strict blood glucose control by means of artificial pancreas**

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**Purpose:** Analysis of insulin metabolism in severely ill patients with glucose intolerance is important for appropriate nutritional support. Significance of the measurement of insulin clearance (IC) and the factors which influence IC in septic patients were investigated.

**Method:** Twenty septic patients in whom blood glucose (BG) levels were strictly controlled by means of bedside-type artificial pancreas (AP) (STG-22: manufactured by NIKKISO corporation in Japan) were studied. IC was calculated from the data obtained

by euglycemic hyperinsulinemic glucose clamp method performed by means of AP twice for each patient (first measurement was done in acute condition or within 3 days after admission, second measurement was done 1 week after the first measurement basically. Clamped BG level: 80 mg/dl. Insulin infusion rate [IIR]: 1.12 and 3.36 mU/kg min. I1/I3 and C1/C3, the blood insulin levels, and the C-peptide reactivity levels, when IIR is 1.12/3.36 mU/kg min respectively. Glucose disposal rate: M value [mg/kg min]). IC was calculated from the following



**P130 Sepsis progression is associated with a gradual depletion of both insulin-like growth factor I (IGF-I) and insulin-like growth factor binding protein-3 (IGFBP3) and a progressive elevation of growth hormone (GH) serum levels**

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Critical illness is associated with increased protein catabolism that is resistant to nutritional support. There is some evidence that an acquired resistance to GH anabolic action appeared in these situations, may be partly responsible. Moreover, in the same conditions, IGF-I and IGFBP-3 serum levels concentrations are low, despite high circulating concentrations of GH. Among several critical illnesses, sepsis is one that GH/IGF-I axis has never systematically studied, and mainly in regard to its progression from uncomplicated sepsis to severe sepsis and/or septic shock. Thus, the aim of this study was to investigate the GH/IGF-I axis in septic phenomenon, especially with regard to its evolution. We measured, by commercially available radioimmunoassays (ELISA), the serum GH,

IGF-I and IGFBP-3 levels of 59 septic patients (pts) (24 pts with sepsis [group G1], 12 severe sepsis pts [group G2], 23 pts with septic shock [group G3]) and we compared them with the findings of 15 healthy controls (group H). The definition of the stages of sepsis followed the criteria established by the ACCP/SCCM consensus conference (August 1992). We use one-way ANOVA to compare the results from sepsis, severe sepsis and septic shock patients with the ones from healthy controls. Results were as in the Table.

We conclude that GH/IGF-1 axis impairment increases in parallel with the increasing severity of septic process.

**Table**

	Normal	Sepsis	Severe sepsis	Septic shock	P
GH (ng/ml)	1.12 ± 0.56	5.58 ± 0.27	2.3 ± 1.1	6.3 ± 1.9 <sup>b</sup>	0.013884
IGF-I (ng/ml)	170.9 ± 18.3	124.3 ± 18.6	91.7 ± 24.2	62.1 ± 7.6 <sup>a,b</sup>	0.000163
IGFBP-3 (µg/ml)	2.98 ± 0.14	1.98 ± 0.19 <sup>a</sup>	1.73 ± 0.46 <sup>a</sup>	1.38 ± 0.15 <sup>a</sup>	0.000002

Data are mean ± standard error of mean, <sup>a</sup> statistically different from normal, <sup>b</sup> statistically different from sepsis.

**P131 The effect of enteral and parenteral nutrition on blood and respiratory tract immunoglobulins in intensive care unit patients**

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**Aims:** The immunoglobulin production is influenced by the functional integrity of the intestinal mucosa, as long as 50% of the secretory IgA originates from it. Therefore, the type of nutritional schedule could interfere with immune response of the respiratory tract. The aim of our study was to compare the changes of the immunoglobulins (IgA, IgG and IgM) in the blood and the bronchial secretions in intensive care unit (ICU) patients under enteral (EN) and total parenteral (TPN) nutrition.

hospitalization day. White blood cells were also measured and cultures of bronchial secretions were received.

**Results:** Our results concerning immunoglobulins levels on the 1st and 5th day (mean values ± SD) are presented in the following table (mg/dl).

During the 1st day of the study immunoglobulins did not differ significantly either in blood or in bronchial secretions in both groups.

During the 5th day of the study we did not detect significantly differences ( $P > 0.05$ ) for immunoglobulins in the blood in both

**Methods:** Twenty ICU patients were included in the study. Ten of them received EN and the other 10 TPN. Immunoglobulins (IgA, IgG and IgM) were measured in the blood and the bronchial secretions (samples obtained during bronchoscopy), at the 1st and 5th

**Table**

	IgG		IgA		IgM	
	Enteral	Parenteral	Enteral	Parenteral	Enteral	Parenteral
1st day – blood						
	973.2 ± 433.66	794.1 ± 262.69	214.0 ± 137.4	206.6 ± 128.40	131.1 ± 77.47	112.6 ± 51.67
1st day – bronchial secretions						
	32.2 ± 55.81	20.3 ± 10.73	13.6 ± 18.47	9.99 ± 9.41	15.9 ± 43.62	0.96 ± 1.3
5th day – blood						
	925.5 ± 468.98	880.2 ± 441.96	230.8 ± 149.62	230.7 ± 160.17	146.3 ± 99.69	116.0 ± 61.68
5th day – bronchial secretions						
	43.7 ± 42.69	13.3 ± 9.50	16.0 ± 15.90	2.25 ± 4.17	2.6 ± 2.70	0.7 ± 1.15



**Table**

Day of measurement	1st	2nd	3rd	4th	Last
TDEE (kcal/kg)	52.5	48.6	51.4	48.3	51.4
Energy intake/TDEE	0.8	1.3	1.5	1.6	1.3
RQ (All patients)	0.82	0.88	0.9	0.87	0.88
RQ (PCEB)	0.85	0.88	0.92	0.92	0.89
RQ (NCEB)	0.81	0.86	0.84	0.83	0.83

All values expressed as median, day 5–7 are not shown because of limited data.

**P134 Oxygen consumption in critically ill patients: the relation between calculation by Fick's principle and measurement by gas-mixing chamber indirect calorimetry**

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**Background:** The accurate calculation of Oxygen consumption ( $VO_2$ ) using the Fick equation require accurate measurement of cardiac output (Q), usually by thermodilution, Oxygen content in arterial blood ( $CaO_2$ ) and Oxygen content in venous blood ( $CvO_2$ ). Each of these measurements can carry random errors and proportional errors and this well result in a significant final error in the calculated  $VO_2$  ( $cVO_2$ ). Gas mixing chamber indirect calorimeter has been an extremely valuable tool in measuring  $VO_2$  in critically ill patients ( $mVO_2$ ).

**Objectives:** To compare  $cVO_2$  and  $mVO_2$  in different groups of critically ill patients.

**Subjects and methods:** The study was conducted on 31 critically ill patients admitted to the department of critical care medicine, Cairo University, 25 males and 6 females, mean age  $56.2 \pm 10.4$  (range: 37–75), 11 patients with congestive heart failure (CHF) (class III & IV according to NYHA), 10 males and 1 female, mean age  $53.4 \pm 5.9$  (range: 45–63), 10 patients with acute respiratory failure, 8 males and 2 females mean age  $63.7 \pm 7.97$  (range: 50–75), 10 patients with sepsis or septic shock, 7 males & 3 females, mean age  $52.2 \pm 12.9$  (range: 37–69). Each was subjected to  $VO_2$  measurement utilizing Fick's equation;  $cVO_2 = Q$

**Conclusion:** During mechanical ventilation of critically ill children, TDEE can be predicted in 82% of the patients by performing only one measurement, despite individual differences. RQ is strongly influenced by the ratio energy intake/TDEE and by the cumulative energy balance. We advocate to feed critically ill mechanically ventilated children according to or in excess of their TDEE as soon as possible during admission, in order to optimize nutritional therapy.

( $CaO_2 - CvO_2$ ), the average of three double checked readings over 1 hour is determined. Concomitant measurements utilizing gas mixing chamber indirect calorimeter is carried out, the average of sixty readings over the same hour is recorded ( $mVO_2$ ).

**Results:** Oxygen consumption measured by Fick's method was comparable with that measured utilizing gas mixing chamber indirect calorimetry with no significant difference between means in the whole population ( $162.3 \pm 44.7$  vs  $165.0 \pm 33.4$  ml/min/m<sup>2</sup>, respectively,  $n = 61$ ), in CHF ( $176.4 \pm 57.4$  vs  $177.4 \pm 22.1$  ml/min/m<sup>2</sup>, respectively,  $n = 20$ ), in RF ( $143.8 \pm 40$  vs  $147.2 \pm 30.7$  ml/min/m<sup>2</sup>, respectively,  $n = 17$ ) and in sepsis and septic shock ( $161.9 \pm 35.3$  vs  $170.0 \pm 39.9$  ml/min/m<sup>2</sup>, respectively,  $n = 24$ ). However, correlation was present only in the whole population ( $r = 0.3$ ,  $P < 0.05$ ) and in patients with congestive heart failure ( $r = 0.4$ ,  $P < 0.05$ ).

**Conclusion:** Gas mixing chamber indirect calorimetry is a non-invasive, safe method for measuring Oxygen consumption in critically ill patients. Oxygen consumption measured by Fick's method is comparable with that measured utilizing gas mixing chamber indirect calorimetry, however correlation was absent in patients with respiratory failure, sepsis and septic shock.

**P135 Calculation of unmeasured anions fails to assist outcome prediction in patients in an adult intensive care unit**

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**Introduction:** The anion gap (AG) and base excess (BE) are used to identify the presence of a metabolic acidosis. A method of analysis using physico-chemical principals has been developed by Stewart and refined by Fencl. This technique has recently been demonstrated to detect unmeasured anions, due to metabolic derangement, more readily than the traditional markers of AG and BE. This method may be a more sensitive indicator of patients with circulatory inadequacy or organ dysfunction. The Fencl–Stewart method of assessing unmeasured anions, resulting in the strong ion gap (SIG), has been shown to be more strongly associated with mortality in paediatric patients than BE or AG [1]. This study examines the predictive value of these measurements in an adult population of critically ill patients.

**Methods:** 100 consecutive patients admitted to an adult intensive care unit had electrolyte and blood gas analysis performed on admission. The AG, SIG were calculated on admission and the base excess measured (BE) by blood gas analyser. APACHE II data and 28 day mortality were recorded.

**Results:** 100 mixed medical and surgical patients (48 and 52 respectively) with a mean age 60.5 years (range 18–97) and mean APACHE II score of 20.4 (range 5–40) were enrolled into the study. Twenty-eight day mortality was 31%. Logistic regression analysis showed that the APACHE II score was the best predictor of outcome (OR 1.17 95% CI 1.07–1.26  $P < 0.001$ ). Predictions did not significantly improve when either BE, AG, SIG or lactate were included. From ROC analysis, the best of the acid base variables for prediction of mortality was the BE (area under curve 0.70) followed by AG (AUC 0.66), lactate (AUC 0.66) and then SIG (AUC 0.57).

**Conclusion:** These data indicate that SIG does not have a useful predictive value in the adult patients in our ICU practice. Further studies are required to determine whether the application of SIG differs between adult and paediatric ICU patients.

**References:**

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**Table 1**

**The first day data for hemodynamic and oxygenation parameters**

	ARDS (n = 9)	Non-ARDS (n = 23)	P value
PWP (pulmonary wedge pressure) (mmHg)	14 (12–15)	16 (15–19)	< 0.05
Cardiac output (l/min)	7.3 (6.0–7.6)	8.0 (7.3–9.4)	NS
PCO <sub>2</sub> gap (mmHg)	9.4 (6.6–12.3)	11.7 (7.1–17.1)	NS
PaO <sub>2</sub> /FiO <sub>2</sub>	129.4 (117.5–212.5)	239.7 (197.1–342.2)	< 0.05
Arterial lactate (mmol/l)	2.2 (1.6–2.4)	1.93 (1.31–3.33)	NS
Arteriovenous lactate gradient (mmol/l)	0.11 (0.07–0.15)	0.06 (0.03–0.08)	< 0.05
Lactate flux (mmol/h)	44.37 (33.7–62.7)	31.7 (11.2–40.3)	NS
Mortality (%)	44.4	43.4	NS

oxygen variables, arterial and mixed-venous lactate levels, and gastric mucosal pCO<sub>2</sub> (PgCO<sub>2</sub>) were measured every 8 hours for 5 days. PCO<sub>2</sub>gap (PCO<sub>2</sub>gap = PgCO<sub>2</sub> – PaCO<sub>2</sub>) and pulmonary lactate flux [(arterial lactate – mixed venous lactate) × cardiac output] were calculated. Results were expressed as median and inter-quartile 25–75%. The median values at the first day were used to statistical analyzes. Mann–Whitney U-test was used to evaluate of differences between the groups.

**Results:** Mean age was 57 ± 17 years, being higher among patients with ARDS than the ones without ARDS. Mean APACHE II and SOFA scores were 21.5 ± 6.6 and 9.9 ± 2.5, respectively. The lactate flux showed a trend to be greater in non-survivors than survivors septic patients (P = 0.06).

**Conclusion:** Despite of respiratory failure severity, all septic patients presented pulmonary lactate production, which was significantly greater in patients with ARDS.

**P139 Relationship among sigmoid pHi, blood lactate and outcome in surgical patients of abdominal aortic aneurysm**

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**Introduction:** Many works have shown the relationship between the outcome of surgical critically ill patient and oxygen availability of the body. Many factors cause an insufficient oxygen availability: tissutal traumatism with the consequent beginning of the inflammatory cascade, anemia, hypotension due to the blood losses, anesthesia. Shoemaker has called this alteration as 'oxygen debt' and has demonstrated that patient outcome is directed correlated to it and that this oxygen debt must be extinguished as soon as possible. The higher is the oxygen debt, higher is the risk of multiple organ failure and death. The gut has certainly a prominent role to determine these two last events and previous studies have shown the importance of a low gastric perfusion to cause death, measuring intramucosal pH with a gastric tonometer. A previous study has shown a correlation between II-6 levels and outcome in major abdominal surgery. Now we have done a work to investigate the correlation between gut hyposmia, measured with sigmoid tonometry, during aortic clamping for abdominal aortic aneurysm operation, and patient outcome.

**Materials and methods:** It was a prospective study on a series of 13 patients operated for abdominal aortic aneurysm. These patients were monitored with a sigmoid tonometer and pHi was detected at some times, together with arterial blood lactate and blood lactate of portal vein. These parameters have been detected at these times: at the beginning of anesthesia (t0), before aortic clamping (t1), 30 min after aortic clamping (t2), just after the operation (t4). The portal blood have been taken only in the first two times by the surgeon.

**Results:** Data have been divided in two groups following the developing or not of organ failures (OF) in the postoperative period. Seven patients had not organ failure, while among the other six patients, one died for MOF and the other five developed organ failures: three patients had acute renal and two cardiac failure. Arterial

**Table 1**

	T0	T1	T2	T4
Without		8.38 ± 1.9	11.26 ± 2.2	P = ns
With OF		9.78 ± 2.52	16.97 ± 4.02	P = 0.0172

**Table 2**

	T0	T1	T2	T4
Without	7.374 ± 0.14	7.3 ± 0.18	7.216 ± 0.15	7.25 ± 0.15
With OF	7.23 ± 0.167	7.092 ± 0.16	6.995 ± 0.24	7.00 ± 0.16
	P = ns	P = ns	P = 0.035	P = 0.014

blood lactate trend was not significantly different between the two groups. Tables 1 and 2 show portal blood lactates and pHi trend. Patients with organ failure had a drop of sigmoid pHi with an increase of portal blood lactate after aorta declamping. At T4 pHi was still significantly lower in patients with OF. Fisher exact test has shown a significative relationship between pHi < 7.15 at 30 min after declamping and outcome (P < 0.05).

**Conclusions:** Patients operated for abdominal aortic aneurysm often have organ failures in the postoperative period. The developing of organ failure is correlated with the gut ischemia which happens in the intraoperative period. In fact from these preliminary data patients with a persistent drop of pHi < 7.15 had organ failure in the postoperative period.



**Methods:** ACI rats, IL-6<sup>-/-</sup> and IL-6<sup>+/+</sup> mice underwent a standardized intestinal manipulation (IM) and were sacrificed at various time points postoperatively. One group of rats received repeated i.v. doses of blocking antibodies against the adhesion molecules (1A29 + WT.3) pre- and postoperatively. The small bowel was separated in mucosal and muscularis layers and specimens were used for RNA and protein extraction. STAT protein was quantified using EMSA. IL-6 protein was measured by ELISA in tissue culture and by immunohistochemistry in muscularis whole-mounts.

**Results:** Muscularis extracts demonstrated an early upregulation (12.3 fold at 3 hours) in IL-6 mRNA by RT-PCR. This was in contrast to mucosal extracts that did not show significant changes. Adhesion molecule blockade resulted in a significant decrease in infiltrating cells, but did not change mRNA expression. IL-6 immuno-

histochemistry stained resident muscularis macrophages, smooth muscle cells and infiltrated leukocytes. Muscularis tissue culture after IM demonstrated a significant increase in IL-6 protein compared to untreated control cultures (420 vs 230 pg/100 mg tissue). Postoperatively STAT proteins showed a significant increase in activation (32 fold at 30 min) with a prototypic IL-6 supershift profile (Stat3 $\alpha$ ). IL-6<sup>-/-</sup> mice demonstrated a significantly lower STAT activation following IM compared to IL-6<sup>+/+</sup> mice.

**Conclusion:** These results demonstrate for the first time that operative trauma leads to an early and significant production of IL-6 within the intestinal muscularis. IL-6 is mainly produced by resident cells within the muscularis and has functional activity. Therefore, the intestinal muscularis plays a role in the postoperative production of the proinflammatory mediator IL-6.

**P143 Continuous multi-parameter tissue monitoring during shock and resuscitation**

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**Introduction:** Continuous assessment of tissue perfusion may allow for early detection and correction of hemorrhagic shock. We investigated continuously monitoring pH, pO<sub>2</sub> and pCO<sub>2</sub> of skeletal muscle (SM), subcutaneous tissue (SQ) and bladder wall (BW) as possible sites for following the course of hemorrhagic shock and resuscitation.

**Methods:** Seven anesthetized pigs (25–35 kg) underwent laparotomy, femoral vessel cannulation, cystostomy, and ureteral cannulation. Multi-parameter sensors (Diametrics Medical, MN, USA) were placed in the deltoid (SM), chest wall (SQ), femoral artery, and adjacent to the bladder mucosa (BW). Ventilation was adjusted to keep the PaCO<sub>2</sub> at 40–45 mmHg. Animals were rapidly bled and maintained at a MAP = 40 mmHg by withdrawing and infusing blood as needed. When a constant infusion was required to maintain a MAP = 40 mmHg (decompensation), animals were resuscitated with shed blood + 2x shed volume in LR (20 min) and observed for 2 hours. The time dependence of pH, pO<sub>2</sub> and pCO<sub>2</sub> in each tissue was analyzed using ANOVA

with repeated measures and a *post hoc* Tukey's test for significance (\* *P* < 0.05, † *P* < 0.01).

**Results:** Average blood loss was 48 ± 11%. All tissue sites were found to respond significantly to shock and resuscitation. Both SMpH and SQpH remained significantly lower than baseline until 90 min of recovery, whereas BW returned to normal by 30 min. PCO<sub>2</sub> was significantly elevated at decompensation in all tissues, but returned to baseline by the end of resuscitation. Only SM and BW were found to decrease significantly at the end of decompensation, but returned to normal with resuscitation. Overall, SM afforded the greatest measurable change with the smallest relative variance at each time point.

**Conclusions:** Continuous multi-parameter monitoring of SM, SQ and BW potentially provide a minimally invasive method of assessing shock and resuscitation. Of the tissue sites investigated, SM provides the most sensitive means of monitoring hemorrhagic shock with the least amount of inter-subject variance.

		Baseline	Decompensation	Resuscitation	30 Recovery	60 Recovery	90 Recovery	120 Recovery
	MAP	90 ± 35	37 ± 3 <sup>†</sup>	74 ± 27 <sup>†</sup>	79 ± 26	85 ± 14	78 ± 5	82 ± 4
SM	pH	7.35 ± 0.09	7.02 ± 0.09 <sup>†</sup>	7.04 ± 0.07 <sup>†</sup>	7.10 ± 0.13 <sup>†</sup>	7.14 ± 0.17 <sup>†</sup>	7.23 ± 0.06	7.22 ± 0.07
	CO <sub>2</sub>	53.7 ± 8.2	85.7 ± 23.3 <sup>†</sup>	71.3 ± 19.8	66 ± 13.8	64.9 ± 16.3	55.9 ± 5.2	56.8 ± 4.1
	O <sub>2</sub>	65.7 ± 43.6	7.8 ± 13.5 <sup>†</sup>	44.6 ± 29.3	55.1 ± 29.7	56 ± 29.6	56 ± 12	57.3 ± 12
SQ	pH	7.38 ± 0.08	7.11 ± 0.12 <sup>†</sup>	7.10 ± 0.07 <sup>†</sup>	7.16 ± 0.08 <sup>†</sup>	7.19 ± 0.12 <sup>†</sup>	7.24 ± 0.08	7.24 ± 0.08
	CO <sub>2</sub>	53.5 ± 10.6	84.3 ± 23.6 <sup>†</sup>	66.6 ± 15.1	58.5 ± 15.1	55.4 ± 18.1	48.8 ± 9.5	50.1 ± 8.6
	O <sub>2</sub>	92 ± 75	41.6 ± 63.5	63 ± 53	74.5 ± 58.5	81.4 ± 77.3	110 ± 85.6	96.8 ± 46.2
BW	pH	7.33 ± 0.08	7.01 ± 0.2 <sup>†</sup>	6.99 ± 0.36 <sup>†</sup>	7.09 ± 0.2	7.09 ± 0.21	7.11 ± 0.19	7.11 ± 0.18
	CO <sub>2</sub>	49.3 ± 5.6	71.4 ± 18.7 <sup>†</sup>	60 ± 12.1	53.3 ± 12.9	56.7 ± 21.9	51.7 ± 9.9	53.8 ± 9.8
	O <sub>2</sub>	114.5 ± 81	27.1 ± 20 <sup>†</sup>	75.3 ± 53.4	75.7 ± 47.1	46.1 ± 36.7	37.1 ± 28.9	38.7 ± 26.1



**P146 Dose-response of arginine-vasopressin (AVP) on blood pressure (MAP), renal macro and micro cortical and medullary flows in anesthetized rabbits**

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AVP is a vasopressor used in various clinical vasoplegic situations. Little is known about AVP effect on intact animal for MAP and renal circulation. Anesthetized (pentobarbital) ventilated New Zealand rabbits (2.5–3.3 kg) were studied.

**Measured parameters:** MAP, systolic (SVRen) and diastolic (DVRen) renal blood flow velocities (20 MHz pulsed Doppler); laser Doppler cortical  $FI_{cort}$  and medullary  $FI_{med}$  flows.

**Baseline values:**

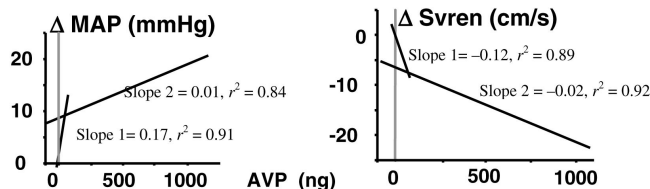
MAP (mmHg)	SV <sub>ren</sub> (cm/s)	DV <sub>ren</sub> (cm/s)	FI <sub>cort</sub> (TPU)	FI <sub>med</sub> (TPU)
78.5 ± 14.5	51.6 ± 16.8	20.4 ± 11.8	37.3 ± 6.0	16.8 ± 4.7

Incremental boluses of AVP (1, 2.5, 5, 10, 25, 50, 100, 250, 500 and 1000 ng, 1 ng = 0.4 mU) were i.v. injected. Recording maximal effect, data were expressed in absolute difference from baseline ( $\Delta$  related to AVP dose).

**Data processing:** Best statistical curve fit (Fig. 1).

**Results:** Two linear curves for MAP, SVRen variations were observed (Fig. 1) with two different slopes (slope1 [doses from 1 to 25 ng AVP] = 0.17 & -0.12 and slope 2 [doses from 50 to 1000 ng AVP] = 0.01

**Figure 1**



& -0.02 respectively). EC50 (AVP dose inducing half of the response) was calculated from both curves: EC1<sub>MAP</sub> = 9 ng; EC2<sub>MAP</sub> = 662 ng; EC1<sub>SVRen</sub> = 13 ng; EC2<sub>SVRen</sub> = 349 ng. The shift from curve 1 to curve 2 occurred at 40 ng for MAP and 68 ng for SVRen of AVP. For DVRen, FI<sub>cort</sub>, FI<sub>med</sub> no linear relation was observed at low AVP doses. For higher AVP doses, similar negative slopes have been calculated: DVRen -0.01; FI<sub>cort</sub> -0.01; FI<sub>med</sub> -0.003.

**Conclusion:** MAP and SVRen react strongly to low AVP doses whereas DVRen FI<sub>cort</sub> FI<sub>med</sub> did not. At higher dose, FI<sub>med</sub> is better preserved than DVRen and FI<sub>cort</sub>.

**P147 Corticosteroids reduce inotrope requirements in hypotensive liver failure**

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**Introduction:** Corticosteroids improve haemodynamic profile in patients with septic shock [1,2]. Adrenal dysfunction is common in patients with acute hepatic necrosis (AHN) and haemodynamic instability [3].

**Methods:** We studied 13 patients aged between 19 and 63 years with liver failure defined by the presence of encephalopathy and hypotension requiring noradrenaline (NA) support despite adequate fluid resuscitation. Eleven patients had AHN and two decompensated alcoholic cirrhosis. Treatment with 300 mg hydrocortisone daily by infusion was started when BP required NA support. Baseline, incremental rise and peak cortisol following 250 µg intravenous synacthen were recorded, as were NA requirements and mean arterial BP for 24 hours before and 24 and 48 hours after the start of corticosteroids.

**Results:** NA was given for a median of 2 days prior to steroid therapy. Three patients survived, eight died and one underwent liver transplantation (OLT).

Of those who came off NA (seven), three required further NA and all died; four required no further inotropes of which three survived and one underwent OLT.

	After 24 hours steroids		After 48 hours steroids	
Withdrawal of noradrenaline	1/13	8%	7/12	58%
Reduced dose of noradrenaline	7/12	58%	9/11	82%

There were no differences between baseline, increment and peak cortisol between those who became inotrope independent and those who did not using the Mann-Whitney test.

**Conclusion:** Low dose corticosteroids improve the haemodynamic profile in patients with hypotensive liver failure and may improve survival. This may not be dependent upon endogenous adrenal function.

**References:**

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- Breigel et al: *Crit Care Med* 1999, **27**:723–732.
- Harry et al: *Int Care Med* 2000, **26**:S275.



were taken as reference values. Bias and precision were calculated as mean difference and standard deviation between the rebreathing and reference values in relation to the reference values. The mean difference between  $Co_{2,rb}$  and reference value was  $-3.6\%$  (bias), with a standard deviation of  $\pm 10.9\%$  (precision). The mean difference between  $QVA/Q_{t,rb}$  and reference value was  $17.5\%$ , with a standard deviation of  $14.0\%$  respectively;  $VO_2$  was determined with a bias of  $3.4\%$  and a precision of  $\pm 15.4\%$ . The mean difference between duplicate measurements related to their mean value accounted for  $3.5\%$ .

**Conclusion:** The present results suggest, that cardiac output, venous admixture and oxygen consumption may be reliably estimated by the proposed rebreathing technique.

Supported by INNOVISION, Denmark, providing the gasanalyser and the computer software for the calculation of pulmonary blood flow and oxygen consumption (AMIS 2001 system).

**P150 Pulmonary embolism detected by transesophageal echocardiography during cemented total hip surgery: the effects on hemodynamic, hemogasanalytic, and pulmonary shunt values**

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**Introduction:** During insertion of a cemented total hip arthroplasty, the rise of the intramedullary pressure in the femur, causes embolisation of fat and bone marrow into the pulmonary circulation. The goal of this study was to relate the embolic events observed by transesophageal echocardiography to the changes in hemodynamic, hemogasanalytic, and calculated pulmonary shunt values.

**Material and methods:** In this clinical trial entered 65 patients (>65 years). During the surgical period continually monitoring included ECG, measurement of invasive arterial pressure, pulseoximetric oxygen saturation, endtidal carbondioxid concentration as well as transesophageal echo-cardiography. A blinded observer graded embolic events from videotapes off-line after published criteria [1]. Hemogasanalysis was performed at defined points of the perioperative period. Preoperative clinical status of the patients was assessed according to the classification of the ASA. Pulmonary shunt-values were calculated with the formula of Ries *et al* [2].

**Results:** Cementation of the stem caused a cascade of fine emboli of less than 5 mm with an opacification of the right atrium and ventricle. In the same set of patients, after reduction of the hip joint, it was followed by macroemboli up to 3 cm (49 patients, 75%). No important embolic phenomena were observed during other surgical steps. Both embolic events were followed by changes in hemodynamics (increase in heart rate in 18%,  $P < 0.05$ ; hypotension more

than 20 mmHg in 62%) and blood gas parameters ( $paO_2$  decreased for 7.7%, 41.4 mmHg;  $P < 0.05$ ).  $PetCO_2$  decreased for a mean of 2.9 mmHg ( $P < 0.05$ ). Pulmonary shunt values increased after embolisation for a mean of 30.5% ( $P < 0.05$ ). They did not turn back to baseline values in the postoperative period in patients classified ASA III and IV. A significant correlation ( $P < 0.05$ ) was found between the clinical state before surgery and the duration and intensity of hemogasanalytic changes after insertion of the stem.

**Conclusion:** There is a correlation between embolic events quantified by transesophageal echo-cardiography and the grade of hemodynamic and hemogasanalytic changes of patients during cemented total hip arthroplasty. Patients with high anesthesiological risk can suffer severe cardiopulmonary complications from fat and bone marrow embolisation, that last even into the postoperative period and may cause intensive care treatment.

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**P151 Continous right ventricular monitoring under lysis with rt-PA in acute pulmonary embolia**

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**Introduction:** During postsurgical treatment on our ICU by six patients occurred an acute lung embolia Grade III/IV. Right after resuscitation we placed prior to angiography a Swan-Ganz-Catheter with  $SVO_2$  in a pulmonary arteria. Typical signs of a lung embolia like increased PAP, PCWP and decreased  $SVO_2$  and CO were obtained. We used the right-ventricular monitoring during lysis with rt-PA.

**Methods and patients:** Six patients with average age of 68.3 were monitored. Prior to embolia none of the patients had insufficient heart function or irregular heart rhythms. After resuscitation all patients showed increased  $PAP_{sys}$  higher than 50 mmHg, CI lower than 2.5 and  $SVO_2$  lower than 75%. All patients were treated with administration of rt-PA in fraction of 5 mg each 90 s. Success of lysis was shown by angiography and right-ventricular monitoring.

**Results:** By four patients there was a rapid normalisation after administration of highest 15 mg rt-PA. The result was to be seen first at angiography than on  $SVO_2$ . Cardiac parameters took 5–8 min to normalize. One patient needs administration of 40 mg rt-PA for normalization. One patient died during lysis without any remarkable normalization and after unsuccessful resuscitation.

**Discussion:** It was shown that continous right-ventricular monitoring is a capable feature for monitoring during lysis at thecritically ill patient. Even angiography is more sensitive the  $SVO_2$ -monitoring provides usefull information. If there is no way to have an angiography, right-ventricular monitoring is a valuable system. Placement of catheters can easily be performed and is even in unstable patients practicable.



**Table**

Changes	200 ml group 2 (n = 26)			50 or 100 ml group 1 (n = 42)		
	T0	T0-T10	T10-T20	T0	T0-T10	T10-T20
CI (l/min/m <sup>2</sup> )	3.86 ± 0.9	0.3 ± 0.09	0.11 ± 0.07	3.9 ± 0.9	0.12 ± 0.06	-0.36 ± 0.04*
SI (ml/m <sup>2</sup> )	42.3 ± 12.2	3.5 ± 0.8	1.9 ± 0.1	42.5 ± 10.4	1.74 ± 0.7	0.09 ± 0.56 *
ITBV (ml/m <sup>2</sup> )	867 ± 245	12 ± 11	40 ± 15	862 ± 124	61.3 ± 10.7	-18.6 ± 10.8*
MSAP (mmHg)	77.3 ± 11.6	4.9 ± 1	1.6 ± 0.5 *	73.3 ± 8.5	3.6 ± 0.5	-0.3 ± 0.1 *
CVP (cmH <sub>2</sub> O)	5.8 ± 2.8	1.9 ± 0.2	-0.07 ± 0.2 *	9.95 ± 1.75	1.2 ± 0.2	-0.05 ± 0.13 *

\* P < 0.05 changes from T10 to T20 vs changes from T0 to T10.

**Discussion:** In the 200 ml group, 10 min after the end of volume expansion, the increase in MSAP and CVP disappears, whereas ITBV, CI and SI increases remain unchanged and even shows for ITBV a trend toward increase. This suggest a post-expansion effect which is not observed on CVP values. In group 2 who had a higher baseline CVP and a lower volume expansion, the increases in MSAP, CVP, ITBV and SI observed at the end of volume expansion disappear 10 min later, suggesting the absence of a post-expansion effect when the baseline CVP is high and/or the volume infused is low.

**Conclusion:** ITBV measurement may be a useful guide for the evaluation of volume expansion and post-volume expansion effect when baseline CVP is low and/or volume expansion is 200 ml.

**Reference:**

1. Weil MH, Henning RJ: **New concepts in the diagnosis and fluid treatment of circulatory shock.** *Anaesth Analg* 1979, **58**:2.

**P155 Usefulness of an expert software for hemodynamic evaluation: results of the HEMODYN™ Survey**

**P Squara**

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In an earlier study, we clinically validated an expert computer program (Hemodyn™) designed to assist in interpreting pulmonary artery catheterization data [1]. The present study in seven European centers assessed the influence of Hemodyn™ on the therapeutic strategies of experienced residents.

Patients with a pulmonary artery catheter inserted were included in the study if they had hemodynamic disorders unresponsive to standard therapy and/or if their condition raised a therapeutic problem that PAC was expected to solve. Each resident examined and collected PAC data from the study patients in their center, under the supervision of the local study coordinator. Then, the resident completed a data form and made one or more choices among the diagnostic possibilities listed on the form. The same PAC data were then entered into the software. Based on the software's diagnostic evaluation, the resident could either maintain or change his or her diagnosis and treatment. Finally, a senior intensivist accepted or rejected the resident's final diagnosis and treatment plan. Agreement between the residents' initial evaluation and the software's evaluation was poor (kappa < 0.6).

Sixty-four hemodynamic profiles from 44 patients were used for the study covering a broad spectrum of critical situations. Before computer assistance, the residents suggested at least one treatment change (to improve hemodynamics) in 83% of patients and a mean of 2.2 treatment changes per patient. After computer assistance and evaluation by the local study coordinator, the residents changed their treatment suggestions in 94% of patients, making a mean of 1.9 changes per patient. Therapeutic agreements before and after computer assistance are shown in the Table (\* P < 0.05 vs other comparisons).

After computer assistance, agreement was very good between residents and seniors and between seniors and the software. Com-

**Table**

	Number of disagreements	Kappa coefficient
Before computer assistance		
Resident-computer	5.7 ± 2.2	0.64 ± 0.14*
After computer assistance		
Resident-computer	1.9 ± 2.0	0.88 ± 0.12
Resident-senior	1.2 ± 1.7	0.92 ± 0.10
Senior-computer	0.9 ± 1.2	0.95 ± 0.07

puter assistance led the residents to change at least one suggested treatment in 63% of cases; in 55% of cases, the change was not minor. Analysis of the points of disagreement showed that the residents often underused fluids and vasodilators: these two points contributed 42% of changes after computer assistance. In only 20% of the cases in which the patient received a vasodilator was this treatment suggested initially by the resident. For the other treatments, the proportions of inappropriate use and inappropriate absence of use were similar.

Expert software capable of helping residents to interpret PAC data properly may improve the quality of care given to critically ill patients.

**Reference:**

1. Squara P, Dhainaut J, Lamy M, Perret C, Larbuisson R, Poli S, Armanidis A, de Gournay J, Bleichner G: **Computer assistance for hemodynamic evaluation.** *J Crit Care* 1989, **4**:273-282.



itorization for their treatment. A Swan-Ganz catheter (Baxter Healthcare 131F7) was placed on all by the usual form. The esophageal echo-Doppler (Hemosonic 100, Arrow International) was placed via oral/nasal passages and simultaneous measurements of CO were given, with interval of 3 min between each. The investigator was blinded by the CO by Swan-Ganz. The therapeutic decision were guided by the value of the SG catheter. For the statistical analysis we will the paired samples for patients and time of measurement. We used software SPSS 8.0. We made a analysis correlation for Pearson and a comparison between group with 'U' Mann-Whitney for a significant statistic between populations of  $P < 0.05$ . We obtained difference of the medications by descriptive statistic, the inferential analysis was made with IC 95%.

**Results:** We studied 12 patients; 3 of them it was imposible insert the probe, in 4 patients it was difficult to get a well measurement because the lack of vision of diameter aorta and correct flow

curves. And in 5 patients we made a total of 38 measurements with each of the described methods, for a total of 76 measuments. With the SG catheter the mean CO were  $6.94 \pm 2.1$  l/min (IC 95% 6.2–7.2, range 3.1–11.2). The measurements of aortic blood flow with the esophageal echo-Doppler were  $5.14 \pm 1.9$  l/min (IC 95% 4.5–5.7, range 1.8–8.5). The measurements of CO with esophageal echo-Doppler were  $6.90 \pm 2.2$  l/min (IC 95% 6.17–7.63, range 2.9–10.5). The comparison between groups was NS. The Pearson correlation between SG and echo-Doppler ABF was 0.838 ( $r^2 = 0.70$ ), between SG and CO by echo-Doppler was 0.819 ( $r^2 = 0.67$ ).

**Conclusion:** The preliminary report showed that the correlation between the measurements of ABF with esophageal echo-Doppler is good. This new method offers advantage that are minimally invasive and quickness in obtaining results; however it requires replacing the esophagus transducer every time the patient is mobilized and not in all patients could be used.

#### P159 Accuracy of blood volume measurement using an integrated fiberoptic monitoring system in septic shock

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**Objectives:** To compare the accuracy of an integrated fiberoptic monitoring system in measuring blood volume (BV) with standard method using chromium-51-tagged erythrocytes in septic shock.

**Design:** Prospective animal laboratory study.

**Measurement and main results:** Twenty anaesthetised, and mechanically ventilated pigs ( $20.9 \pm 1.9$  kg) were investigated over a period of 8 h. Septic shock was induced with faecal peritonitis (1 g/kg body weight autologous faeces). A central venous catheter was used for the injection of the indicator dyes. BV was measured by detecting indocyanin green by reflection densitometry using a fiberoptic thermistor tipped catheter inserted into right carotid artery (4F PV 2024, Pulsion Medical Systems). Haemodynamic treatment scheme was aimed at maintenance of a central venous pressure of 12 mmHg. Data were analysed using Bland-Altman analyses, linear regression and correlation. Forty data pairs of

simultaneous BV-measurements were yielded during haemodynamic consistency with a mean BV measured by integrated fiberoptic monitoring system of  $66.6 \pm 20.3$  ml/kg (range: 24.5–122.6 ml/kg). Mean BV measured by chromium-51-tagged erythrocytes was  $76.1 \pm 17.9$  ml/kg (range: 49.7–121.6 ml/kg). Linear regression equation was: BV by integrated fiberoptic monitoring system =  $0.65 \times$  BV: chromium-51-tagged erythrocytes + 17.6;  $r = 0.57$ ,  $P < 0.01$ . The mean bias was 9.6 ml/kg (95% confidence interval: 3.7–15.4 ml/kg), with limits of agreement of –26.5 to 45.6 ml/kg and a precision of 16.8 ml/kg.

**Conclusion:** In this model of porcine septic shock we could show a significant correlation in blood volume measurement between fiberoptic monitoring system and chromium-51-tagged erythrocytes. The relatively wide limits of agreement might be due to pronounced circulatory alterations including slow mixing compartments, prolonged equilibration and sequestration in septic shock.

#### P160 Patterns and kinetics of cardiac troponin I and T after coronary artery bypass grafting

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**Objective:** Cardiac troponins have shown to be specific markers of myocardial injury. Aim of this prospective study was to compare patterns and kinetics of troponin I and T after Coronary Artery Bypass Grafting (CABG) with or without perioperative myocardial infarction (PMI).

**Methods:** 119 patients (male/female: 96/23, age  $64 \pm 10$  years) underwent first-time elective CABG. Preoperative mean ejection fraction was  $55.8\% \pm 15.6\%$ . The mean number of grafts was  $3.1 \pm 1.1$ /patients, in 85.7% the internal mammary artery was used. Cardiac troponin I and T levels, total creatine kinase and creatine kinase isoenzyme MB activities in the serum were measured before operation, at arrival on the ICU and 6, 12, 24, 48 and 120 hours after declamping. Twelve-lead electrocardiograms were recorded preoperatively and at day 1, 2 and 5. The relationship between perioperative data and postoperative cTnI and cTnT levels were statistically identified.

**Results:** Two patients died due to refractory myocardial failure early postoperative. For further evaluation patients were grouped according to their postoperative ECG (group I: Patients without PMI,  $n = 107$ ; group II: Patients with PMI,  $n = 10$ : six of them with Q-wave and four of them with non-Q-wave PMI). Best cutoff values were calculated with ROC analysis for cTnI (8.35 µg/l) and for cTnT (0.768 µg/l). Serum concentrations of cTnI, and cTnT were preoperatively normal and significantly increased after surgery in both groups. In both groups cTnI reached its medium peak level after 24 h: (group I:  $cTnI_{\text{median peak}} = 2.7$  µg/l, 95% CI: [2.1, 3.2]); group II: 70.5 µg/l). cTnT reached its medium peak level in group I without PMI after 48 h ( $cTnT_{\text{median peak}} = 0.298$  µg/l, 95% CI: [0.254, 0.354]) in group II with PMI not until 120 h (3.0 µg/l). In Group II serum level of both troponins remained considerably high at 120 h ( $cTnI_{\text{median}} = 10.75$  µg/l,  $cTnT_{\text{median}} = 3$  µg/l).



**Conclusion:** In acute coronary syndromes, the use of platelet glycoprotein IIb/IIIa blocker tirofiban could effectively reduce GP IIb/IIIa receptor activity, enhance myocardial perfusion, improve

salvage of myocardium, reduce residual ischemia and improve short term outcome.

**P163 Early stenting vs conservative treatment after thrombolysis in acute myocardial infarction: results of a randomized trial**

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Thrombolysis (T) in acute myocardial infarction (AMI) is limited by TIMI III-flow rates of 60% and reocclusion of the infarct related artery in 5 to 10%. Prior studies showed no benefit of PTCA following T in AMI. Recent studies have demonstrated superiority of primary stenting versus PTCA alone in AMI.

We are conducting a multicenter, randomized, prospective, controlled trial to compare the strategy of early coronary stenting (group A) with conservative treatment (group B) following T within 12 hours after onset of AMI. Patients of group A are transferred to the interventional center within 6 hours after T for coronary angiography including stenting of the infarct related artery. Group B has elective coronary angiography after 2 weeks. Primary endpoint is a combined endpoint of death, reinfarction, and target lesion revascularization.

So far (November 2000) 176 pts have been randomized. There are no significant differences regarding sex, age, infarct localization, risk factors, ck-elevation and cardiogenic shock. Mean follow-up time is 158 ± 97 days.

**Results:**

	Group A (n = 71)	Group B (n = 75)	P value
Combined end point	22.5%	37.3%	0.038
Death	5.6%	10.7%	ns
Reinfarction	2.8%	2.7%	ns
Target lesion revascularization	16.9%	25.3%	ns

Bleeding complications occurred in 11% of pts in group I vs 8% in group II (ns).

**Conclusion:** Early stenting after T in AMI is safe. This preliminary data indicate a clinical benefit by this approach compared to conservative treatment after T in AMI.

**P164 Myocardial infarction on elder 80 years old patients: women handicap**

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**Objective:** To analyze epidemiology and evolution differences between sex on elder 80 years old patients with myocardial infarction.

**Methods:** It is a retrospective analysis. Were included all patients elder 80 years admitted from 1-1-1990 to 31-10-1998 with a myocardial infarction. We used  $\chi^2$  test and  $P < 0.05$  to establish a statistically significant association.

**Results:** Were included 211 patients, 50.71% males. Myocardial infarction was anterior 71.09% cases and 81.04% patients developed Q wave. Pathological antecedents were: arterial hypertension 38.38%, coronary disease 33.17% and diabetes mellitus 26.54%.

Patients developed next complications: 13.74% supraventricular tachycardia, 6.16% complete atrioventricular block, 58.76% left ventricular failure, 35.07% cardiogenic shock and dead 40.28%.

Women had more antecedents of diabetes mellitus (32.69% vs 20.56%,  $P < 0.05$ ), and developed more complete atrioventricular block (9.61% vs 2.80%,  $P < 0.05$ ) and exitus (47.11% vs 33.64%,  $P < 0.05$ ).

There was no statistically significance to compare pathological antecedents of arterial hypertension (38.46% vs 38.31%) and coronary disease (34.61% vs 31.77%), localization anterior (70.19% vs 71.96%), development of Q wave (80.76% vs 81.30%) and the development of left ventricular failure (59.61% vs 57.94%), cardiogenic shock (36.53% vs 33.64%) and supraventricular tachycardia (16.34% vs 11.21%).

**Conclusions:** Women have a higher mortality rate and more complete atrioventricular block.

**P165 Epidemiology of gender-related differences of arrhythmias in the ICU**

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**Background:** Studies have revealed sex-specific differences in the electrophysiology with respect to rate, sinus node function, refractory periods, conduction time of accessory pathways and the type and duration of arrhythmias. However, data on sex-specific differences of arrhythmias are lacking in critically ill patients.

**Aim of the study:** From November 1996 until July 1999 a prospective study was conducted in the ICU of a university hospital

to assess sex-specific differences in all consecutive tachyarrhythmias.

**Results:** 278 episodes of tachyarrhythmia (wide QRS complex  $n = 168$ , narrow QRS complex  $n = 108$ , ventricular fibrillation  $n = 2$ ) were recorded in 119 patients (83 m, 36 f, age  $65 \pm 12$ , APACHE II  $19.6 \pm 18$ ). There was no significant sex-specific difference ( $P = 0.49$ ) in the incidence of wide QRS complex tachycar-



**Results:** Only 8% of hospitals have a dedicated telephone number for the emergency team. In 44% of cases a beeper is used, in 40% of cases the personnel call directly the ICU. In the remaining 8% of cases the Anaesthesiologist on duty is called. Only in 27% of cases the beeper allows bi-directional communication. In 42% of cases the number corresponding to the beeper is always the same, while in the remaining cases it may change even daily or from day to night.

The ALS team includes one Anaesthesiologist and one nurse in 20% of cases, one Anaesthesiologist and one optional nurse in 40% of cases and only one Anaesthesiologist in 40% of cases. The ALS equipment carried by the crash team includes a monitor-defibrillator, intubation equipment and drugs in 12% of cases, intubation equipment with drugs in 52% of cases and no equipment at all in 36% of hospitals. In these last cases, the crash team relies on the equipment available in the wards, but only 75% of them have protocols to check it regularly. In 20% of hospitals there is a defibrillator in every ward, in 24% there is one defibrillator per floor and in 56% less than one per floor. In 79% of these last cases, the crash team does not carry the defibrillator, which has to be found by the personnel in other ward of the same floor or in other floors of the hospital, and has to be carried by hand or by elevator. In two hospitals a transthoracic emergency pacemaker is not available; in only one hospital the pacemaker is included in the crash cart carried by the emergency team; in the remaining cases, it is available, but it has to be found in CCU, ITU or OR.

Fifty-six percent of hospitals do not have standard ALS protocols; 28% have them, while in 16% of hospitals some providers use them, others do not. Only in two hospitals the Utstein style for reporting cardiac arrest is used.

Despite the fact that the majority of hospitals have a regular BLS training programme for the personnel, in 88% of hospitals the emergency team members complained of insufficient CPR training of general ward personnel, on which they rely to perform ALS on arrival.

The time for arrival in the farthest ward of the hospitals ranges from 30 s to more than 15 min (average 3 min 30 s ± 4 min 27 s SD). The majority of hospitals are on a single building with less than six floors, but seven of them have separate buildings, and two have 11 floors.

**Conclusions:** The majority of hospitals in Rome do not have a dedicated telephone number for emergencies and do not use international ALS protocols for cardiac arrest treatment. Only in 12% of cases the crash team carries a complete ALS equipment on the scene, while the majority of ALS teams prefer to move with a limited equipment, relying on materials available on the wards. However, only in 20% of hospitals there is a defibrillator in every ward. In the majority of hospitals there is regular training on CPR for general ward personnel, but the majority of emergency team members complaint of insufficient CPR training of general ward personnel.

**P168 Sudden death resuscitation announcing acute myocardial infarction: early outcome and mortality factors**

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Between January 1999 and June 2000, we analysed in a prospective study patients admitted for sudden death with positive resuscitation (SD) after acute myocardial infarction (AMI). All patients were assigned to undergo immediate PTCA.

About 588 AMI were recruited during this period, and 38 patients (6.46%) have presented a SD. Mean age of patients of this group is 65.3 years ± 12.3 (37–88). Sex-ratio is 3/1. Patients with Killip grade over III represent 44.7%, and cardiogenic shock is present in 47.3%. Myocardial localisation of infarction is anterior in 60.5%, and inferior in 34.2%. The culprit lesion interests left main coronary artery in 7.9%, LCA in 39.4%, circumflex in 5.3%, and right coronary in 42.1%. An angiographic occluded vessel is present in 94.7%, and we have one-vessel disease in 50.0%, two-vessels disease in 15.8% and three-vessels disease in 34.2%. Successful procedure after PTCA is obtained in 93.5%, with stent implantation in 71.0% of the cases. 53.6% patients are under mechanical ventilation (MV), 31.6% have a cardiac pump assistance by IABP, and 50.0% have β-mimetic medication. In-hospital mortality rate is 31.6%, among which 13.2% in the first day. If we analyse the two groups with or without cardiogenic shock, we obtain:

	Cardiogenic shock (n = 18)	Without cardiogenic shock (n = 20)	P
Successful procedure	92.8%	94.1%	ns
MV	83.3%	25.0%	< 0.01
IABP	44.4%	20.0%	< 0.01
β-Mimetic medication	83.3%	20.0%	< 0.01
In-hospital mortality	66.7%	0.0%	< 0.01
First day mortality	27.8%	0.0%	< 0.01

**Conclusion:** Mortality rate after successful resuscitation for sudden death during acute myocardial infarction is depending on the haemodynamic status at admission. In presence of cardiogenic shock, two thirds of patients will die. Without shock, no death is observed.

**P169 Quality of life after cardiac arrest – evaluation with EQ-5D**

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**Background:** Evaluation of outcome after cardiac arrest focuses mainly on survival. Survivors of cardiac arrest end up in different states of health and survival alone may not be a sensitive measure for successful cardiopulmonary resuscitation (CPR).

**Objectives:** To evaluate health-related quality of life (HR-QOL) of cardiac arrest survivors with EQ-5D, a generic instrument developed by the EuroQol group.



**P172 A report on emergency service by ambulance with doctor on board of the Emergency Department of Prato, Italy**

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In the urban area of Prato (population 172,473 01.01.2000), the Emergency Department runs three ambulances with doctor on board coordinated by the emergency number 118. Here we analysed the typology of 798 consecutive services carried out by our ambulance from 01.08.1998 to 31.01.1999. Twenty-eight services (3.5%), canceled for various reasons, were excluded by the statistical analysis. 770 patients were visited; 402 (52.2%) were males and 368 females (47.8%); males were significantly younger than females ( $53.8 \pm 24.2$  vs  $59.9 \pm 17$  years,  $P = 0.001$ ). 75.5% of services concerned non-traumatic cases, 17.9% traumatic cases and 6.6% transfers between hospitals. The services for non-trauma group, concerned dyspnoic symptoms (15.7%), cases of lipothimia (15.2%), chest pain (11.1%), mental disorders (7.9%), cerebrovascular pathology (6.8%), abdominal pain (4.4%), use of psychotropic substances (4.3%), epileptic and not epileptic convulsions (3.5%). Metabolic disorders (diabetes, hypoglycemic crises, hyperthyroidism) accounted for 2.4% of cases, hypertensive crises 2.4%, tachycardia 2.2%, support to patients with terminal

cancer 2.2%, vertigo 2%, allergies 1.1% and obstetric pathology 0.9%. 1.9% of cases required cardiopulmonary resuscitation. 15.9% was a miscellany of services including poisonings, migraines, haemorrhages, flu syndromes. Trauma cases were road accidents (64.7%), falls (27.2%), work-related accidents (4.4%) and aggression (3.7%). 75.8% of patients were admitted to hospital; the others (24.2%) were not urgent or refused hospitalisation. According to Sonsin *et al* [1], the most frequent services were related with cardiorespiratory pathologies, cases of lipothimia and trauma so as the % of non-hospitalised patients (24.2% vs 23%). The % of our traumatic cases is like that found by Brismar *et al* [2] in Sweden urban areas (17.9% vs 20%). Cases of cardiopulmonary resuscitation were 1.9%, similar to 1.8% found by Hu *et al* [3]. Further studies are in progress.

**References:**

1. Sonsin *et al: Aust Fam Physician* 1989, **18**: 233-234.
2. Brismar *et al: Ann Emerg Med* 1984, **13**: 1037-1039.
3. Hu *et al: J Formos Med Assoc* 1995, **95**: 2s 87-93.

**P173 Impact of interhospital intensive care unit transfers**

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Duke University Medical Center is a tertiary referral level one trauma hospital with a 16 bed surgical intensive care unit (SICU) averaging 1100 admissions per year. SICU patients include trauma, gastrointestinal, vascular, transplant, urology, orthopedics, otolaryngology and gynecology services. SICU admissions consist of postoperative, trauma via emergency room, intrahospital floor transfer and interhospital direct transfer. Transfers from outside institutions are often critically ill patients who have a significantly prolonged length of stay (LOS) and use vast amounts of resources.

All SICU admissions were compared with interhospital transfers for the last 3 fiscal years.

Interhospital transfers account for 5% of ICU admissions but 10% of total costs. These patients generate increased cost per case of over \$11,000. The ICU LOS is significantly increased from 3.3 days for all patients to 7.5 for transfers. Likewise, the SICU mortality of these cases is significantly increased from 7.3% to 28.6% and hospital mortality from 9.6% to 33.5%

We continually review our practices to dedicate our resources where they do the most good. We must continue to take salvageable, critically ill patients in transfer early in the course of their illness when appropriate SICU management can favorably influence outcome. In our experience, interhospital transfer of critically

Fiscal year	Total admits	ICU average LOS (days)	ICU mortality (%)	Hospital mortality (%)
97	1175	3.4	8	10
98	1044	3.5	7	9
99	1039	3.1	7	10

Fiscal year	Total transfers	Transfers ICU average LOS (days)	ICU mortality for transfers (%)	Hospital mortality for transfers (%)
97	40	7.5	32.5	37.5
98	52	8.2	23.1	32.7
99	69	6.7	30.4	30.4

ill patients identifies a group with overall poor prognosis. There is a need for a means to evaluate and appropriately triage outside referrals in order to maximize clinical outcomes. Analysis of these transfers is underway to identify prospective predictors of potentially futile care to allow better utilization of available resources.

**P174 Hypothermia is a marker for adequacy of resuscitation in severe truncal injury**

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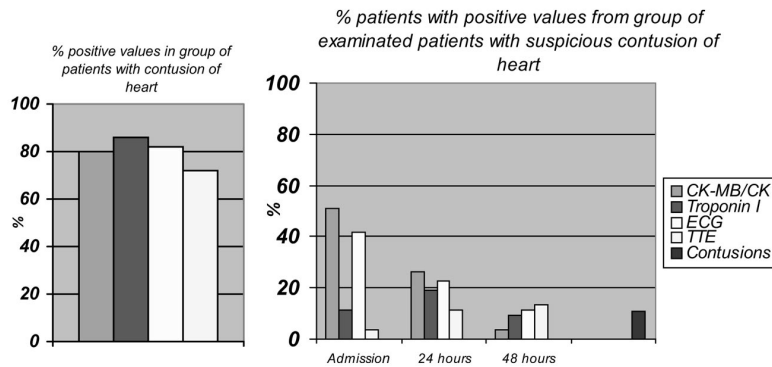
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**Introduction:** Hypothermia after massive resuscitation is known to lead to coagulopathy, myocardial depression, and a depressed immune response. Attempts at prevention or correction of hypothermia in the perioperative period frequently fail in spite of uti-

lizing aggressive rewarming modalities. We hypothesized that the response to rewarming is directly correlated to control of bleeding and adequacy of resuscitation.



Figure



transesophageal echocardiography) is still not fully used and in many hospitals is not accessible at all.

**Methods:** The group of 101 patients hospitalized in traumatology and general ICUs (1998–2000) with diagnosis: multiple trauma (including trauma of chest) or isolated thoracic trauma. The only including criterion – admission to our ICU within 24 hours from the injury. We have tried to determine the incidence of heart contusion and to compare all accessible methods of diagnosis and its importance. The aim of this study was to assess the validity of diagnostic procedures and possibility of its simplification.

**Results:** The incidence of heart contusion in our group was 11.8%. See the Figure.

**Conclusion:** The Figure demonstrates that validity of CK-MB/CK-total ratio is very low. Also changes of ECGs are not specific. Values of troponin I and results of TTE are mostly correlating and are the most conclusive for diagnosis. For these patients assessment of CK-MB/CK is useless and brings higher economic charges.

**P177 Long-term follow up of traumatic multiple rib fractures**

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We investigated the prognosis of patients with multiple rib fractures for 2 years after discharge from the hospital, and whether the pain control management during the initial respiratory care influence the respiratory function or neurological findings. The ethical committee in Fukushima Medical University approved this study.

221 patients with chest blunt trauma were admitted in our hospital from 1990 to 1996. We found 61 cases that had more than 4 rib fractures with or without pulmonary contusion. The subjects that were 51 patients who had traffic or some other accidents can be followed by phone and investigated. Forty-one cases were received mechanical ventilation for from 5 to 18 days. All of 51 cases were administrated oxygen and drugs that controlled the chest pain. Nineteen of 51 patients (EPI group) were undergone the epidural anesthesia with xylocain for the first 7 days (5–9 days). The other patients (non-EPI group) were administrated narcotics or non-steroid anti-inflammatory agents.

Measurements were arterial blood gasses, respiratory functions, chest X-ray, physical and neurological findings. The subjects were 48 patients who had traffic or some other accidents. Respiratory care was required in 20 cases for  $5 \pm 18$  days. PaO<sub>2</sub>, PEFr (peak expiratory flow rate) were gradually increased after discharge. The improvement was not associated between both of pain controls. Chest deformities were seen in 12 of 51 cases. Râle sound was audible in three cases. Neurological findings (spontaneous pain, tenderness, hyperesthesia, sensory disturbance) were found less frequent in patients who were treated under epidural anesthesia. The epidural anesthesia sometimes induced hypotension, however, fluid resuscitation improved. The epidural anesthesia was better than the other narcotics or anti-inflammatory drugs from the points of neurological prognosis. Sensory disturbance is not associated with chest deformities but pain control.

Epidural anesthesia was one of the useful pain management to avoid neurological complications after long-term of multiple rib fractures of chest trauma.

**P178 Decompressive craniectomy as an ultimate therapy for post-traumatic brain swelling**

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**Introduction:** Decompressive craniectomy can be the ultimate therapeutic possibility of severe traumatic brain edema. Indications, surgical techniques and results are presented.

**Patients and methods:** Seven patients with severe head injuries, 5 girls (8–18 years), 2 boys (11–16 years) and increased intracranial pressure not responding to conventional treatment were



Treatment group (n)	PMV oedema (µm <sup>2</sup> )	Endothelial area (µm <sup>2</sup> )	Luminal area (µm <sup>2</sup> )
Septic (5)	80.20 ± 5.347	16.27 ± 2.139	30.49 ± 2.197
Non-septic (5)	26.20 ± 2.666	12.34 ± 1.258	20.56 ± 1.063
Dopexamine/septic (5)	39.80 ± 5.546	16.11 ± 1.294	26.53 ± 1.163
ICI 118,551/septic (4)	62.20 ± 6.339	17.75 ± 1.844	24.99 ± 0.709
Methoxamine/septic (5)	58.26 ± 5.944	26.28 ± 2.581	23.54 ± 1.952
Methox/non-septic (4)	60.80 ± 11.785	23.00 ± 1.080	20.83 ± 0.994
Dopex/methox/septic (4)	43.23 ± 7.655	23.00 ± 2.836	26.75 ± 4.473

non-septic pigs. The mean cerebral microvessel lumen area was significantly larger in septic than in non-septic pigs ( $P = 0.012$ ). None of the drug treatments used resulted in a mean lumen area significantly different from that of non-septic pigs.

Therefore, sepsis resulted in PMV oedema, which was protected against by dopexamine treatment. Conjoint methoxamine treatment did not impair this protective effect of dopexamine in septic pigs,

but methoxamine alone caused PMV oedema formation in non-septic pigs.  $\beta_2$  adrenoceptor blockade did not affect the formation of PMV oedema in sepsis. Methoxamine treatment resulted in the swelling of microvessel endothelial cells in both septic and non-septic pigs, but conjoint dopexamine treatment did not prevent this swelling. These results suggest that  $\beta_2$  adrenoceptor stimulation is beneficial and  $\alpha_1$  adrenoceptor stimulation is detrimental to the treatment of septic encephalopathy.

**P181 Prognostic features and outcome of surgically treated aneurysmal subarachnoid haemorrhage**

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**Introduction:** Aneurysmal subarachnoid haemorrhage (SAH) is a challenging pathology which remains a cause of considerable morbidity and mortality. We attempted to classify patients with aneurysmal SAH according to prognostic estimates, identifying cases with a certain risk profile.

**Method:** Retrospective chart review of 80 SAH patients admitted in our ICU following surgical ligation of cerebral aneurysm. The following clinical details were recorded: age, sex, ASA physical status (ASA-PS), timing of angiography and surgical treatment, pre-operative Glasgow Coma Scale, Hunt–Hess grade, admission angiographic features, length of sedation and ICU stay. Functional outcome was assessed by Glasgow Outcome Scale (GOS) upon ICU discharge. For statistical purpose two subgroups according to outcome were identified: a) GOS 1–3 (unfavorable outcome) and B) GOS 4–5 (good recovery). Statistical analysis was performed using Students' *t*-test and  $\chi^2$  analysis.

**Results:** History of longstanding hypertension was recorded in 45% ( $n = 36$ ) of the cases, while cigarette smoking in 48.7% ( $n = 39$ ). Male to female ratio was 1.3:1. Early operation (within the first 3 days after the bleed) was performed 8.7% ( $n = 7$ ) of the cases with a mortality rate of 43% ( $n = 3$ ). Calcium antagonists (nimodipine) were administered to 90% of the patients in the study group.

In addition early hints for poor neurological outcome were also acquired from ASA-PS, pre-operative Hunt–Hess, evidence of

**Table**

	GOS 1–3 ( $n = 20$ )	GOS 4–5 ( $n = 60$ )	<i>P</i>
Age (years)*	55.8 ± 9.9	50.2 ± 10.8	< 0.05
Time to angiography (days)*	11.8 ± 9.4	12.3 ± 8.2	ns
Time to surgery (days)*	24.1 ± 17.6	25.8 ± 14.4	ns
GCS*	11.1 ± 3.8	14.2 ± 0.7	< 0.001
Sedation in ICU (days)*	4.5 ± 4	0.8 ± 0.4	< 0.001
ICU stay (days)*	15.2 ± 21.9	2.3 ± 5.6	< 0.001

\* Mean ± SD.

angiographic spasm and presence of severe brain swelling intra-operatively ( $\chi^2$ -test,  $P < 0.001$ ). Overall mortality rate was 5% ( $n = 4$ ).

**Conclusion:** Our results indicate that age, neurological status upon admission, pre-existing medical condition, evidence of vasospasm and cerebral oedema are the most important determinants of outcome for patients with aneurysmal SAH, regardless of treatment utilized.

**P182 Intracranial pressure monitoring in patients with subarachnoid haemorrhage**

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**Introduction:** ICP monitoring is part of intensive care management of subarachnoid hemorrhage patients (SAH). However, patterns of

ICP and their relationship with cerebral ischemia or quality of outcome have not yet been clearly defined.



antipyretic effect of DCF. NSAIDs were associated with deeper CPP reductions and not all febrile episodes were completely

managed. We, preliminary, concluded that DCF at low dosage was advantageous and effective.

**P185 Plasma sodium and sodium balance following sub-arachnoid haemorrhage (SAH)**

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**Introduction:** Following SAH a massive diuresis, natriuresis and hyponatraemia may occur, termed 'cerebral salt wasting'. The aetiology of this condition is unclear and its existence has been questioned [1,2]. This study aimed to document sodium balance in a patient cohort treated by the same protocol following SAH, hoping to further elucidate the mechanism of this condition.

**Patients and methods:** Prospectively entered data from a computerised database of SAH patients admitted to an eight-bedded neurosurgical ICU were analysed to assess the correlation of sodium flux with the course of the disease. For up to 18 consecutive days plasma sodium was measured, 24-hour urinary collections were analysed for sodium loss and the daily intravenous sodium intake was calculated from the charted intravenous fluids.

Patients underwent check cerebral angiography on day 5–7 following admission or earlier if there was clinical evidence of vasospasm. Papaverine was administered to patients with vasospasm who then underwent further angiography and hypertensive therapy with noradrenaline. The total doses of papaverine and noradrenaline administered were used as markers of the severity of spasm.

**Results:** Data from 39 patients was analysed. In 15 patients urinary sodium excretion and hence sodium balance could be calculated for 8 or more days. The median sodium input was 360 mmols/day (range 15–4868), see Figures for daily plasma sodium and sodium balances.

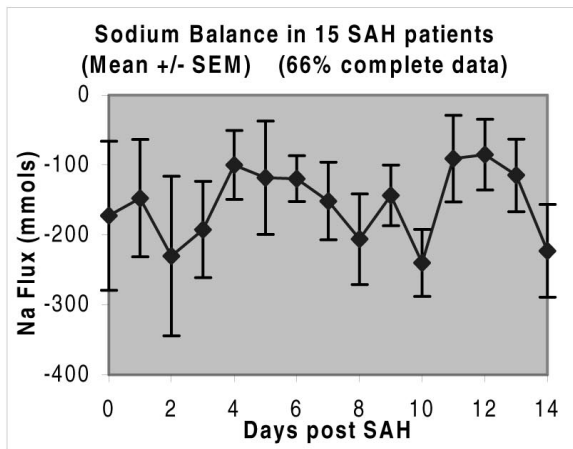
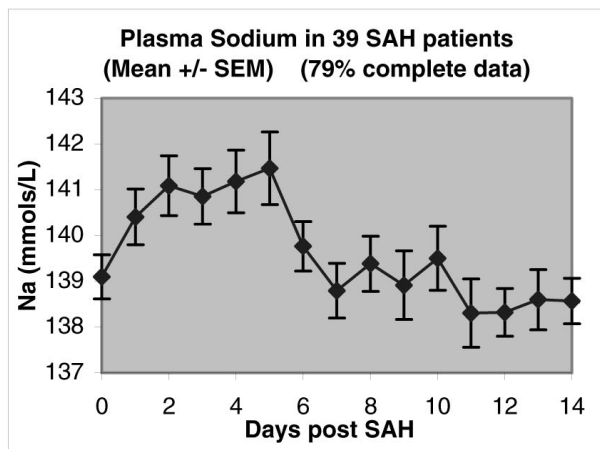
Measured sodium balance was consistently negative in this population. There were no significant differences between high and low papaverine and noradrenaline groups.

**Conclusions:** In this limited dataset, following SAH and saline loading, plasma sodium increased in these patients but there was no obvious natriuretic phase. Cerebral salt wasting was not clearly demonstrated by these data.

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**Figures**



**P186 Secretion pattern of melatonin after head injury**

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**Introduction:** The circadian rhythm of melatonin secretion is a most reliable biochemical marker of the endogenous biological rhythm of the organism. Plasma melatonin levels are low during the day (1–5 pg/ml) and normally increase to about 50–100 pg/ml at night. The objective of the present study was to investigate any potential disturbances of melatonin's secretion pattern after head injury.

**Materials and methods:** The sample consisted of eight subjects (seven males and one female) admitted at the Intensive Care Unit after head injury. Mean age ± SD of subjects was 41 ± 17.91 years, mean APACHE II Score was 15.5 ± 3.75, mean Glasgow Coma Score was 7.11 ± 3.14, mean duration of stay in the ICU was 23.44 ± 12.23 days, and mortality rate was 11.1%. All



studied by TCD and at the same time EEG recording was performed. Twenty-five of 30 patients clinically presented with brain death. Undetectable flow despite accurate bone window or the demonstration of isolated systolic spikes or diastolic reverse flow without forward flow in TCD examination and isoelectricity in EEG recording were accepted as confirmation of brain death. TCD examination was repeated in clinically brain death patients in whom TCD demonstrated initially systolodiastolic forward flow or diastolic forward flow and reverse flow in middle cerebral artery (MCA).

**Results:** Five of 25 patients who were brain death excluded from the study because of the lack of accurate bone window in TCD examination. In only 9 (45 %) of 20 patients who were clinically brain dead, three wave-form patterns that confirmed brain death were seen at the initial of TCD examination. Various wave-form patterns were detected in 11 patients in the first examination. Repeated TCD examination of 9 of these 11 patients who initially had forward flow patterns later demonstrated flow patterns which confirmed brain death. In 2 of 11 patients TCD examination could not be reperformed because of sudden cardiopulmonary arrest. In one of 5 patients who

were not clinically brain death, TCD showed systolic spikes and no diastolic flow. The sensitivity and specificity of TCD for brain death were found to be 45% and 80%, respectively.

**Discussion:** TCD is a simple and noninvasive imaging modality that is easily performed at the patient's bedside in order to evaluate cerebral perfusion. A number of authors have presented very similar results concerning the specificity (100%) and sensitivity (91–100%) of this method [1,2]. However, we found 11 (55%) false negative and one false positive (20%) results which are higher rates than the results of previous studies [1,2]. Finally, in our study we interestingly found that the specificity and sensitivity of TCD examination in confirming brain death were lower than in previous studies.

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**P189 A prospective multicenter study of ICU acquired paralysis**

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**Objectives:** Although the incidence of electrophysiological and muscle histological abnormalities in ICU patients has been largely described, the clinical incidence of ICU acquired paralysis (ICUAP) remains poorly explored. The objective of this study was to assess clinical incidence, risk factors and outcome of ICUAP.

**Method:** All consecutive patients without pre-existent neuromuscular disease were daily screened for awakeness in the 5 participating ICUs after 7 days of mechanical ventilation (MV). The first day patient was considered awake (based on a specific awakeness scale) was Day 1. Patients with a neuromuscular score (NMS) < 48 (on a scale ranging from 0, totally paralyzed to 60, normal muscle strength) on Day 7 were considered as having ICUAP. These patients underwent an electrophysiologic (EP) examination within the next 72 hours. Patients with persistent paralysis (NMS < 48) on Day 14 underwent a muscle biopsy. Potential risk factors (including demographic, metabolic, drug-related and organ failure-related variables) were recorded between ICU admission and Day 1. Odd ratios (OR) with 95% CI were separately computed for each potential risk factor. Then, significant factors were simultaneously included in a multivariate logistic regression model (BMDP software).

**Results:** Among the 95 patients who satisfactorily woke up, the incidence rate of ICUAP was 25.3% (95% CI 16.9–35.2). EP examination showed a sensory-motor axonopathy in all cases. A specific muscle involvement, not exclusively related to the nerve involvement, was observed in all the patients who underwent a muscle biopsy. The median duration of ICUAP was 21 days. ICUAP patients had a significantly longer duration of MV after Day 1 (18.2 ± 36.3 vs 7.6 ± 19.2 days, *P* = 0.03) and longer ICU length of stay after Day 1 (27.6 ± 31.4 vs 14.6 ± 19.6 days, *P* = 0.02), compared to patients without ICUAP. Two patients remained paralyzed after 6 months. In multivariate logistic regression, the number of days with organ failure ≥ 2 (OR 1.28 [1.11–1.49]), duration of MV (OR 1.10 [1.00–1.22]), administration of corticosteroids (OR 14.90 [3.20–69.8]) prior to day 1, and female sex (OR 4.66 [1.19–18.3]) were independent predictors of ICUAP.

**Conclusion:** Clinically detected ICUAP was a frequent finding among patients mechanically ventilated ≥ 7 days and was associated with a prolonged duration of MV and ICU length of stay. Both the peripheral nerve and the muscle were involved in the paralysis. Some risk factors might be accessible to preventive measures.

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**P190 The clinical course of acute quadruplegia of the critically ill**

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**Aim of the study:** To describe the clinical course of acute quadruplegia of intensive care.

**Setting:** Ten bed medical ICU in university hospital Hradec Králové.

**Patients:** Twelve consecutive patients with acute quadruplegia that occurred during critical illness.

**Study period:** Fifteen months.

**Design:** Prospective observational study.

**Methods:** For precise diagnosis of the neuromuscular disorder, clinical, biochemical, electrophysiological examinations and skeletal muscle biopsies were performed. During the whole stay in the hospital, skeletal muscle strength was clinically examined and quantified



aim of this study was to investigate the probable correlation between BIS and the Ramsay and Cook scales.

**Material and methods:** Twenty-six patients (18 males and 8 females) of a mean age of  $55.46 \pm 21.25$ , APACHE II Score  $13.50 \pm 5.21$ , who were hospitalized from August 4 to October 31, 2000 and were subjected to respiratory mechanical support were investigated. Patients who had damage of the neurological system or those who had received muscle relaxants were excluded from the study. All the patients, during evaluation and measurements were under stable sedation and analgesia (Fentanyl, Propofol or Mydazolam) under continuous intravenous infusion. The evaluation of the level of sedation was carried out during the same time period by means of two different scales: The Ramsay (0–6), Cook's (4–19) and BIS (0–100). The BIS registration lasted 60 min and the final value was calculated from the average of the total recorded 10 min values. The measurements were taken under consideration if the SQI (Signal Quality Index) was higher than 80%. The statistical analysis was carried out by the Jonckheere–Terpstra test.

**Results:** The results are depicted analytically in Table 1. Between BIS and the Ramsay Scale, a correlation or a degree statistically significant ( $P = 0.012$ ) were observed. The Cook Scale was not statistically significant ( $P = 0.091$ ).

**Table 1**

BIS vs Ramsay	$P = 0.012$
BIS vs Cook	$P = 0.091$

**Conclusions:** BIS is satisfactory correlated with the Ramsay scale and its indications correspond to the clinical condition of the patient, where the sedation level is concerned, as opposed to the Cook scale for which no significant correlation was established. The BIS values in the ICU and the corroboration of our results require further study.

### P193 Assessment of sedation level and EEG recovery after major operation by spectral entropy

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Entropy quantifies the amount of disorder in a system and characterizes chaotic behaviour. The complexity of a signal can be characterized by spectral entropy, which gives the amount of disorder in frequency space [1]. If an EEG signal includes a wide spectrum of frequencies, its spectral entropy has a high value (near one), and in case of few relevant frequencies spectral entropy is low (near zero). Spectral entropy has been shown to be an effective tool in measuring depth of anaesthesia [2].

In this study, we investigated whether spectral entropy can distinguish between the different sedation levels corresponding to the Ramsay Scores 2, 4, and 6. In order to study spectral entropy during different sedation levels, EEG was recorded from 26 patients scheduled for an elective cardiopulmonary bypass operation with propofol/alfentanil/isoflurane/pancuronium anaesthesia [3]. Postoperative sedation was maintained with propofol to keep the sedation level at Ramsay Score 6 (not responding to any commands) until the patients were hemodynamically stable. EEG was recorded 5 times for each patient: 1 day before the operation (Ramsay Score 2), after premedication 1 hour before the operation (Ramsay Score 2 or 3), immediately after the operation (Ramsay Score 6), after the patient had opened his eyes for the first time (Ramsay Score 4), and the following morning (Ramsay Score 2 or 3). The EEG signal was recorded bipolarly between electrodes Fz–M1, Cz–M2, C3–P3 and C4–P4. It was amplified and digitized continuously at 100 Hz using the Datex-Ohmeda EEG module and stored to a PC for off-line analysis. Spectral entropy values were evaluated for 5 s epochs in two frequency bands: 0.5–32 Hz and 7–32 Hz. Epochs including artefacts were removed from the data before the calculation.

Spectral entropy for the range 0.5–32 Hz differentiated statistically significantly whether the patient was awake (Score 2) or asleep (Scores 4–6) ( $P < 0.05$ ). Spectral entropy for 7–32 Hz was able

to differentiate the sedation levels 4 and 6 ( $P < 0.001$ ). Sedation levels 2, 4, and 6 could thus be distinguished by using spectral entropy. For comparison, we analyzed whether spectral edge frequency or auditory evoked potentials can distinguish between these levels. These methods failed in separating levels 6 and 4. There was considerable variation in spectral entropy values between the patients having the same Ramsay Score. This may be due to the physiological variation of different EEG-patterns between individuals.

We divided the patients into two groups according to how the EEG, measured the following morning after the operation, was recovered compared to the EEG 1 day before the operation. In both recordings the patients were awake. The spectral entropy values 1 day after the operation were significantly lower in the group in which the EEG was not at all recovered compared to the group in which the EEG was almost recovered.

Our results indicate that spectral entropy can be a useful tool for assessment of the sedation level of a patient. The performance of spectral entropy in distinguishing Ramsay Score levels 2, 4, and 6 was superior in comparison to spectral edge frequency and auditory evoked potentials. However, in patients with postoperative EEG significantly slower compared to preoperative EEG, spectral entropy remained at a low level and was not able to indicate whether the patient had waken up. A relation between postoperative EEG slowing and mild subclinical cerebral injuries has been discussed by Vanninen *et al* [4]. Our results suggest that spectral entropy might provide diagnostic information of such a state.

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**P196 Pharmacokinetics of dexmedetomidine infusions for patients in the intensive care unit**

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**Introduction:** To date the pharmacokinetics of the sedative agent, dexmedetomidine, has only been reported in volunteers [1,2]. This study investigated the pharmacokinetic profile of dexmedetomidine infusions in human patients requiring postoperative sedation and ventilation in the ICU.

**Methods:** Ten adult patients who were expected to require a minimum of 6 hours of postoperative sedation and ventilation were studied. Patients received a loading dose of dexmedetomidine (DEX) of 2.5 µg/kg/h over 10 min (approx 0.42 µg/kg) followed by a maintenance infusion rate of 0.7 µg/kg/h. Alfentanil infusion was commenced if additional analgesia was required. The Ramsay sedation score and Bispectral Index (BIS) were used to measure depth of sedation. Blood samples were obtained for measurement of plasma concentrations of DEX immediately prior to infusion start ( $t = 0$ ), at 5, 10, 20, 30, 45, 60, min, 2, 3.5, 6, 10, 14, 19 and 24 h if the patient was still receiving a DEX infusion. Samples were also obtained at 0, 10, 25, 40, 60, 90 min and 2, 3, 4, 5, 6, 12, 24 h post infusion termination. Plasma DEX concentrations were measured using a gas chromatographic-mass spectrometer method

(Oneida Research Services Inc, Whitesboro, NY, USA). Pharmacokinetic parameters were estimated by noncompartmental methods [3].

**Results:** Median (interquartile range) Ramsay, BIS and APACHE II scores were 4.5 (4.2–4.6), 53 (45–58), 13 (12–16) respectively. Tabular results are expressed as mean (SD).

**Conclusion:** Previously reported [2] DEX subjects' clearances range from 46.3 (8.3) to 35.3 (6.8) l/h,  $V_{ss}$  range from 88.7 (22.9) to 102.4 (20.3) l and  $t_{1/2}$  from 1.78 (0.30) to 2.5 (0.61) h. Although these patient pharmacokinetic values appear slightly greater, the results are generally comparable to those previously reported for subjects.

Supported by Abbott UK.

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Weight (kg)	Duration of DEX infusion (h)	Half-life (h)	Clearance (l/h)	Volume of distribution (l)	Mean residence time (h)
74 (14)	10 (4)	3.14 (0.62)	48.3 (15.9)	173 (52.5)	3.86 (1.59)

**P197 Short-term propofol sedation increases serum levels of parathyroid hormone independent of calcium levels in normal subjects**

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**Introduction:** Propofol (Diprivan®, AstraZeneca) is a surgical anesthetic and an intensive care sedative that contains 0.005% disodium edetate (EDTA) as an antimicrobial agent. EDTA is also a chelating agent that may affect the function of the parathyroid-calcium axis, predisposing patients to the development of hypocalcemia.

**Purpose:** To compare the effect of propofol with and without EDTA on the parathyroid-calcium axis in normal healthy volunteers.

**Methods:** In a randomized, double-blind, age-stratified, crossover trial, 50 normal subjects were randomly treated with propofol or propofol EDTA as a bolus containing 2 mg propofol/kg iv (1 mg/kg if aged > 65 years), followed by randomly selected infusions (25, 50, 100, or 200 µg/kg per min). The alternate treatment was given 15 to 29 days later. Changes in ionized Ca, total Mg, and intact parathyroid hormone (PTH) levels were measured. The normal range for PTH is 9 to 46 pg/ml.

**Results:** Eighteen women and 32 men were equally distributed among 3 age groups (19–34, 35–65, > 65 years). Ionized Ca and total Mg remained within the normal range for both treatments throughout the study. However, PTH levels significantly increased from baseline ( $40.7 \pm 19.8$  pg/ml and  $40.4 \pm 16.7$  pg/ml for propofol and propofol EDTA, respectively) to  $54.3 \pm 24.7$  pg/ml and  $55.8 \pm 23.0$  pg/ml, respectively, ( $P < 0.05$ ) 4 min after the bolus injection and returned to baseline within 60 min. Propofol infusions significantly ( $P < 0.05$ ) increased PTH levels in a step-wise fashion. PTH levels increased 31% and 43% for the 100 and 200 µg/kg per min infusions of propofol, respectively. These PTH levels are similar to those seen in hyperparathyroidism and hypocalcemia. Age did not affect PTH responses.

**Conclusion:** Propofol was associated with a dose-dependent increase in PTH levels that were not related to changes in ionized Ca, total Mg, or EDTA.



prolonged infusion the effects of R do not accumulate. Its major metabolite, remifentanyl acid (RA) is eliminated by the kidneys and its elimination is prolonged as a result of increasing renal dysfunction. However RA has been reported to have 1/4600 mu-opioid potency of the parent compound. This study assessed the offset of pharmacodynamic (PD) effects of R in ICU patients with varying degrees of renal dysfunction receiving R for provision of sedation and analgesia.

**Methods:** R (starting rate 6–9 µg/kg/h) was administered as a continuous infusion for up to 72 hours in 40 ICU patients (10 normal/mild renal impairment, creatinine clearance ≥ 50 ml/min; 30 moderate/severe renal impairment, creatinine clearance < 50 ml/min) who required sedation and analgesia. At scheduled times (8, 24, 48 and 72 hours) R was down titrated until the offset of PD effects (eg changes in sedation, pain intensity, respiratory function or haemodynamic variables) were seen. On confirmation of the offset of PD effects, R was continued at the original rate.

**Results:** See Table.

**Conclusions:** The offset of the PD effects of R were consistent and independent of the duration of infusion even in patients with a

**Table**

Time of down titration (h)	Renal status: normal/mild PD offset (min) (mean, SD)	Renal status: moderate/severe PD offset (min) (mean, SD)
8	15.6 ± 7.4 (n = 10)	19 ± 15.7 (n = 27)
24	13.8 ± 7.7 (n = 10)	20.3 ± 11.7 (n = 20)
48	16.1 ± 7.2 (n = 8)	15.4 ± 7.4 (n = 12)
72	14.8 ± 5.7 (n = 6)	25.3 ± 12.6 (n = 11)

significant degree of renal dysfunction. R was well tolerated in these patients. R may therefore be an ideal agent for provision of sedation and analgesia to patients with varying degrees of renal dysfunction in the ICU.

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**P201 Phenobarbital: a good choice for long-term sedation**

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Sedation is an essential part of intensive care medicine. The most common agents used for sedation in intensive care units are midazolam or propofol in combination with opioids. These sedatives have short half-life times, rapid onset after application and a short duration depending on the dose that is given.

A small part of patients in our intensive care unit need long-term sedation. Most of these patients have multiple organ failure caused by septic shock or cardiac shock.

Short acting sedatives are very expensive and a relevant economic factor in intensive care units.

Drugs used in long term sedation should be as safe and as comfortable for the patient as continuous given midazolam or propofol. Patients ventilated for two or more weeks often need some days to wake after discontinuation of sedation and they awake with discomfort from sedation with midazolam.

In long-term sedation we used phenobarbital in combination with fentanyl since more than 5 years in about 40 adult patients. After stabilization of the patient we switch from continuous application of midazolam to bolus application of phenobarbital 200 mg given every 6–8 hours. A patient with 70 kg bodyweight needs about 1000 mg per day phenobarbital for a deep sedation. The level of sedation could be controlled easily. The Ramsey sedation scale should be used to measure the level of sedation. Plasma levels could be controlled. Phenobarbital is a safe drug and the patient are comfortable sedated. There is no significant decrease in blood pressure after bolus application. There is no prolongation of sedation in contrast to continuous given midazolam. All patients waked up comfortable.

Cost of sedation with midazolam 240 mg/day (10 mg/h): 85 Euro/day. Cost of sedation with Phenobarbital 1000 mg/day: 6.2 Euro/day. Phenobarbital has an important cost-benefit.

**Conclusion:** Phenobarbital is a recommendable drug for long-term sedation.

**P202 Repetition of self-poisoning and self-injury: a retrospective 4-year study**

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**Objectives:** Repetition of self-poisoning and self-injury presents us serious problems because there are some important reasons. Not only may it represent the establishment of a maladaptive pattern of coping, but it also the probability of fatal suicide. The purpose of this study was to investigate characteristics of patients who attempted suicide repeatedly.

**Methods:** This study was undertaken in the emergency department of Fukushima Medical University Hospital. We conducted a

retrospective cohort study of consecutive patients with attempting suicide for over 4-years period between April 1996 and March 2000. Patients who attempted suicide were picked up from the records of emergency room and then all records where the attending doctor diagnosed self-poisoning and self-harm were identified.

**Results:** The total number of attempters of suicide was 215 (0.38%, whom 74 were men and 141 women (male to female ratio 1:1.9). Of these, the number of repeaters was 41, whom 5 were



Decontamination prior to PICU admission was associated with a shorter hospital stay (median 3 vs 5 days) for survivors ( $P = 0.028$ ), but not with a lower rate of complications ( $P = 0.73$ ) or mortality ( $P = 0.34$ ). The presence of a tachyarrhythmia was associated with an increased mortality ( $n = 4/9$ ; 44% vs  $n = 0/45$ ; 0%) ( $P = 0.0004$ ).

**Conclusion:** More children than expected were from rural areas. Mortality in children with organophosphate poisoning is related to the presence of tachyarrhythmias. Early decontamination is associated with shorter hospital stay but not with decreased mortality.

**P205 End-tidal CO<sub>2</sub> (EtCO<sub>2</sub>) and QTc period: can it help us in the prognosis of patients with organophosphate poisoning?**

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**Introduction:** In our area, organophosphate poisoning is a frequent method of committing suicide, with a relatively high mortality rate (12–16%, data from literature). Defining and observing the QTc period and EtCO<sub>2</sub> enables us to make an additional estimate of the handicap and prognosis, or better the possibility of complications (respiratory failure).

**Methods:** The contribution presents our experience in the period from February 1997 to September 2000. During this period, either in the emergency ward or during interventions we met 61 patients (37 male and 24 female; age varied from 18 to 75 years with a mean  $57.4 \pm 18.3$ ), for whom the diagnosis organophosphate poisoning was confirmed by means of anamnesis/heteroanamnesis and laboratory analysis (serum cholinesterase). In prehospital setting we collected from each patient EtCO<sub>2</sub>, SaO<sub>2</sub>, QTc period, pre- and postintervention values of the MEES. The APACHE II score was recorded on the day of admission to the hospital. We compared two groups (with complications [group I] and without complications [group II]). A  $P$  value  $< 0.05$  was chosen to rejected null hypothesis.

**Results:** See Table.

**Table**

	Group I	Group II	$P$ value
End-tidal CO <sub>2</sub> (mmHg)	38.3 ± 8.5	56.4 ± 10.3	< 0.05*
SaO <sub>2</sub> (%)	75.3 ± 9.2	89.5 ± 6.3	< 0.05*
QTc (s)	0.69 ± 0.17	0.45 ± 0.11	< 0.05*
MEES (postintub.)	18.3 ± 6.1	22.4 ± 3.3	< 0.05*
APACHE II	32.7 ± 9.4	20.6 ± 5.8	< 0.05*
Intubation-Y/N	22/7	11/21	< 0.05†
Ratio dead/survive	11/19	3/28	< 0.05†

\* Student's  $t$ -test; †  $\chi^2$  test.

**Conclusion.** In the initial nursing of patients with organophosphate poisoning, monitoring (ECG, capnometry) and observation of the QTc period and EtCO<sub>2</sub> is essential, for it helps us in the prognosis of the patient and suggests precaution due to the danger of complications (respiratory failure).

**P206 Cardiac troponin I as a marker of myocardial injury in paracetamol induced acute liver failure**

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**Background:** Anecdotal case reports and necropsy studies have suggested that severe paracetamol poisoning may cause cardiac injury in addition to fulminant hepatic failure. Cardiac troponin I (cTnI) is a regulatory protein highly specific for myocardial injury which has not been evaluated in paracetamol poisoning.

**Aim:** To assess the incidence of myocardial toxicity in paracetamol induced fulminant hepatic failure in a prospective, controlled trial.

**Methods:** Patients admitted with paracetamol (POD) and non-paracetamol acute hepatic failure were studied (subjects and positive controls). Healthy volunteers were enrolled as negative controls for serum sampling. Patients with pre-existing cardiac disease, chronic liver disease or chronic alcoholism were excluded from the study. Cardiac investigations included baseline ECG and transthoracic echo (TTE) on admission, invasive haemodynamic monitoring and daily cardiac output studies in those in whom a pulmonary artery floatation catheter was clinically indicated. Serum creatinine kinase MB isoenzymes and cTnI were followed for the first week of admission.

**Results:** Nineteen patients were enrolled from September 1999 to October 2000. Eleven had paracetamol induced liver failure and eight had other aetiologies. Thirteen were female and the mean age was 35.79 (range 17–59). Fourteen patients were admitted to

ICU, 12 were ventilated and underwent invasive haemodynamic monitoring. Eleven had intracranial pressure (ICP) monitoring. None of the 13 patients who had TTEs showed evidence of myocardial dysfunction. ECG was normal in 11 patients and showed sinus tachycardia in 7 patients. One patient had terminal ventricular tachycardia. 53% of patients (subjects and positive controls) had cTnI above the upper limit of the laboratory normal range on day 1 and subsequent days of admission ( $0.67 + 1.01$ ). cTnI was higher in the paracetamol group than the positive controls, but this difference was not statistically significant,  $1.02 \pm 1.2$  (POD) versus  $0.23 \pm 0.24$  (non-POD). Negative control values fell within the normal range. By multivariate analysis there was an independent significant correlation between noradrenaline requirements and cTnI ( $P = 0.004$ ). In addition, cTnI levels above the normal range were associated with a low LVSWI ( $P < 0.01$ ), an increased heart rate ( $P < 0.05$ ) and CVP ( $P < 0.05$ ).

**Conclusions:** In this study, we have demonstrated that previously fit young patients with acute hepatic failure developed myocardial injury. This was more severe in those treated with noradrenaline. There was a trend towards worse myocardial injury as evidenced by raised cTnI, but not by TTE, in patients with paracetamol induced hepatic failure. A larger study is required to establish whether myocardial damage seen in acute liver failure is a direct effect of paracetamol.



**Discussions:** 1. Tachycardia induced by positive inotropes or cardiac pathology comes down to an acceptable rate when Magnesium is given in an average of 45 min. 2. Patients are protected from Tachyarrhythmia (Atrial and Ventricular arrhythmia). Incidences of drug-induced arrhythmias when Magnesium is given concomitantly with inotropes or bronchodilators are nil. 3.

Magnesium improves energy production (ATP) and stimulates metabolism. This is advantageous as patients requiring inotropes are always in shock. 4. The affect of Magnesium therapy on Base Deficit (Lactic Acidosis) is to be studied further, because we got normal base values within 5–6 hours of Magnesium.

**P208 Critical illness is associated with elevated parathyroid hormone**

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**Introduction:** Propofol (Diprivan®, AstraZeneca) is a reliable sedative frequently used in critically ill patients (pts). The modified formulation contains 0.005% disodium edetate (EDTA) as an antimicrobial agent. EDTA is also a chelating agent and may impact calcium balance; therefore, three clinical trials were performed in which ionized calcium (Ca<sup>2+</sup>) and parathyroid hormone (PTH) levels were assessed. PTH plays a major role in calcium homeostasis but is generally not considered to be a stress hormone.

**Purpose:** Evaluate PTH levels in critically ill pts sedated with propofol or propofol EDTA.

**Methods:** Serum intact PTH, total Mg, Ca<sup>2+</sup>, and total Ca were measured in 212 pts in 3 randomized, double-blind, controlled

trials (85 medical ICU, 37 renal impaired ICU, and 90 cardiac surgical pts).

**Results:** See Table. For the medical ICU pts, baseline PTH levels were unexpectedly increased above the normal range (unrelated to propofol and Ca<sup>2+</sup>). Baseline PTH levels in pts undergoing elective cardiac surgery were normal. Pts with impaired renal function had high PTH values presumably secondary to hyperparathyroidism.

**Conclusion:** PTH levels were elevated at baseline in critically ill medical ICU pts without renal failure. This finding was not related to propofol or low Ca<sup>2+</sup> levels. The explanation is unknown, but perhaps PTH should be reconsidered as being a stress hormone. Patients with impaired renal function had high PTH values, presumably secondary to decreased Ca<sup>2+</sup> levels and/or hyperparathyroidism.

**Table**

**Intact PTH Levels in pg/ml (mean ± SEM; normal range: 9–46 pg/ml)**

	Medical ICU pts		Renal impaired pts		Cardiac surgery pts	
	Baseline	24 h after sedation	Baseline	48 h after sedation	Baseline	1 h after extubation
Propofol	84.9 ± 15.1 (n = 26)	69.2 ± 19.2 (n = 22)	126.3 ± 23.6 (n = 19)	119.9 ± 44.7 (n = 15)	40.6 ± 2.4 (n = 46)	62.3 ± 5.3 (n = 46)
Propofol EDTA	92.0 ± 18.6 (n = 21)	72.1 ± 26.4 (n = 14)	234.4 ± 52.2 (n = 18)	141.1 ± 33.6 (n = 13)	40.0 ± 2.9 (n = 44)	67.6 ± 5.5 (n = 44)

**P209 Hypocalcemia in children with septic shock**

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**Introduction:** Ionized calcium is essential for maintenance of myocardial function and vascular tone. Ionized hypocalcemia is seen frequently in critically ill patients and is associated with poorer prognosis. It is unclear whether calcium administration is beneficial in these patients.

**Objective:** To evaluate the incidence of ionized hypocalcemia (Ca<sup>2+</sup>-level < 1.0 mmol/l), the time course of serum ionized calcium (Ca<sup>2+</sup>) in children with septic shock, the effect of calcium administration and the relationship with survival.

**Methods:** We retrospectively studied 37 children with septic shock. We analyzed Ca<sup>2+</sup> levels on admission and after 8 and 24 hours, the dose of intravenous calcium administration in the first 24 hours and survival.

**Results:** The group consisted of 22 boys and 15 girls with a median age of 2.3 years (0.2–16.1 years). The median PRISM-score was 23. There were nine non-survivors. On admission 26 patients (68%) were hypocalcemic (19 survivors and 7 non-survivors). There was a significant negative correlation between PRISM-score and Ca<sup>2+</sup> levels on admission ( $r = -0.46, P < 0.01$ ). On admission there was not a significant lower Ca<sup>2+</sup> level in non-survivors compared to survivors (0.89 mmol/l vs 0.96 mmol/l, NS). During the first 24 hours after admission 14/28 survivors and 8/9 non-survivors received calcium administration intravenously. All 22 patients received calcium in a slow infusion during the first 24 hours, 3/14 survivors and 3/8 non-survivors also received a bolus of 0.1 mmol/kg in 30–60 minutes. There was a significant difference in the Ca<sup>2+</sup> level on admission between survivors with and without Ca<sup>2+</sup> administration (0.91 mmol/l vs 1.00 mmol/l,



agreement a third evaluation was asked. The kappa value was established for the CT evaluation. The variables shock, renal failure, MODS and Balthasar for the mortality prognosis were evaluated.

**Results:** (See Table.) The review of the Balthasar score had a kappa of 0.88, our results show a low specificity and predictive positive value of Balthasar score C, D, and E, to predict the probability of mortality. The variables shock, renal failure and MODS show more certainty to the prediction of mortality.

**Conclusion:** The Balthasar score does not predict with certainty the probability of mortality by itself. Other variables related with the severity of SIRS as shock more certainty the mortality in patients with acute pancreatitis.

**Reference:**

Balthasar EJ et al: *Radiology* 1985, **185**:767-772.

**Table**

	Sensitivity	Specificity	Predictive positive value	Predictive negative value
Balthasar score (C, D, and E)	87.7%	45.2%	20%	95%
Shock	85.7%	92%	66%	97%
Renal failure	85.7%	92%	66%	97%
MODS	85.7%	90%	60%	97%

**P212 Acute renal failure due to crush injury and prolonged positional compression on a muscle group**

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**Introduction:** Widespread muscle crush injury and prolonged positional compression on a muscle group are often associated with myoglobinuric acute renal failure (ARF). Treatment consists of early massive volume replacement and forced alkaline solute diuresis. With this regimen it is possible to increase survival of life and limbs, and prevent myoglobinuric ARF.

**Methods:** The present study was carried out to describe clinical pattern of ARF caused by crush injury and prolonged positional compression on a muscle group. Clinical and laboratory data of 61 crush or positional compression injury patients transferred to ICU were analyzed. All patients were evaluated by physical examination, determinations of serum levels of electrolytes, urea, creatinine, acid-base balance. Also we recorded the following data: a) the period from the onset of injury to the commencement of treatment; b) the form of ARF; c) need of hemodialysis; d) complications; e) the mortality rate. The only indications for fasciotomy were lack of a distal pulse or open lesions.

**Results:** Sixty-one patients were admitted to our ICU with ARF caused by crush injury (25 patients) or prolonged positional compression on a muscle group (36 patients). These patients con-

sisted of 55 men and 6 women with a mean age of  $40.9 \pm 13.4$  years, ranging from 19 to 85. All the patients demonstrated kidney failure with increased concentrations of serum urea ( $13.22-79.40$  mmol/l) and creatinine ( $172-1398$   $\mu$ mol/l). ARF was highly associated with massive muscle damage and insufficient initial fluid resuscitation. The period from the onset of symptoms and signs of the injury to the commencement of treatment with hemodialysis varied from 4 hours to 9 days. Fifty-nine (97%) patients were oliguric. Fifty-eight (95%) of these patients were treated with hemodialysis from 1 to 21 days. Hyperkalemia ( $5.6-8.1$  mmol/l) was present in 38 (62%) patients. More than in half cases hyperkalemia was diagnosed before azotemia. Six (9.8%) patients underwent fasciotomies and 6 (9.8%) patients underwent amputations. The outcome was favorable in 43 (70%) patients, 18 (29.5%) patients died. The half causes of death were infection and sepsis.

**Conclusions:** 1. Hyperkalemia, and metabolic acidosis appear before azotemia and within hours of the rescue of casualties with traumatic rhabdomyolysis. 2. Very early, aggressive volume replacement followed by forced solute-alkaline diuresis therapy may protect the kidney against acute renal failure.

**P213 Experience with continuous venovenous hemofiltration (CVVH) in the ICU: a report from a single center**

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During the last 7 years in our ICU, CVVH was used as renal support in 101 critically adults (79 M, 22 F, median age 57, range 17-86) with acute renal failure (ARF). Patients who were treated with CVVH for less than 24 hours were excluded from this report.

APACHE score at admission was 23 (median, range 8-42). The majority of the patients was on mechanical ventilation (98%) and needed vasopressor support (91%). Vascular access was performed with the use of a blood pump. Conventional heparin was used for anticoagulation in the most of the cases (90%).

In 31 of the patients (group A) CVVH was initiated upon their first day of admission while in the rest 70 pts (group B) CVVH was started on the 9th day, median (range 2-32) of their hospitalization in the ICU.

Uremia was satisfactory controlled in most of the cases with a mean amount of ultrafiltrate of  $38.7 \pm 0.6$  SEM, l/day (range 27-49.5). Patients of group A remained on CVVH treatment for a median of 5 days (range 1-40), while those of group B for 4.5 days (range 1-29),  $P = NS$ . Although serum creatinine levels at the initiation of CVVH did not show any difference between the groups (group A  $4.9 \pm 0.4$  SEM, group B  $5.2 \pm 0.5$  SEM,  $P = NS$ ), the corresponding BUN level were lower in patients of group A ( $86.0 \pm 7.1$  SEM vs  $112.8 \pm 6.9$  SEM,  $P = 0.021$ ). The duration of hospitalization (days) in the ICU was also lower in the group A patients ( $10.7 \pm 2.2$  SEM vs  $24.2 \pm 2.0$  SEM,  $P = 0.0001$ ). Ten (10) patients of group A (32.2%) and 15 pts of group B (21.4%) were survived and discharged from the ICU,  $\chi^2 = NS$ , with a mean serum creatinine and BUN levels that did not differ between these two groups. The overall mortality was 75.2%.



**P216 Dosing patterns for continuous renal replacement therapy in the United States**

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**Introduction:** There is evidence that increasing the dose of continuous renal replacement therapy (CRRT) is associated with improved survival in critically ill patients with acute renal failure (ARF) [1]. In the US, CRRT is usually provided with an ultrafiltrate (UF) and/or dialysis flow rate of 2 l/h irrespective of the patient's weight. Patients undergoing CRRT frequently have their therapy interrupted and hence receive a much lower dose than prescribed. Hence we retrospectively reviewed the records of all patients with ARF, who received CRRT in our hospital in the past year, to determine dosing patterns.

**Methods:** Computerized records of all patients ( $n = 115$ ) who received CRRT for ARF in our institution from September 1999 to August 2000 were reviewed. Patients were included in analysis if they received CRRT for at least 2 days and their hospital discharge outcome was known. All but four patients met these inclusion criteria. The patient's CRRT dose for each day was inferred from the hourly UF/dialysis flow rate and the duration (in hours) of CRRT for that day. A mean UF/dialysis flow rate (in l/h) for each patient was then calculated. Other patient demographic characteristics including age, weight and duration of therapy were obtained from the patient's records.

**Results:** The average number of hours/day on CRRT was 16.1, with a mean flow rate of 1.36 l/h. The mean CRRT dose for these patients was only 16.50 ml/kg/h, much lower than the lowest dose (20 ml/kg/h) used by Ronco *et al* [1].

**Table**

CRRT characteristic	Mean value
Age	55.50
Weight (kg)	88.90
Number of days on CRRT	9.23
Number of hours/day on CRRT	16.10
Hourly flow rate (l/h)	1.36
Dialysis dose (ml/kg/h)	16.50
Hospital mortality (%)	65.76

**Conclusion:** In the US, many patients are prescribed a lower dose of CRRT than supported by current evidence. Moreover, the actual dose delivered is much lower than that prescribed. Immediate changes in dosing practices are necessary to achieve the doses recently shown to be beneficial in patients with ARF [1]. A weight-based dosing regime may enable physicians to achieve increased dosing of CRRT in such patients.

**Reference:**

1. Ronco C *et al*: *Lancet* 2000, **355**:26–30.

**P217 A preliminary investigation of the nephroprotective effects of the adenosine antagonist aminophylline in patients undergoing abdominal aortic aneurysm repair**

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Infra-renal clamping of the abdominal aorta during aneurysm repair is associated with a significant reduction in renal blood flow. Adenosine has been implicated as a mediator of renal ischemia in a number of human and animal models and its antagonism with theophylline has led to the attenuation of these effects. In order to investigate the possible attenuation of renal arterial vasoconstriction associated with infrarenal cross clamping of the aorta we prospectively randomised 8 consecutive patients undergoing abdominal aortic aneurysm repair to receive aminophylline 5 mg/kg ( $n = 5$ ) in 500 ml normal saline or placebo ( $n = 3$ ) on the morning of surgery followed by an infusion of 6 mg/hour of aminophylline or placebo for 24 hours. Staff, investigators and patients were blinded. Inulin clearance as an indicator of glomerular filtration rate (GFR) was measured pre-operatively and again on the 2nd post-operative day. *N*-Acetyl- $\beta$ -glucosaminidase (NAG) activity (mmol PNP/hour/mol creat) and Retinol Binding Protein (RBP) excretion (mg/mol creat) were measured to assess renal tubular damage and albumin excretion (mg/mol creat) as a marker of glomerular injury.

**Results:** There was a significant increase between the pre and post operative measurements in NAG activity (45.53 to 248.96,  $P = 0.0078$ ), RBP excretion (10.68 to 3851.92,  $P = 0.0078$ ) and albumin excretion (1.165 to 7.88,  $P = 0.0078$ ) however there was no difference between the treatment and control groups. Contrary to expectation inulin clearance was marginally increased in the postop-

erative period (80 vs 76 ml/min/1.73 m<sup>2</sup>,  $P = 0.36$ ) in spite of a significant reduction in urinary volumes (85 vs 40 ml/hour,  $P = 0.05$ ).

**Table**

Characteristic	Pts
Sex M/F	6/2
Age (median)	70
IHD (%)	6 (75)
LVF (%)	1 (12.5)
Diabetes (%)	1 (12.5)
Hypertension (%)	4 (50)
ACE inhibition (%)	2 (25)
Calcium channel antagonists (%)	4 (50)

**Conclusions:** 1. Infrarenal aortic aneurysm repair is associated with significant renal ischemia that does *not* result in a sustained fall in GFR. 2. Urine volumes are not an accurate reflection of GFR in this setting. 3. Measurement of perioperative GFR is not a suitable way to assess the effects of adenosine antagonism in this model of renal ischemia.



**P220 Trends in post-operative mortality in patients requiring renal replacement therapy following cardiothoracic transplantation**

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Renal failure requiring renal replacement therapy (RRT) increases mortality after any operation. Cardiothoracic surgery carries a high risk of post-operative renal failure, but the effect of the management of RRT on mortality is unclear in these patients. The aim of this study was to determine the changes in mortality over a 15-year period in patients requiring RRT following cardiothoracic transplantation. We performed a retrospective review of all 406 patients who received a heart ( $n = 359$ ) or lung ( $n = 49$ ) transplant in a single tertiary care centre from November 1986 to October 1999. Two patients underwent a second heart transplantation and one patient received a combined heart/renal transplant during this period.

The requirement for RRT has not significantly altered over the time period of the study. However there has been a dramatic reduction in the 30-day mortality in patients treated with RRT which is sustained through to the end of the first year. This is likely to be due to earlier implementation of RRT with its associated improvements in nutrition and homeostasis.

Date of Tx	Need for RRT in first 30 days	30-Day mortality in patients requiring RRT	1-Year mortality in patients requiring RRT
1986–1990	12/71 (16.9%)	10/12 (83.3%)	11/12 (91.1%)
1991–1995	29/202 (14.4%)	19/29 (65.5%)	24/29 (82.8%)
1996–10/1999	26/135 (19.3%)	11/26 (42.3%)	15/26 (57.7%)
<b>1986–10/1999</b>	<b>67/408 (16.4%)</b>	<b>40/65 (61.5%)</b>	<b>50/65 (76.9%)</b>

**P221 Outcome of renal transplant recipients and graft survival in the ICU**

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**Objective:** To determine renal transplant recipients outcome and graft survival in ICU setting.

**Design:** Retrospective cohort study.

**Setting:** Ten-bed adult medical ICU in a university hospital.

**Patients:** Consecutive adult renal transplant recipients admitted to an ICU over a period of 13 years. In our institution postoperative monitoring is not performed in ICU.

**Measurements:** For each patient the following data were recorded: demographic characteristics, prior duration of transplantation, immunosuppressive therapy, indications for admission to ICU, data necessary for the calculation of SAPS II and APACHE II, duration of mechanical ventilation, length of stay in ICU, mortality and graft survival at both ICU and hospital discharge. Patient and graft survival were also collected 6 months after ICU discharge.

**Results:** Thirty ICU admissions in 26 adult renal transplant recipients were studied. The median of prior post-transplant duration was 3 months (10 days–90 months), and of end-stage renal disease was 68 months (5–340). Reasons for admission were: sepsis ( $n = 11$ ), hemorrhage ( $n = 4$ ), cardiopathy/fluid overload ( $n = 4$ ), coma ( $n = 4$ ), abdominal crisis ( $n = 4$ ), others ( $n = 3$ ). The overall ICU mortality was 33%. There was no difference between the observed hospital mortality (40%) and the expected mortality as predicted by SAPS II (36.6%) or APACHE II (50%). The area under the receiver operating characteristic curve was  $0.85 \pm 0.08$  for SAPS II and  $0.84 \pm 0.08$  for APACHE II. The variables associated with ICU mortality were: (i) ICU admission without hospital discharge after transplantation (RR = 2.5), (ii) mechanical ventilation requirement (RR > 20), (iii) vasoactive drugs use (RR = 5.6). Use of immunosuppressive drugs was not different between survivors and nonsurvivors. At ICU discharge, graft survival among survivors was 48%. At 6 months, 5 additional renal transplant recipients had died.

**Conclusion:** The mortality of renal transplant recipients admitted in ICU is high and graft loss during ICU stay is frequent.

**P222 ICU acquired acute renal failure carries a higher mortality than acute renal failure on admission to ICU**

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Acute renal failure (ARF) has a significant impact on outcome of critically ill patients [1]. The aim of this study was to identify any differences between patients with ARF on admission to the intensive care unit (ICU) and patients developing ARF during their stay in the ICU. We retrospectively analysed data from The Riyadh Intensive Care Program (RIP) database which contains demographic data of 26,669 patients admitted to 21 ICUs in the United Kingdom (UK) during the time period June 1989 until September 1996. ARF was defined according to the organ system failure scoring system by Knaus *et al* [2]. Patients with chronic renal failure were excluded.

**Comment:** Our study confirms that ARF increases mortality in ICU patients with a further marked increase amongst patients who require renal replacement therapy (RRT). Patients who develop ARF during their stay in the ICU have a significantly worse outcome compared to patients with ARF on admission to ICU.

**References:**

1. Levy EM, Viscoli CM, Horwitz RI: **The effect of acute renal failure on mortality – a cohort analysis.** *JAMA* 1996, **275**:1489–1494.
2. Knaus WA, Draper EA, Wagner DP, Zimmermann JE: **Prognosis in acute organ-system failure.** *Am Surg* 1985, **202**:685–693.



Receptor Operator Curve (ROC) was used to determine the LOD's power of discrimination. The 'Goodness of Fit' test (Hosmer–Lemeshow) was applied to evaluate the calibration in our population.

**Results:** 448 patients were included in the study. Thirty percent of patients who met LOD criteria developed severe multiple organ failure (MOF). The average LOD score was  $1.83 \pm 2.26$  with a predicted probability of death of  $9.47 \pm 11.30\%$ . The global mortality rate was 17.6% (80 patients); therefore the OM/PM ratio was

1.85. The global percentage of accurate prediction was 85.71% for a cut off point of 50% of probability of death. The area under the ROC was 0.834 (CI 95% 0.781–0.886). The Hosmer–Lemeshow test showed a GOF of 20.59.

**Conclusion:** In our hands, the LOD system proved to be capable of discriminating among critically ill patients those likely to die. It, however, did not prove an appropriate calibration in our population of patients. We emphasize the need for proper regional validation in populations different from those in which the tools were developed.

**P225 Value of SOFA (Sequential Organ Failure Assessment) score and total maximum SOFA score in 812 patients with acute cardiovascular disorders**

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**Objectives:** The SOFA score is composed of scores from six organ systems (respiratory [R], cardiovascular [C], hepatic [H], coagulation [Co], renal [Re], and neurological [N]) graded from 0 to 4 according to the degree of dysfunction/failure. The aggregate score (total maximum SOFA score [TMS]) is calculated summing the worst scores for each of the organ systems ( $TMS_{ORG}$ ) during the ICU stay. We investigated the outcome discrimination of the TMS and the association with ICU length of stay (ICU-LOS) in patients (pts) with acute cardiovascular disorders.

**Methods:** 812 consecutive pts (age  $62 \pm 13$  years, 69.7% male, SAPS II  $29 \pm 14$ , 266 pts acute myocardial infarction, 161 pts unstable angina, 96 pts rhythm disturbances, 63 pts heart failure, 47 pts cardiac arrest, 179 pts other admission diagnosis) were included between 4/99 and 4/00. SOFA score was determined daily and TMS was calculated. Discrimination power of TMS for survivors (S) and non-survivors (NS) (hospital mortality [HM]) was assessed by the area under the Receiver Operating Characteristic (AUROC) curve. Survival curves were determined for  $TMS \leq$  and  $> 6$  (criterion value) and compared with log-rank test. Association between TMS and survival was assessed with Cox regression analysis.

**Results:** 130 (16%) pts died. ICU-LOS was 3.8 (1–80) days. SOFA score was significantly higher for NS on day 1 to day 10.  $TMS_{ORG}$  for N, Re and H correlated significantly with ICU-LOS.  $TMS_{ORG}$  for R, C, N and Re were significantly associated with HM (risk ratio [RR] + 95% confidence interval [CI]: R 1.8 [1.3–2.5], C 1.5 [1.2–1.9], N 1.4 [1.2–1.7], Re 1.5 [1.2–2.0]). TMS correlated only moderately with ICU-LOS ( $r = 0.45$ ,  $P < 0.001$ ) but was strongly associated with HM (RR 1.5 [1.4–1.6]). The AUROC for TMS was  $0.915 \pm 0.015$ . Log-rank test demonstrated a significant difference ( $P < 0.001$ ) between pts with  $TMS \leq 6$  and  $TMS > 6$ . RR for HM was 13.2 [8.6–20.1] in pts with a  $TMS > 6$ .

**Conclusion:** SOFA score is an excellent tool to describe the extent of organ dysfunction in critically ill cardiovascular pts. Moreover, the degree of organ dysfunction is associated with ICU-LOS and mortality. Survival rates were higher in pts with  $TMS \leq 6$ , pts with a  $TMS > 6$  were 13.2 times more likely to die.

Therefore SOFA score may be utilised for quality assessment or appraisal of new therapeutic strategies.

**P226 Short-term prognosis in critically ill patients with liver cirrhosis: use of the SOFA score**

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**Introduction:** In patients with liver cirrhosis who develop extra-hepatic organ failure hospital mortality rates of 63–100% have been reported [1]. For ethical reasons but also due to limited resources physicians need early and reliable outcome predictors to identify cases where aggressive treatment for cure or potential liver transplantation is merited, as well as those where such care is likely futile. We therefore analysed the prognostic accuracy of the Child–Pugh (CP) classification, the Acute Physiology and Chronic Health Evaluation (APACHE) II prognostic system and the Sequential Organ Failure Assessment (SOFA) [2] in predicting hospital mortality of cirrhotic patients on the first day after admission to a medical ICU.

**Patients and methods:** All patients with hepatic cirrhosis admitted to our medical ICU were eligible. Prospectively collected data included demographics, reason for ICU admission, acute diagnosis and mortality rates. Prognostic data were assessed 24 hours after ICU admission. Discriminative power of the scores was evaluated using the area under the receiver operating characteristic (AUROC) curve.

**Results:** 143 consecutive patients with hepatic cirrhosis were enrolled. 62% were male, median age was 53 years. Hospital mortality was 46%. CP category (A/B/C; n) was 6/40/97, mean CP points  $10.1 \pm 2$ , mean APACHE II  $20.6 \pm 10.7$ , mean SOFA  $8.6 \pm 4.7$ . The total SOFA score on the first ICU day had the best predictive ability (AUROC 0.94, standard error (SE) 0.02). No significant differences were seen between APACHE II (AUROC 0.79, SE 0.04) and CP points (AUROC 0.74, SE 0.04). A cut-off of 8 SOFA points had an overall correctness of 91%, a positive predictive value (PV) of 87% and a negative PV of 96% with regard to hospital mortality.

**Conclusion:** In our population of critically ill patients with cirrhosis the total SOFA score on the first ICU day was found to be a very reliable scoring system to discriminate between hospital survivors and non-survivors.

**References:**

1. Zimmerman JE: *Hepatology* 1996, **23**:1393.
2. Vincent JL: *Intens Care Med* 1996, **22**:707.



**Method:** We measured SOFA and LODS scores at ICU admission and daily. Survivors and non-survivors median scores for both descriptors were compared using Mann–Whitney *U*-test; the relative risk (RR) was also calculated.

**Results:** The mean age was  $51 \pm 18$  years and mean APACHE II was  $19.8 \pm 6$ . The best cut-off value for SOFA and LODS score were 11 and 6, respectively. The overall mortality rate was 48.9%.

**Conclusion:** Both SOFA and LODS score discriminated adequately survivors and non-survivors septic patients.

**P229 Outcome prediction in ICU admitted end-stage renal disease patients**

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**Objective:** To determine predictors of ICU mortality in end-stage renal disease (ESRD) patients treated with haemodialysis or peritoneal dialysis and requiring ICU admission.

**Design and setting:** Retrospective/prospective cohort study in an adult 10-bed medical ICU in a university hospital.

**Mesasurements and main results:** Over a 4-years period, out of 104 ICU admissions, 92 ESRD patients were studied. The etiologic diagnosis of ESRD was diabetes mellitus ( $n = 23$ ), glomerulonephritis ( $n = 19$ ), hypertension ( $n = 13$ ), polycystic kidney disease ( $n = 11$ ), pyelonephritis and obstructive uropathy ( $n = 6$ ), interstitial nephritis ( $n = 5$ ), congenital abnormalities ( $n = 5$ ), others or unknown ( $n = 10$ ). The prior mean duration of dialysis was  $68 \pm 83$  months. 86 patients were on hemodialysis and 18 on peritoneal dialysis. The admission diagnosis was sepsis ( $n = 32$ ), cardiac failure/fluid overload ( $n = 19$ ), hemorrhage ( $n = 12$ ), postoperative ( $n = 10$ ), mesenteric ischemia and peripheral arterial thrombosis ( $n = 7$ ), stroke ( $n = 6$ ), cardiac arrest ( $n = 6$ ), hyperkalemia ( $n = 5$ ), others ( $n = 7$ ). The mean length of stay in ICU was  $6 \pm 9$  days. The overall ICU mortality was 29.8% (31/104). The survival rate for

patients requiring mechanical ventilation was significantly less than for those not mechanically ventilated 13/36 (36%) vs 8/68 (12%), respectively ( $P < 0.0001$ ). There was no significant difference between ICU survivors and nonsurvivors according to prior duration of dialysis, type of dialysis, and etiology of ESRD. In this target population, the mean SAPS II and APACHE II were  $50.3 \pm 20.9$  and  $24.9 \pm 9.1$ , respectively. The discrimination as determined by the area under the receiver operating characteristic curve was not different between SAPS II and APACHE II: 0.859 vs 0.878, respectively ( $P = 0.62$ ). For both models, the Hosmer–Lemeshow goodness-of-fit test revealed a poor performance. The H test result was  $P = 0.013$  for SAPS II and  $P = 0.0006$  for APACHE II. The C test result was  $P = 0.008$  for SAPS II, and  $P = 0.005$  for APACHE II. The ICU mortality among ESRD patients trend to be higher than that of other ICU admitted patients during the same period (21.8%),  $P = 0.063$ .

**Conclusions:** SAPS II and APACHE II were not well calibrated in ESRD patients. These models probably need to be customized to accurately predict mortality and analyse quality of care or performance among ICUs when applied to this target population.

**P230 Comparison of prediction of hospital mortality by ICU medical staff and referring parent team doctors**

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**Introduction:** There is much interest in outcome prediction for ICU patients and many studies have evaluated the accuracy of predictions made by ICU medical staff [1]. There is little data on the accuracy of outcome prediction made by the ward-based doctors who refer these patients for ICU admission.

**Method:** As part of an on-going prospective study comparing the accuracy of prediction of hospital mortality by ICU medical staff

and referring parent team doctors we analysed the first 100 completed data sets. The most senior doctor from both the referring parent team and receiving ICU team were asked to give their prediction of the likely hospital mortality for all emergency adult admissions to our 22 bedded ICU. Predictions as a percentage chance of dying in hospital were made at the time of referral to ICU, there was no conferring between the ICU and parent team and all results were confidential. MPM II<sub>0</sub> was scored in all patients.

**Table 1**

**ICU doctors' prediction**

Decile	Av. predicted mortality (%)	Observed mortality (%)
1	0.0	10.0
2	2.8	10.0
3	9.5	10.0
4	11.0	10.0
5	20.0	50.0
6	28.0	30.0
7	42.0	50.0
8	54.0	60.0
9	76.0	70.0
10	92.0	80.0

**Table 2**

**Referring doctors' prediction**

Decile	Av. predicted mortality (%)	Observed mortality (%)
1	0.0	0.0
2	4.8	0.0
3	10.0	20.0
4	12.5	40.0
5	20.0	50.0
6	23.5	10.0
7	34.0	50.0
8	50.0	90.0
9	57.5	60.0
10	89.0	60.0



procalcitonin at the day of admission, whereas testosterone, cortisolone, dehydroepiandrosterone, thyroidea stimulating hormone, gonadotropines or prolactin were not different between groups. We have compared the results of the radio-immuno-assay with HPLC and found perfectly matched results.  $\beta$ -Estradiol was elevated up to 25-times the normal range even at day of admission.  $\beta$ -Estradiol increased further in the next days reaching a maximum at day 4–7 and decreased thereafter. Patients on chronic steroid therapy had no different  $\beta$ -estradiol level than untreated patients.  $\beta$ -Estradiol was not influenced by body

weight. Even women after hysterectomy and ovariectomy had elevated  $\beta$ -estradiol levels in plasma indicating that the gonads are not the source of  $\beta$ -estradiol.

In the survival analysis with Kaplan–Mayer analysis, increasing  $\beta$ -estradiol was highly associated with increasing mortality for both sexes, men and women ( $P < 0.001$ ).

**Conclusion:** Men and women had similar survival rates. In men and women  $\beta$ -estradiol influence outcome.

**P233 Incidence and risk factors for mortality in acute respiratory distress syndrome. Do we have the same predictors?**

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**Objectives:** To know the density of incidence and annual punctual prevalence, mortality and main factors for death in Acute respiratory distress Syndrome (ARDS) in our patients.

**Materials and methods:** Cohorte study, retrolective and prolective. Secular period: All the admissions of the intensive care unit (ICU) in 1 year (March-1-99 to Feb-29-00). Zero point was considered the admission of the ICU continuing follow up until the outcome: discharge from the ICU or death. We included all those patients that completed criteria of ARDS according to the American–European consensus (1994). The risk factors were defined to all factors associated with ARDS during the first 24 hours and were classified as direct or indirect. The following variables were defined: age, gender, number of days in ICU and hospital, comorbidity, APACHE II (admission), factors associated to the development of ARDS, time between risk factors and start of mechanical ventilation and duration of the same with complications, less  $\text{PaO}_2/\text{FiO}_2$ , maximum PEEP, use of Swan–Ganz catheter and amines (dopamine

$> 5 \mu\text{g}/\text{kg}/\text{min}$ , norepinephryne and epinephryne), type of nutrition and causes of death.

**Statistical analysis:** Program SPSS 9.0 was used, unvaried analysis with  $\chi^2$  and exact Fisher tests.  $P$  was considered significant  $< 0.05$ .

**Results:** 550 cases were reviewed. Forty fulfilled criteria of ARDS (18 men and 22 woman). The punctual prevalent was 8.8% and the incidence was 19 per 100 anual. The mortality was 55%. Of the evaluated variables  $P < 0.05$  was found between living and death: the number of days in ICU and hospital stay, APACHE II (admission) and less  $\text{PaO}_2/\text{FiO}_2$ . The risk factors found associated were direct (30%), indirect (45%) and both (25%).

**Conclusions:** The punctual prevalence was 8.8%. The Incidence was 19 per 100 anual. ARDS is an important cause of death (55%) and the independent variables for mortality found were: APACHE II  $> 18$  and less  $\text{PaO}_2/\text{FiO}_2 < 100$  with OR 50.66 and CI 95% (7.51–341).

**P234 Acute lung injury in paediatric intensive care: course and outcome**

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**Introduction:** Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) carry a high morbidity and mortality (10–90%). ALI is characterised by non-cardiogenic pulmonary oedema and refractory hypoxaemia of multifactorial aetiology [1]. There is limited data about outcome particularly in children.

**Methods:** This retrospective cohort study of 85 randomly selected patients with respiratory failure recruited from a prospectively collected database represents 7.1% of 1187 admissions. They include those treated with High Frequency Oscillation Ventilation (HFOV). The patients were admitted between 1 November 1998 and 31 October 2000.

**Results:** Of the 85, 49 developed acute lung injury and 47 had ARDS. There were 26 males and 23 females with a median age and weight of 7.7 months (range 1 day–12.8 years) and 8 kg (range 0.8–40 kg). There were 7 deaths giving a crude mortality of 14.3%, all of which fulfilled the Consensus I [1] criteria for ARDS. Pulmonary occlusion pressures were not routinely measured. The A–a gradient and  $\text{PaO}_2/\text{FiO}_2$  ratio (median + [95% CI]) were 37.46 [31.82–43.1] kPa and 19.12 [15.26–22.98] kPa respectively. The non-survivors had a significantly lower  $\text{PaO}_2/\text{FiO}_2$  ratio (13 [6.07–19.93] kPa) compared to survivors (23.85 [19.57–28.13] kPa) ( $P = 0.03$ ) and

had a higher A–a gradient (51.05 [35.68–66.42] kPa) compared to survivors (36.07 [30.2–41.94] kPa) though not significant ( $P = 0.06$ ). Twenty-nine patients (59.2%) were oscillated (Sensormedics 3100A) including all 7 non-survivors. There was no difference in ventilation requirements for CMV prior to oscillation. Seventeen of the 49 (34.7%) were treated with Nitric Oxide including 5 out of 7 non-survivors (71.4%). The median (95% CI) number of failed organs was 3 (1.96–4.04) for non-survivors compared to 1 (0.62–1.62) for survivors ( $P = 0.03$ ). There were 27 patients with isolated respiratory failure all of whom survived. Six (85.7%) of the non-survivors also required cardiovascular support.

**Conclusion:** A crude mortality of 14.3% compares favourably to published data. The A–a gradient and  $\text{PaO}_2/\text{FiO}_2$  ratio may be of help in morbidity scoring in paediatric ARDS. Use of Nitric Oxide and HFOV is associated with increased mortality, which probably relates to the severity of disease. Multiple organ failure particularly respiratory and cardiac disease is associated with increased mortality. ARDS with isolated respiratory failure carries a good prognosis in children.

**Reference:**

1. Bernard GR, Artigas A, Brigham KL: **The American–European Consensus Conference on ARDS.** *Am J Respir Crit Care Med* 1994, 149:818–824.



**P237 The impact of demographics, chronic health status and severity of disease on outcome from mechanical ventilation: a prospective cohort study**

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**Objectives:** 1) To describe the characteristics of the ICU patients undergoing prolonged mechanical ventilation (MV) and estimate its incidence. 2) To evaluate the impact of demographics, chronic health status and severity of disease on the duration of MV and on short-term mortality.

**Setting:** A 20 bed multidisciplinary ICU of a 650 bed tertiary university hospital.

**Design:** A prospective dynamic cohort study. Impact on outcome was analyzed by univariate (attributable risk, relative risk increase and survival analysis), and multivariate analysis (relative risk of disconnection [HR] and of mortality [OR]), by the Cox proportional hazards and logistic regression models).

**Patients:** From a whole population of 591 patients admitted to the ICU between November 1998 and October 1999, we enrolled 205 patients who received MV for more than 12 hours.

**Results:** Incidence of MV 34.7%. Age  $57.8 \pm 1.2$  years. Males 136 (66%). SAPS II scoring:  $42.01 \pm 1.23$  (mean  $\pm$  EE), APACHE II scoring:  $17.78 \pm 0.53$  (mean  $\pm$  EE), multisystem organ failure (MSOF): 1 (0–2) (median and 25–75% interquartile range), a simplified organ failure index (s-OFI): 1 (1–2) (median and 25–75% interquartile range). ICU mortality: 25.4% (52), hospital mortality: 33.7% (69). Duration of MV:  $13.9 \pm 2.4$  days. Weaning time:  $8.8 \pm 2.2$  days (62.3% of total ventilation time). The mean duration of MV was longer in respiratory pathology ( $29.6 \pm 13.9$  days), followed by neurologic ( $14.9 \pm 6.3$  days) and trauma ( $12.8 \pm 1.9$  days). It was longer in nonsurvivors  $15.6 \pm 5.1$  versus  $10.8 \pm 1.6$  days in survivors (log-Rank,  $P < 0.00005$ ). ICU length of stay (LOS)  $16.6 \pm 2.1$  days, hospital LOS  $41.9 \pm 3.3$  days.

APACHE II (hazard ratio [HR] 0.92; 95% CI: 0.89–0.95), body mass index (HR 0.97; 95% CI: 0.93–0.99), sepsis with or without associated pneumonia (HR 0.36; 95% CI: 0.19–0.70), and ARDS (HR 0.20; 95% CI: 0.06–0.68) reduced independently the rate of disconnection from MV. Surgical vs medical category (HR 1.68; 95% CI: 1.1–2.56), and the presence of chronic respiratory disease (HR 1.71; 95% CI: 1.02–2.90) increased the rate of disconnection.

Female gender with an attributable risk of hospital mortality of 14.8% (95% CI: 1.0–28.7%), an attributable fraction in exposed population of 34.0% (95% CI: 3.8–54.8%);  $\chi^2$  4.49,  $P = 0.034$ , and an adjusted odds ratio (OR) of 2.80 (95% CI: 1.22–6.41), degree of malnutrition (OR 2.80; 95% CI: 1.35–5.84), SAPS II (OR 1.07; 95% CI: 1.03–1.10), cardiac arrest on arrival (OR 34.42; 95% CI: 6.90–171.58), postoperative respiratory failure (OR 3.65; 95% CI: 1.20–11.03), and cardiac failure (OR 5.93; 95% CI: 1.56–22.48) increased hospital mortality risk, whereas age (OR 0.97; 95% CI: 0.94–0.99) decreased it.

**Conclusions:** ICU patients undergoing prolonged MV represented an important subset of the whole ICU population (one third of total admissions, half of them medical category). Prolonged MV was associated with a relatively high short-term (ICU and hospital) mortality and prolonged ICU and hospital LOS. Gender category, chronic health condition and several early-acquired clinical data successfully predicted both the duration of MV and short-term mortality. Severity scoring indexes behaved as useful tools to predict the duration of MV (APACHE II) and the risk of mortality (SAPS II). Increasing age was not necessarily associated with an adverse outcome.

**P238 Management of hematological patients in ICU: a retrospective study of 110 patients**

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**Introduction:** Intensive care in hematological patients remains challenging. In despite of an aggressive and sometimes prolonged treatment, outcome in ICU remains poor, particularly in septic patients.

**Methods:** A retrospective review of hematological patients suffering from acute leukemia (AL), non-Hodgkin's lymphoma (NHL) and Hodgkin's lymphoma (HL), hospitalized in our ICU from January 1995 to October 2000, has been performed. We studied demographic data, mortality rates and risk factors associated to mortality both for all patients (excepted allogeneic transplants patients) and for septic patients.

**Results:** 110 patients have been included in our study and 10 of them benefited from an allogeneic bone marrow transplantation. Mean age was 47.49 years (range 16–77), and sex-ratio male/female was 1.08. 58% suffered from AL, 36% from NHL and 6% from HL. Sepsis, respiratory and neurologic failures represented the most frequent causes of admission. Mean SAPS II, SOFA max and OSF scores were respectively 51.41, 9.07 and 2.40. Mean OSF decreased significantly between 1997 and 2000

(2.66 vs 1.90;  $P = 0.04$ ). Mean mortality rate was 56%. In univariate analysis, SAPS II, SOFA max, OSF scores, mechanical ventilation, extrarenal replacement and use of amines were significantly associated with mortality. Renal, hepatic, neurologic and circulatory failures at admission were also significant.

Among the 110 patients, 53 (48.18%) had septic conditions (severe sepsis and septic shock). Mean age was 47.51 years. Mean SAPS II, SOFA max and OSF scores were respectively 59.11, 10.68 and 2.98. Mean mortality rate was 75.47%. Comparisons between septic patients during these 5 years showed no statistical differences, excepted for mean SAPS II which increased significantly between 1995 and 1999 (40.71 vs 77.63;  $P = 0.04$ ). Severity-of-illness scores, use and duration of mechanical ventilation, extrarenal replacement (ERR) and amines were significantly associated with mortality. Interestingly, only hepatic, neurologic and circulatory failures at admission were also significantly associated to a poor outcome. Mortality rates in patients with no organ supply, with 1, 2 and 3 supplied organs were respectively 0%, 66.66%, 86.66% and 92.59%. Type of disease was not associated to an increased mortality rate. Performing chemotherapy in



Numbers	Survivors		Non-survivors	
	Day 1 (n = 33)	Day 3 (n = 23)	Day 1	Day 3 (n = 32)
Age (years)	51 (16–76)		52 (15–74)	
Sex	1:2		1:2.1	
APACHE II	26.5 (11–35)	22 (9–30)	27 (10–44)	26 (14–38)
Organ failure score	26.3 (11–37.8)	20 (9.2–32.4)	27.6 (10–47.5)	27.3 (14.4–41)
Number of organ failure	2 (0–3)	1 (0–3)	2 (0–4)	2 (0–4)
P/F ratio	187.5 (52–497)	206 (67–543)	190 (48–520)	134 (42–324)

**P241 Outcome of neonates operated on for congenital diaphragmatic hernia**

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**Introduction:** Congenital diaphragmatic hernia (CDH) is a severe disorder in neonates. The prognosis has been improved in the past 10 years by a combination of HFO ventilation, sedation and analgesia, nitric oxide and delayed surgery. Extracorporeal oxygenation (ECMO) has been proposed by certain teams. A decrease in mortality from 70% to approximately 40% has recently been reported [1,2]. However, little is known about the outcome of such patients. We report the outcome of a group of patients after 10 years' follow-up.

**Patients and methods:** A retrospective review was undertaken of neonates admitted to the paediatric intensive care unit after 1 January 1992 (date at which new treatment methods were introduced in the department) and operated on for congenital hiatus hernia.

**Results:** Nineteen neonates were reviewed, of whom seven died (36%) and 74% had left hernia. Two of the 12 remaining survivors had other malformations (cardiac and urogenital). Mean age at the time of surgery was 17 hours. Median ventilation duration was 6 days. Median duration of intensive care was 12.5 days. 58% chil-

dren were discharged from intensive care unit with oxygen therapy and median hospitalization duration was 31 days. Mean age at the last consultation was 18 months (SD 18). Six infants required readmission and four had severe respiratory disorders (one with severe bronchiolitis, one with asthmiform bronchitis and one with chronic clinical respiratory insufficiency). One infant was hospitalized for more than 12 months and required left pneumonectomy and tracheotomy. Six infants had gastro-esophageal reflux, of whom one required surgery. This infant also had residual hiatus hernia and scoliosis. Three infants had neurological sequelae (one with psychomotor retardation and two with overall hypotonia, one of whom had problems with swallowing).

**Discussion:** Our results showed that 1) the mortality was similar to those reported by the other two French series [1,2] (36%) despite the lack of use of ECMO and 2) middle-term morbidity was low compared to the mortality reported after ECMO [1].

**References:**

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**P242 The intensive care unit in paediatric oncology: 10 years experience**

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We report the results of a retrospective study of the intensive care outcome of 196 children admitted with malignancy at a tertiary referral institution over a period of 10 years from 1988 to 1997. A total of 165 children required 196 admissions for a median of 3 days. Their mean age was 5.82 years and there were 100 boys (51%) and 96 girls (49%). Their admission median Apache II score was 18. A total of 150 children (76.5%) survived intensive care. Nonsurvivors had a higher Apache II score than survivors (23 vs 15 respectively,  $P < 0.001$ ). Patients were divided into those needing postoperative care ( $n = 55$ ), patients with respiratory infection ( $n = 39$ ), systemic infection ( $n = 30$ ), neurological complications ( $n = 20$ ), respiratory failure with no evidence of infection ( $n = 17$ ), metabolic effect ( $n = 13$ ), tumour mass effect ( $n = 9$ ), GI bleed ( $n = 5$ ), cardiac failure ( $n = 4$ ), post cardiac arrest ( $n = 3$ ). The overall survival, defined as those who survived 1 week after discharge from PICU, was 73.4%. Invasive monitoring including arterial and central venous pressure line were inserted in 143 (72.9%), mechanical

ventilation was required for 133 (67.8%), ionotropic support for 66 (33%), pulmonary artery floatation catheter insertion and monitoring in 23 (11.7%) and renal replacement therapy for 13 (6.6%) children. The profile of diseases in children admitted in PICU appears to be changing since last report from this unit in 1992 [1]. The most common reason for admission was need for postoperative care (28%) and survival in this group was 100%. There also is a significant improvement in survival rate of patients with systemic infections (63%) needing ventilatory support and children with respiratory (with or without infection) failure (67%) [2].

**Reference:**

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± 14.9 years. Sixteen (34%) patients died. Of the 16, 11 (68.8%) were admitted with a GCS ≤ 4.11 (35.5%) of the survivors had an admission GCS ≤ 4. MVA's accounted for 66% of head injuries, followed by assault injuries at 25.5%. 81.25% of the patients died as a result of the primary brain damage. No association could be established between poor outcome and the presence of concomi-

tant injuries, non-operative management and the number of brain lesions.

**Conclusion:** Mortality from head trauma is high. An initial low GCS ≤ 4 is associated with poor outcome. A few patients with an initial low GCS do recover fully.

**P246 Factors influencing the functional outcome in a neurointensive care unit**

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**Introduction:** The aim of the present study was to investigate the factors that affect the outcome of patients with central nervous system pathology.

**Method:** One hundred and thirty patients (head injury [*n* = 43], multiple trauma [*n* = 40], cerebral hemorrhage [*n* = 36] and emergency cerebral aneurysm repair [*n* = 11]) were investigated for age, GCS, CT-Scan grade, ISS, and APACHE II. Male to female ratio was 96/34. The patients were divided in five groups according to Glasgow Outcome Scale: 1) group A, *n* = 50 (GOS 1, death), 2) group B, *n* = 5 (GOS 2, severe brain damage), 3) group C, *n* = 17 (GOS 3, moderate brain damage), 4) group D, *n* = 28 (GOS 4, mild disability) and 5) group E, *n* = 30 (GOS 5, full recovery).

**Table**

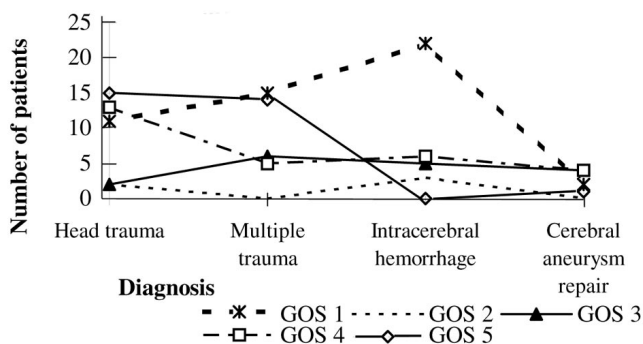
Groups	Age (years)	GCS	CT-Scan grade	ISS	APACHE II
A	42.3 ± 17.5**	6.1 ± 2.5*	3.5 ± 0.5*	29.1 ± 9.3	19.9 ± 4.5
B	53 ± 20.8*	5.8 ± 1.0	3.2 ± 0.8	25 ± 0	15.6 ± 6.8
C	43.7 ± 19.7*	6.6 ± 3.0	3 ± 0.8	36.6 ± 8.3*	21.5 ± 4.5*
D	37.6 ± 16.2	7.0 ± 3.1	2.7 ± 0.7	24.6 ± 6.1	18.4 ± 4.8
E	28.2 ± 15.1	8.2 ± 3.4	2.8 ± 0.8	26.1 ± 8.2	16.9 ± 4.9

Mean ± SD. \* *P* < 0.05, \*\* *P* < 0.01.

**Results:** Total mortality was 38.4%. There was a statistically significant difference (one way analysis of variance ANOVA) regarding: 1) age: groups A, B and C versus E, 2) GCS: group A versus E, 3) CT-Scan grade: group A versus D and E, 4) ISS: group C versus D and E and 5) APACHE II score: group C versus E (Table). Patients with head injury or multiple trauma had better outcome than patients with cerebral hemorrhage (Fig.).

**Conclusion:** Age, GCS and CT-Scan grade were related to the patient outcome regarding life or death whereas diagnosis, age, ISS and APACHE II determined the severity of disability.

**Figure**



Relation of diagnosis to GOS

**P247 Prolonged intensive care unit stay: predictors and impact on resource utilization**

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**Objective:** To evaluate the predictors of prolonged ICU stay its impact on resource utilization.

**Methods:** We collected the following data prospectively on all ICU admissions between 2/1999 and 9/2000: demographics, ICU stay, APACHE II and SAPS II scores, the main reason for ICU admission, re-admissions and ICU outcome. We documented the presence of coma, oliguria, coagulopathy and infection as well as the need for mechanical ventilation or vasopressors in the first 24 hours. ICU stay was considered prolonged if it exceeded 14 days. We calculated the utilization of ICU days and ventilator days. We identified predictors of prolonged stay using univariate analysis.

**Results:** Eleven percent of patients (104/947) stayed in ICU > 14 days. This group of patients used 45% (2880/6392) of ICU days and 56% (2556/4604) of ventilation days. Prolonged stay patients had higher APACHE II (21 ± 8 vs 19 ± 9, *P* = 0.016) and SAPS II

scores (43 ± 16 vs 37 ± 20, *P* = 0.003), although ICU mortality was not different (19% vs 21%). Patients were more likely to have prolonged stay if the main reason for admission was respiratory (OR 2.2, CI 1.4–3.6) or trauma (OR 2.1, CI 1.4–3.4) and less likely if it was non-trauma surgical (OR 0.27, CI 0.13–0.54). Prolonged stay occurred more likely with re-admissions (OR 2.1, CI 1.1–3.8) and in patients with oliguria (OR 1.8, CI 1.1–3.1), coagulopathy (OR 1.5, CI 1.01–2.3), infection (OR 2.3, CI 1.5–3.5), mechanical ventilation (OR 1.9, CI 1.3–2.9) and vasopressor therapy (OR 1.8, CI 1.2–2.7).

**Conclusions:** Although patients with prolonged stay constitute a small fraction of ICU patients, they consume a significant proportion of ICU resources. Patients admitted for respiratory or trauma indications are more likely to have prolonged stay. Attempts to shorten ICU stay, such as by development of clinical pathways, should especially target these patients. Caring after some of these patients in a step-down unit may have a great impact on resource utilization.



**P250 Incidence and course of early cardiac failure in long term ICU patients**

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**Introduction:** Cardiac failure is a potential motor of multiple organ failure in long term ICU patients [1]. The aim of our study was to monitor incidence on admission of cardiac failure in long term ICU patients. The early course (first 72 hours) of cardiac failure was also evaluated.

**Materials and methods:** ICU database was used for data acquisition. Long term patients were defined as those who survived > 3 days in the ICU. Cardiac failure was defined as cardiac SOFA points ≥ 3.

**Statistics:** Chi-square, Fisher exact test, Mann-Whitney U-test and Manova for repeated measures when appropriate. Data are presented as means ± SD. *P* < 0.05 was considered significant.

**Results:** Out of 110 patients admitted from January 1 to October 15, 72 (65%) stayed in the ICU > 3 days. Forty-six patients (65%) survived and 26 died. Survivors (S) and non-survivors (NS) did not differ in age (55.2 ± 15.9 and 60.5 ± 15.9 years, respectively; *P* = 0.18). S had significantly higher APACHE II score on admission than NS (24.2 ± 7.2 and 29.2 ± 7.0, respectively; *P* < 0.01).

S had significantly lower incidence of cardiac failure on admission (< 24 hours) compared to NS (13 [28%] and 17 [65%], respectively, *P* < 0.001). This difference was attenuated but remained significant by day 2 when additional 5 S developed cardiac failure (8 developed, 3 recovered) and there was no change in NS (*P* < 0.05). Non-survivors had a trend to more severe forms (cardiac SOFA points 4) of cardiac failure in the first two days of hospitalisation (*P* = 0.1). The course of cardiac failure during the first 3 days of ICU stay did not differ between S and NS (Manova time effect *P* = 0.23). Only 2 survivors without cardiac failure during the first 48 hours (*n* = 25) developed cardiac failure during their further ICU stay (both later than 72 hours after admission).

**Conclusions:** Long term ICU patients who do not survive have greater incidence of cardiac failure on admission. Nevertheless the course of cardiac failure during the first 3 ICU days does not differentiate between survivors and non-survivors.

**Reference:**

1. Nalos M *et al*: **Incidence, severity and mime course of cardiovascular failure in patients requiring prolonged intensive care.** *Intensive Care Med* 1997, **23** (suppl 1):52.

**P251 Premature discharge of patients from ICU increases mortality**

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The pressure on intensive care beds has led to the discharge of patients before clinically indicated. It has been shown that discharging patients with high TISS scores increases mortality [1], and it has been stated that 'premature' discharge is likely to worsen outcome [2]. We postulated that premature discharge would increase mortality, and that this would be independent of the different TISS scores that were likely to occur.

All ICU patients discharged alive to the ward during 1997-1999, whose reason for discharge had been recorded by the ICU consultant as fully fit or premature were studied. We excluded those discharged for palliative care. We compared the groups APACHE II, admission risk of death, length of ICU stay and last TISS using ANOVA. We then assessed the relative risk of hospital mortality and investigated the association between TISS on day of ICU discharge, reason for discharge and mortality using ordinal regression analysis.

552 patients were identified (Premature Group 145, Fully Fit Group 407). ANOVA identified a significant difference in last TISS, but no significant difference in APACHE II, risk of death or ICU length of stay (Table 1). The hospital mortality was greater in the premature group (relative risk 2.1, 95% CI 1.3-3.5). Both last TISS and discharge reason were found to be independent indicators of hospital mortality (Table 2).

Patients who leave ICU before they are considered fit for discharge are twice as likely to die, despite minimal difference in their risk of death on ICU admission. Although they are receiving more care when they are discharged the excess mortality in those discharged prematurely is equivalent to that associated with a further increase in last TISS of 14 points.

**References:**

1. Smith L, Orts CM, O'Neil I *et al*: *Intensive Care Med* 1999, **25**:1061-1065.
2. Goldhill DR, Sumner A: *Crit Care Med* 1998, **26**:1337-1345.

**Table 1**

**ICU data for patients**

	<i>n</i>	Hospital deaths ( <i>n</i> )	APACHE II mean	Risk of death (%) mean	ICU stay (days) median	Last TISS median
Premature	145	24	17.1	26	1.80	24
Fully fit	407	32	16.3	23	1.60	22
<i>P</i>			0.18	0.1	< 0.001	0.73

*P* values from ANOVA.

**Table 2**

**Ordinal regression for hospital mortality using last TISS and premature discharge**

	Threshold	Last TISS	Premature
Parameter	3.69	0.034	0.738
<i>P</i>	< 0.001	0.006	0.012



**Table 1**

Variable	$\beta$ (SE)	$r$
Age	0.017 (0.0074)	0.0893
Sex	-0.409 (0.25)	-0.0394
MPM II <sub>0</sub>	2.25 (0.77)	0.1236
Constant	-1.94 (0.56)	

**Conclusion:** Our data suggest that in a large ICU age, sex and MPM II<sub>0</sub> but not ratio of nursing workload to nurses on duty are related to outcome. The difference between our findings and those of Tarnow-Mordi *et al* [1] may reflect differences in size and organization of the respective units.

**References:**

1. Tarnow-Mordi WO, Hau C, Warden A, Shearer AJ: **Hospital mortality in relation to staff workload: a 4-year study in an adult intensive-care unit.** *Lancet* 2000, **356**:185-189.
2. Intensive Care Society. *Intensive Care Audit.* London: Intensive Care Society, 1990.

**P254 Terminal weaning from mechanical ventilation in critically ill patients with or without severe brain damage**

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**Introduction:** The withdrawal of mechanical ventilation as a terminal care process occurs with increasing frequency. The aim of the study was to evaluate patients undergoing terminal weaning (TW) with or without severe brain damage.

**Methods:** A prospective, descriptive study of all patients experienced TW during 2 years period was conducted. Apache II, SOFA, length of ICU stay (days) before decision of TW (LOS), method (step-wise reduction or withdrawal of ventilatory support), using analgesia/sedation during TW procedure and length of TW (LTW) in minutes were recorded. Data as mean (SD), median (25-75%), *t*-test, Mann-Whitney Rank Sum Test (SigmaStat Statistical Software) were used,  $P < 0.05$  was considered statistically significant.

**Results:** Sixteen patients were studied, Apache II and SOFA score were 32 (6.9) resp. 12.9 (3.7). Eleven patients with severe brain damage (group BD), five patients without brain damage (group NBD). All patients died during TW. The LOS was shorter in BD

group comparing to NBD group, 2.9 (1.9) resp. 17 (9.3),  $P < 0.0001$ . The TW procedure was step-wise reduction of ventilatory support in 5 patients and as a ventilator withdrawal in 11 patients. The length of TW was 17 (12-87) in BD group and 187 (16-605) in NBD group. Analgesia/sedation was employed in eight patients, there were no statistically significant differences in LTW between patients with or without analgesia/sedation (223, 13-662, resp. 15, 12-43,  $P = 0.232$ ).

**Discussion:** LOS before decision of TW was significantly longer in patients without brain damage. There were no significant differences in length of TW as between groups BD and NBD as between patients with or without analgesia.

**Reference:**

- Campbell LM, Bizek KS, Thill M: **Patients responses during rapid terminal weaning from mechanical ventilation: a prospective study.** *Crit Care Med* 1999, **27**:73-77.

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**P255 Limitation of life-support therapy in critically ill patients: family response and attitudes**

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**Introduction and aim:** Despite modern intensive therapy, 10-20% of patients admitted to ICU will not survive [1,2]. Dealing with family issues surrounding death is therefore an important aspect of ICU care. The purpose of this study was to record aspects of the experience of families whose relative had undergone LOT and identify the views of the family regarding who should be involved in the process of LOT.

**Methods:** Consent for a telephone interview and demographic data were obtained from the representative of all families whose relative had died in the ICU. Four weeks later, the representative was contacted for a structured telephone interview. Questions explored the respondents experience of anxiety related to the process of LOT, their understanding of the explanation and the reasons for LOT, and the adequacy of time to participate in the decision. Respondents were asked who should be involved in the decision process.

**Results:** The relatives of 88 patients who died were interviewed. Sixty-six (75%) patients had undergone LOT. The majority of respondents (90%) expressed that the explanation of LOT was clear and understood, but 18% felt pressurized into decision

making, and 16% felt that inadequate time was allowed for discussion before the decision was made. Participating in the LOT decision provoked anxiety in 45% of respondents. However, when compared with respondents whose relatives did not undergo LOT, the expression of anxiety was lower ( $P < 0.01$ ). Respondents indicated that LOT decisions should be made by the doctor and patient and/or family group (41%), family and/or patient alone (32%), or doctor alone (22%).

**Discussion and conclusion:** While most family members understand the process of LOT, it is still associated with significant anxiety. Allocating more time to the decision making process and improving communication techniques may be important. Family members believe that they should be part of the decision making process.

**References:**

1. Smedira NG *et al*: **Withholding and withdrawal of life support from the critically ill.** *N Engl J Med* 1990, **322**:309-315.
2. Turner JS *et al*: **Limitation of life support: frequency and practice in a London and a Cape Town intensive care unit.** *Intensive Care Med* 1996, **22**:1020-1025.



Springfield, MA. Data collected in the ICU for the Project IMPACT database was merged with cost data from the hospital's cost accounting system to obtain costs based on actual use, not cost/charge ratios.

**Methods:** Patients were identified as early sepsis based on one of the following criteria; 1) primary acute ICU admission diagnosis of SIRS, septic shock, or Multi Organ Dysfunction Syndrome (MODS); 2) notation in the ICU log book of sepsis on admission; 3) infection at 24 hours plus evidence of hypotension, hypoperfusion or multiple organ dysfunction. Resource use measures computed for each patient included: a) total hospital costs incurred during the ICU stay, b) mean costs per ICU day, c) total costs incurred from ICU admission to hospital discharge, d) costs per day during ICU stay for specific cost categories (pharmacy, lab, imaging, respiratory therapy), e) ICU and total hospital (from ICU admission) length of stay (LOS).

**Results:** 14.2% of patients admitted to ICU had early sepsis ( $n = 155$ ). Comparison groups were respiratory diagnosis at ICU admission ( $n = 273$ , 25.1%) and all others ( $n = 660$ , 60.7%). Mean ( $\pm$ SD) cost of the ICU stay for early sepsis patients (\$29,582  $\pm$  39,399) was greater than for respiratory (\$16,757  $\pm$  15,439) and all other (\$17,544  $\pm$  23,712). Mean ICU LOS for early sepsis was 10.4 ( $\pm$  12.6) days compared to 6.8 ( $\pm$  6.1) days

for respiratory and 5.8 ( $\pm$  8.2) days for all other. Mean cost per ICU day for early sepsis was \$2844 compared to \$2464 for respiratory and \$3025 for all other. Mean total costs and LOS (ICU admission to hospital discharge) for early sepsis patients (\$39,949  $\pm$  45,278), (19  $\pm$  19.4 days) was greater than that for respiratory (\$24,824  $\pm$  21,347), (13.3  $\pm$  11.7 days) and all others (\$26,022  $\pm$  29,870), (12.6  $\pm$  12.7 days). Results for specific costs are as follows.

**Mean cost for ICU stay**

	Early sepsis patients	Respiratory patients	All other patients
Pharmacy	2625 $\pm$ 3555	1443 $\pm$ 1767	1436 $\pm$ 2495
Lab	2463 $\pm$ 3109	1127 $\pm$ 1220	1224 $\pm$ 2009
Imaging	1217 $\pm$ 1389	683 $\pm$ 653	784 $\pm$ 1100
Respiratory therapy	2387 $\pm$ 3245	1791 $\pm$ 1809	1213 $\pm$ 2117

**Conclusion:** Compared to respiratory and other patients, mean total costs for patients admitted to ICU with early sepsis is 50% higher.

**P259 The cost in different subgroups of critically ill patients: a multicentric study in Czech Republic**

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**Introduction:** Intensive care units account for a large proportion of hospital expenditures. The aim of the study was to evaluate different subgroups of patients for clinical outcome and cost of care.

**Methods:** 1368 patients were prospectively studied. Demographic data, APACHE II and SOFA score, diagnostic group (TR = trauma, TBI = traumatic brain injury, COPD = chronic obstructive pulmonary disease, CPR = cardiac arrest, ARDS = acute respiratory distress syndrome, INTOX = intoxication), length of ICU stay (LOS), clinical outcome and cost of care in CZK were recorded. Relationship among between cost, diagnostic groups and severity score were evaluated. Data as mean (SD), median (25–75%),  $t$ -test, Mann–Whitney Rank Sum Test,  $z$ -test, ANOVA, linear regression (SigmaStat Statistical Software) were used,  $P < 0.05$  was considered statistically significant.

**Results:** Selected results are presented. The longest LOS and most expensive care were observed in ARDS patients. The independent variable of cost is LOS ( $r = 0.679$ ,  $P < 0.001$ ).

**Discussion:** There were significant differences among selected groups of patients concerning clinical outcome, LOS and cost of care. Obtained data may be of importance in ICU budgeting and in comparing different intensive care units.

**Reference:**

Ingelhart JK: **The American health care system: expenditures.** *N Engl J Med* 1999, **340**:70–76.

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	Number of patients	Apache II	SOFA	Mortality
All	1368	24 (8.9)	8.1 (5.1)	258 (18.8%)
TR	115	21.8 (8.2)	8.6 (3.8)	16 (13.9%)
TBI	137	23.3 (7.7)	6.8 (3.3)	12 (10.9%)
COPD	86	23.3 (6.8)	7.1 (3.4)	11 (12.7%)
CPR	184	32.1 (7.9)	10.3 (3.4)	53 (28.8%)
ARDS	76	25.6 (8.1)	10.7 (3.9)	15 (19.7%)
INTOX	425	21.2 (8.7)	7.5 (4.4)	83 (19.5%)

	TR	TBI	COPD	CPR	ARDS	INTOX
Apache II	19 (17–26)	23 (18–29)	22 (19–23)	32 (27–38)*	26 (19–31)	21 (15–27)
SOFA	7 (6–11)	6 (4–9)	7 (4.5–9)	10 (8–13)†	10.7 (8–13)	6 (4–11)
LOS (days)	10.5 (3–19)	5.5 (4–9)	12.5 (5–21)	5 (2–17)	14 (8–21)	3 (2–7)
Cost (CZK)	168,951 (55,910– 329,056)	127,835 (29,950– 263,849)	213,223 (98,711– 363,445)	63,054 (22,748– 169,757)	322,913‡ (143,822– 519,927)	41,720 (15,567– 127,117)

35 CZK = 1 EUR. \* vs all subgroups ( $P < 0.05$ ), † vs COPD, INTOX ( $P < 0.05$ ), ‡ vs COPD, TBI, INTOX ( $P < 0.05$ ).



**P262 Accidental withdrawal of tubes, sounds and catheters**

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	Number of patients with catheter	Number of catheters	Number of catheter-days	Number of AW	Number of AW per 100 catheter	Number of AW per 100 catheter-days
OT	223	245	1802	14	5.71	0.77
CVC	251	454	3212	12	2.64	0.37
DC	68	96	717	2	2.08	0.27
IYVC	172	195	1112	6	3.07	0.53
SVC	87	117	1007	3	2.56	0.29
FVC	36	46	376	1	2.17	0.26
AC	232	348	2031	28	8.04	1.37
RAC	220	310	1702	23	7.41	1.35
FAC	35	38	329	5	13.15	1.51
NGS	232	380	2114	148	38.94	7
VS	246	334	2444	1	0.29	0.04
ETPE	122	122	400	0	0	0
IABC	7	7	16	0	0	0
TDT	138	270	575	0	0	0
ADT	21	41	316	0	0	0
IPC	17	21	199	0	0	0

**Objective:** To determine accidental withdrawal (AW) of tubes, sounds and catheters.

**Design:** Prospective observational study.

**Setting:** A 20-bed medical-surgical Intensive Care Unit (ICU).

**Patients:** All patients admitted in ICU from 1-5-2000 to 31-10-2000.

**Results:** 253 patients were admitted (64.03% males). Mean age was 57.64 ± 16.71 years. APACHE-II was 12.48 ± 5.52. Mortality was 15.81%. Patients distribution was: 48% cardiac surgery, 14% cardiologic, 10% neurologic, 8% traumathology, 7% pulmonary, 6% digestive and 7% others. Patients need the following monitoring:

88.14% orotracheal tube (OT), 99.20% central venous catheter (CVC), 26.87% drum catheter (DC), 67.98% internal jugular vein catheter (IYVC), 34.38% subclavian vein catheter (SVC), 16.14% femoral vein catheter (FVC), 91.69% artery catheter (AC), 86.95% radial artery catheter (RAC), 13.83% femoral artery catheter (FAC), 91.69% nasogastrical sounds (NGS), 96.09% vesical sound (VS), 48.22% epicardial temporary pacemaker electrode (ETPE), 2.76% intraaortic balloon counter pulsation catheter (IABC), 54.54% thoracic drainage tube (TDT), 8.30% abdominal drainage tube (ADT) and 6.71% intracranial pressure catheter (IPC).

**Conclusions:** This study permit to know our current levels of accidental withdrawals and comparing them with other ICU and with our results in the future.

**P263 Evaluation of daily fluid balance during continuous hemodialysis and filtration (CHDF)**

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**Introduction:** In critical care, accurate assessment of daily fluid balance is both necessary and important. We evaluated the accuracy of the calculated daily fluid balance during continuous hemodialysis and filtration (CHDF) by checking the relationship between two values: (a) daily fluid balance calculated from the balance sheet, and (b) daily body-weight change, a standard way of evaluating daily fluid balance.

**Materials and Methods:** We studied data obtained from patients who underwent CHDF using one of two machines, CHF-1 or JUN-500 (Ube Medical Corporation, Tokyo, Japan). CHDF patients were randomly assigned to one or other of the machines: Group-A (14 patients) to CHF-1 and Group-B (7 patients) to JUN-500. We also studied the relationship between the two values, (a) and (b), above in 10 patients (Group C) not undergoing CHDF. Within

each group, the correlation between values (a) and (b) was studied by regression analysis. Significance was defined as  $P < 0.05$ .

**Results:** The number of time-points studied was 32 in Group A, 22 in Group B, and 45 in Group C. Within each group, we saw a significant relationship for (a) versus (b), the coefficient numbers ( $r^2$ ) being 0.400 in Group A, 0.663 in Group B and 0.757 in Group C.

**Discussion:** JUN-500 has three pumps, providing a stricter regulation of rates of infusion and removal of fluids; this may have given more accurate management under CHDF than that achieved with CHF-1. During CHDF, a large amount of water may be infused

and/or removed, and so a slight error in pump calibration can lead to a considerable inaccuracy in the daily fluid balance calculated from the balance sheet. This would result in a fairly low correlation number for (a) versus (b). In our Groups A and B, although we found significant relationships between the two values, the  $r^2$  numbers were not particularly high. Therefore, using the above reasoning, we would have been unwise to draw conclusions about changes in daily fluid balance using balance-sheet data alone.

**Conclusion:** During CHDF, daily fluid balance still needs to be based on data obtained by measurement of daily weight change, not solely on data obtained from the fluid-balance sheet.