22nd International Symposium on Intensive Care and Emergency Medicine

Brussels, Belgium, 19–22 March 2002

Published online: 1 March 2002

(Print ISSN 1364-8535; Online ISSN 1466-609X)

Critical Care 2002, **6(suppl 1)**

P1 Epidemiology of ARDS in a Brazilian ICU

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Purpose: To describe the epidemiology of the acute respiratory distress syndrome (ARDS) in a Brazilian ICU.

Methods: This prospective observational, non-interventional study, included all consecutive patients with ARDS criteria [1] admitted in the ICU of a Brazilian tertiary hospital, between January 1997 and September 2001. Were collected in a prospective fashion the following variables: age, gender, APACHE II score at ICU admission and at ARDS diagnosis, cause of ARDS, presence of AIDS, cancer and immunosuppression, occurrence of barotrauma, performance of traqueostomy, mortality, duration of mechanical ventilation (MV), length of stay (LOS) in ICU and in hospital. The lung injury score (LIS) [2] was used to quantify the degree of pulmonary injury in the first week of ARDS.

Results: There was 2182 patients (P) admitted in ICU during the study period, of whom 141 (6.46%) had ARDS criteria. Seventy-six (54%) were men, the mean age was 46 ± 18 years, APACHE II 18 ± 7 and 19 ± 7 at admission and at ARDS diagnosis, respectively. Septic shock accounted for 42% (60 P) of the ARDS causes, sepsis 22% (31 P), diffuse pulmonary infection 16% (23 P), aspiration pneumonia 11% (15 P), non-septic shock 5% (7 P) and others 4% (5 P). Ten percent (14 P) had AIDS, 30% (43 P) cancer and 25% (36 P) immunosuppression. All patients were mechanically ventilated with Tidal Volume between 4 and 8 ml/kg. Only 3.5% (5 P) had barotrauma and 10% (14 P) performed traqueostomy. Mortality rate was 79% in the ICU. The patients required 12 ± 10 days on MV, ranging from 1 to 55 days. The LOS in ICU and hospital was 14 ± 13 (1–69) days and 28 ± 32 (1–325) days, respectively. There was a time delay of 3.7 ± 4.5 days between admission in ICU and the onset of ARDS. The Murray score (mean ± SD) was 3.2 ± 0.4, 3 ± 0.5, 3 ± 0.5, 2.9 ± 0.6, 2.8 ± 0.7, 2.7 ± 0.7 and 2.6 ± 0.8 in the first 7 days, respectively.

Conclusions: ARDS in our hospital has a similar incidence of reports in the USA and Europe. There was a higher mortality, which could be explained by a high incidence of infection causes of ARDS, mainly septic shock, and elevated combined occurrence of AIDS, cancer and immunosuppression, along the degree of LIS. The incidence of barotrauma was low, as a consequence of the current mechanical ventilation strategies.

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P2 Role of multiple organ dysfunction syndrome in ARDS mortality

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Purpose: To correlate the occurrence and level of organ dysfunction in ARDS with mortality.

Methods: This cohort study includes all consecutive patients with ARDS criteria [1] admitted in the ICU between January 1997 and September 2001. Were collected in a prospective fashion the following variables: age, gender, APACHE II score at the ARDS diagnosis, the occurrence of organ dysfunction determined by the multiple organ dysfunction syndrome (MODS) [2] in the first week, and mortality in the ICU. The occurrence of organ/system dysfunction was considered with a MODS equal to or greater than 1 in any day. The levels 3 or 4 of MODS were considered severe organ/system dysfunction. Statistical analyses were done by Mann–Whitney and chi-square as indicated.

Results: There was 141 patients (P) with ARDS criteria and all were included in the analysis. Seventy-six (54%) were men, the mean age was 46 ± 18 years and APACHE II 19 ± 7. Mortality rate was 79%. In survivors (SV) and nonsurvivors (NSV) mean age was 35 ± 14 years and 49 ± 5 years ($P < 0.0001$), and APACHE II 16 ± 5 and 20 ± 7 ($P < 0.001$), respectively. There was no difference about gender in mortality. In all groups, there was 4.3 ± 1 organ dysfunction, with 10 P (7%) with 2, 20 P (14%) 3, 36 P (26%) 4, 69 P (49%) 5, and 6 P (4%) 6 organ/system dysfunction; mortality rate in these groups was, respectively: 50%, 60%, 81%, 87% and 100%. The number of organ/system dysfunction was in SV 3.7 ± 1.1 and in NSV 4.5 ± 0.9 ($P < 0.01$). The global MODS in the first week in SV and NSV was: 6 ± 2.5 and

8.8 ± 3.1*; 5.8 ± 2.6 and 9 ± 3.5*; 5.9 ± 2.8 and 9 ± 3.5*; 4.9 ± 2.6 and 8.8 ± 3.7*; 4.3 ± 2.7 and 8.6 ± 3.7*; 4.3 ± 3.2 and 8.6 ± 3.6*; 5.2 ± 3.6 and 7.2 ± 3.7**, respectively (* $P < 0.0001$; ** $P = 0.035$). Bivariate analysis of each organ of MODS in separate in the first week vs mortality showed that renal dysfunction was present in 94 P (89%) and 12 P (11%) ($P < 0.001$) and haematological dysfunction in 96 P (86%) and 16 P (14%) ($P < 0.01$), in NSV and SV. Severe cardiovascular dysfunction was present in 79 P (85%) NSV and in 14 (15%) SV ($P < 0.03$). The other variables showed no statistical differences.

Conclusions: The occurrence, level and number of organ/systems compromised in the first week after ARDS, estimated by the MODS, correlated with mortality in our patients. Cardiovascular, renal and hematological dysfunctions were those more influents in mortality; the determination of neurological dysfunction was difficult because patients were sedated for mechanical ventilation. In our patients, mortality was affected by age and the severity of organ dysfunction in the first week, estimated by the MODS.

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P3 Instrument development to conduct a meta-analysis of mortality from ARDS

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Recently, randomized clinical trials of ventilatory management strategies indicate a reduction in mortality associated with acute respiratory distress syndrome (ARDS). However, there is little clarity as to whether mortality has changed over time to provide a benchmark reference for measuring the effects of therapies and for identifying factors that reduce mortality. In preparation to conduct a comprehensive meta-analysis of mortality from ARDS, 14 search terms for ARDS were identified to generate titles from published, electronic, and unpublished sources. The co-investigators independently reviewed a subset of titles (1996–2000) to select abstracts about investigations of a therapy or pathophysiological mechanism likely to yield information about mortality from ARDS.

Titles were excluded from further review if the report appeared to be a single page; single case study; pediatric/neonatal or healthy subject; review or meta-analysis; study sample with chronic respiratory failure, idiopathic pneumonia syndrome, or pulmonary toxicity; or a methods paper of instrument reliability for patients with ARDS. Inter- and intra-rater agreements ranged between 98–100% across 5 years of title reviews. The co-investigators independently reviewed abstracts of acceptable titles to determine the likelihood that the manuscript would contain useful mortality data (inter-rater Kappa [corrected for chance agreement] = 0.76; intra-rater Kappa = 0.86); clarity of distinct study group(s) with ARDS (inter-rater Kappa = 0.71; intra-rater Kappa = 0.94); and sample size of greater than one subject with ARDS (inter-rater Kappa = 0.78; intra-rater Kappa = 0.79).

An instrument is being developed to assess the study quality and outcomes of each manuscript. The purpose of assessing the quality of the manuscript is to derive a total and variable-linked score by which the manuscript can be assessed for the impact of bias and precision on the meta-analysis. Four areas of the study's quality include publication demographics, study methods, statistical analysis, and presentation of results. Publication demographics include publication source, geographic location of the study, biostatistician involvement, and source of support for the study. Study methods are assessed for the design, sampling methods, description of conditions, randomization and blinding strategies, and *a priori* power analysis. Statistical analysis entails determining the clarity of analysis, intention to treat, compliance, and monitoring of adverse effects. Presentation of results is evaluated for the duration of enrollment, comparison of baseline characteristics and prognostic variables, and *post hoc* power analysis.

Inter- and intra-rater agreement of study quality are in process of being analyzed. An instrument to measure variables associated with mortality is also being developed to include general variables (ARDS definition, sample characteristics, groups compared [ARDS versus non-ARDS]), mortality linked with risk groups (sepsis/nonsepsis, direct/indirect risk), nominal/ordinal subject characteristics (gender, ARDS stage, location and cause of death), and interval/ratio subject characteristics (lung injury, illness severity). Instrument development will provide a solid methodological foundation for conducting a meta-analysis of the risks, treatment effects, and mortality associated with ARDS, using clinical studies from 1967 to the most recent findings.

P4 A novel technique of intra-abdominal pressure measurement: validation of two prototypes

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Introduction: Intra-abdominal pressure (IAP) is an important parameter and prognostic indicator of the patient's underlying physiologic status [1]. Correct IAP measurement therefore is crucial. The gold standard measurement method via a bladder catheter first described by Kron poses the risk for infection and needle-stick injury and interferes with urinary output estimations [1]. Cheatham and Safcsak reported a revision of Kron's technique limiting these risks but still interfering with urinary output estimation [2]. All these measurements also interfere with nursing time and cannot be done without manipulation of the Foley catheter. A technique for measuring IAP using the patient's own urine as transmitting medium has been described previously [1]. The aim of this study is to validate IAP measurement via two prototypes (Holtech Medical, Kopenhagen, Denmark) using this technique. A 50 ml container fitted with a bio-filter for venting is inserted between the Foley catheter and the drainage bag. The container fills with urine during drainage; when the container is elevated, the 50 ml urine flows back into the patient's bladder, and IAP can be read from the position of the meniscus in the clear manometer tube between the container and the Foley catheter. The first prototype consisted of a 50 ml plastic bag with a bio-filter, inserted between the Foley catheter and the urine collection bag; a major drawback was occasional blocking of the bio-filter, leading to overestimation of IAP in some cases. Another drawback was the occasional presence of air-bubbles in

the manometer tube, producing multiple menisci leading to misinterpretation of IAP. In addition, the volume of urine flowing back into the bladder was not well defined. Prototype 2 was adapted to correct for the drawbacks of prototype 1, using a rigid 50 ml reservoir with a large bio-filter surface.

Methods: In total 60 paired measurements were performed in five patients with prototype 1, and 119 paired measurements were performed in seven patients with prototype 2. The IAP was calculated using two different methods: the gold standard via an indwelling bladder catheter using a pressure transducer (IAPves) and via the prototypes using the patient's own urine as transmitting medium (IAPproto1 and IAPproto2). The M/F ratio was 4/1, age 71.4 ± 6.6, MODScore 5.4 ± 3.6, SOFA score 8.4 ± 2.9, APACHE-II score 22.6 ± 4.8, SAPS-II score 51.8 ± 14.4 in the five prototype 1 patients and 4/3, 68.4 ± 18.9, 5.9 ± 3, 7 ± 1.9, 16.6 ± 5.2 and 43.4 ± 11.9 respectively in the seven prototype 2 patients. The number of measurements in each patient was 12 ± 2.7 for prototype 1 and 17 ± 9.8 for prototype 2. Calculation of correlation was done with the Prism GraphPad™ software (version 2.00, 31 October 1995), values are mean ± SD.

Results: The values for IAP (mmHg) were 12.6 ± 5.3 (IAPves) versus 11.1 ± 3.7 (IAPproto1) and 10.1 ± 3.6 (IAPves) versus 10.2 ± 3.3 (IAPproto2). There was a good correlation between IAPves and IAPproto1: IAPves = 0.592 × IAPproto1 + 3.666 (R^2 = 0.71, P < 0.0001), but the bias was considerable. The analysis according to Bland and Altman showed that IAPproto1 consistently underestimated IAPves with a mean difference or bias of −1.5 ± 2.9 (SD) mmHg (95% confidence interval −2.2 to −0.7); the limits of agreement were −7.3 to 4.4 mmHg (95% CI −8.6 to −6 for the LLA and 3.1 to 5.7 for the ULA), these intervals are large and thus reflect poor agreement. The correlation was better between IAPves and IAPproto2: IAPves = 0.9 × IAPproto2 + 1.17 (R^2 = 0.96, P < 0.0001). The analysis according to Bland and Altman showed that IAPproto2 was almost identical to IAPves with a mean difference or bias of 0.17 ± 0.8 (SD) mmHg (95% CI 0.03 to 0.3); with small limits of agreement −1.4 to 1.7 mmHg (95% CI −1.6 to −1.1 for the LLA and 1.5 to 2 for the ULA), these small intervals thus reflect good agreement. A drawback of prototype 2 was the appearance of urine leakage from the rigid 50 ml container's bio-filter in 11 out of 13 devices after 16.7 ± 12.3 hours caused by a technical problem during the assembly of the prototypes.

Conclusions: We found a good correlation between all IAP measurements using the gold standard and both prototypes. Prototype 2 represents a major improvement in the quality and reproducibility of the IAP measurement. With this non-invasive technique using the patient's own urine as transmitting medium nursing time and cost can be significantly reduced. IAP measurement can easily be done at each urine output estimation without interference. The risk of infection and needle-stick injury is reduced. The leakage problem of prototype 2 needs to be corrected.

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P5 An observational study on intraabdominal pressure in 125 critically ill patients

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Elevated intraabdominal pressure and the abdominal compartment syndrome seem to be the recent hype at critical care conferences. The objective of this longitudinal, observational study is to document epidemiologic data on intraabdominal pressure (IAP) in patients admitted to a mixed medical and surgical intensive care department (ICU) of an university hospital and to determine the value of routine monitoring of IAP.

All adult patients admitted for an expected minimum stay of 48 hours in the ICU were included, provided that they needed an indwelling urinary bladder catheter. Included patients were followed until discharge from the ICU or until death, whichever came first. Final outcome at hospital discharge was determined. The IAP was measured in a non-invasive manner through the aspiration port of a standard indwelling bladder catheter, in a modification of the procedure as originally described by Kron *et al*. The IAP was measured twice daily until discharge from the ICU or until there was no further need of a bladder catheter (i.e. a bladder catheter was not left in place for the sole purpose of measuring IAP). Furthermore, demographic, pathologic, and diagnostic data, as well as physiologic, hemodynamic, and biochemical parameters were recorded. Several disease severity scores were calculated.

We present the results of the first 125 patients included. A total of 1451 measurements were performed. Patients were stratified into two groups depending on 30-day survival or outcome at discharge from hospital. Forty-one patients (652 measurements) did not survive. Mean IAP for this group was 8.9 (range −6 to 24, SD 4.5). We recorded 130 IAP-values over 12 mmHg (20%) of which seven IAP-values over 19 mmHg (1%) in six patients. Eighty-four patients (799 measurements) had a favourable outcome. Mean IAP for this group was 7.6 (range −6 to 30, SD 4.6). We recorded 112 IAP-values over 12 mmHg (14%) of which 10 IAP-values over 19 mmHg (1%) in five patients. The two-tailed student's *t*-test for the IAP between the two groups was significant (P < 0.0001). However, elevation of IAP-values did not necessarily coincide with demise. We could not demonstrate a linear correlation between IAP-values and values of other parameters.

From our present data we can conclude that IAP is generally higher in non-survivors than in survivors, but that survivors can have elevated values of IAP. Routine monitoring of IAP in all patients admitted to the ICU does not seem warranted.

P6 Relation between transdiaphragmatic pressure and oxygen consumption in patients with intestinal obstruction

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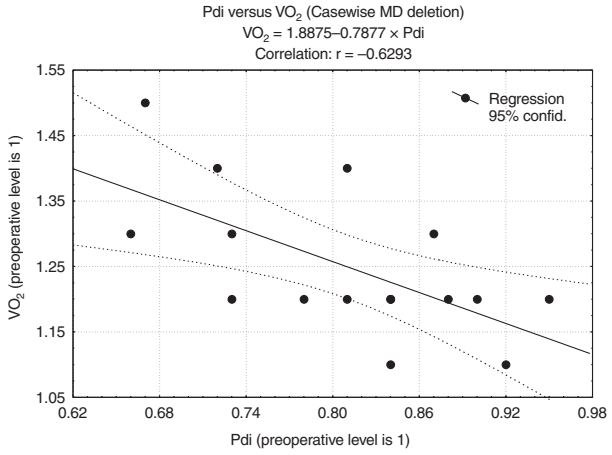
Background and goals: Dysfunction of the diaphragm generally causes an additional load on other respiratory muscles [1]. It may be expressed by the increased oxygen cost of breathing and oxygen consumption (VO_2) [2]. The increased abdominal pressure in patients with an intestinal obstruction may cause the dysfunction of the diaphragm.

Materials and methods: We studied the relation between VO_2 and the end tidal transdiaphragmatic pressure (Pdi_{ET}) in 16 patients with the diagnosis of an intestinal obstruction. The investigations were carried out after operation and before extubation. The average age of the patients was 41 ± 12. The same technique of anesthesia was performed in all patients. The APACHE II count was 22 ± 3. The device Capnomac Ultima™ measured VO_2.

Results: The relation between Pdi_{ET} and VO_2 are submitted in the Figure.

Conclusion: The patients with an intestinal obstruction demonstrate the moderate linear correlation (r=0.63) between Pdi_{ET} and VO_2.

Figure



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P7 Effects of systemic inflammatory response syndrome on intraabdominal pressure and lung compliance

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Introduction: In Systemic Inflammatory Response Syndrome (SIRS) model in rabbits we aim to investigate the relationship between increased intraabdominal pressure (IAP) and lung compliance during mechanical ventilation.

Methods: Twenty-four New Zealand rabbits were randomly divided into three groups (n=8). After sedation with intramuscularly ketamine (50 mg/kg): In group 1: Laparotomy and single cecum puncture was done and, after insertion of an intraabdominal catheter, the abdomen was closed. In group 2: Laparotomy was done and after insertion of an intraabdominal catheter, the abdomen was closed. In group 3: It was the control group. After sedation, nothing was done.

In group 1 and 2, after 1 hour of abdomen closure and in group 3 after 1 hour of sedation, tracheostomy was performed and endotracheal tube was inserted. The rabbits were curarized by atracuriým (0.5 mg/kg, intramuscularly), and ventilated with PC mode for 3 hours and the parameters of ventilation were FiO_2= 1.0, PIP=18 cmH_2O, PEEP=5 cmH_2O, RR=80 breaths/min. Compliance and IAP values were recorded every 30 min. Data were compared by Mann–Whitney U test. P<0.05 was considered to indicate statistical significance.

Results: IAP levels in group 2 were found to be higher than group 3 (P<0.01). However when lung compliance values were compared between groups, no significant differences was encountered. And lung compliance values were found to be significantly decreased when compared to initial values in all groups at the end of the study (P<0.05).

Conclusion: In this experimental SIRS model, at the very beginning, increased IAP values does not seem to effect lung compliance measurements during mechanical ventilation.

P8 The effects of increasing levels of PEEP on inflammation markers and oxygenation in rats with unilateral lung injury

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Introduction: The effects of PEEP on inflammation and oxygenation during acute lung injury are not well known. Accordingly, we investigated the effect of different PEEP levels on local and systemic parameters of lung injury and inflammatory response in a unilateral *in vivo* lung injury model.

Methods: Male Wistar rats (350 g) underwent left-sided lung injury using endobronchial instillation of 0.4 ml HCl (pH 1) (study group) or endobronchial instillation of 0.1 ml NaCl 0.9% (placebo group). Twenty-four hours after treatment the rats were anesthetized, and intravascular catheters inserted for fluid infusion and hemodynamic monitoring. A tracheostomy was performed and the rats were ventilated for 4 hours with tidal volume of 6 ml/kg body weight and randomly assigned to ZEEP, PEEP=5 cmH_2O or PEEP=10 cmH_2O groups. Oxygenation was measured every 30 min and left and right lung lavage was performed lung after 4 hours of ventilation for cell and protein determination. An ANOVA was used for statistical analysis.

Table

	Lung injury with HCl			Controls		
	ZEEP	PEEP5	PEEP10	ZEEP	PEEP5	PEEP10
PaO_2 after 4 h vent. (mmHg)*	127 ± 26	193 ± 4	203 ± 10	138 ± 14	215 ± 10	197 ± 13
Protein left lung (mg/l)**	2841 ± 146	2867 ± 253	1970 ± 300	80 ± 11	62 ± 17	72 ± 17
Protein right lung (mg/l)***	343 ± 69	212 ± 69	195 ± 43	69 ± 7	85 ± 13	92 ± 10
Neutrophils left lung (ml^{-1})**	4082 ± 503	2634 ± 530	1744 ± 453	158 ± 77	157 ± 34	85 ± 29
Neutrophils right lung (ml^{-1})***	456 ± 98	449 ± 147	335 ± 148	155 ± 33	214 ± 56	185 ± 58

Mean ± SEM; Protein and neutrophils: in lavage fluid. * $P < 0.05$ for effects of PEEP; ** $P < 0.05$ for effects of group, PEEP and interaction; *** $P < 0.05$ for effects of group.

Results and conclusion: PaO_2 was higher in the PEEP groups as in the ZEEP groups. Protein and neutrophils in lung lavage fluid of both sides were higher in injured as in placebo rats. Increasing PEEP levels reduced neutrophil count in lavage fluid of the damaged lung in a dose dependent manner. PEEP increases oxygenation and decreased neutrophil infiltration in this model of lung injury.

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P9 The effects of increasing levels of PEEP on oxygenation and lung perfusion in pigs with unilateral lung injury

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Introduction: The effects of PEEP may differ in healthy and diseased parts of the lung. Accordingly, we studied the effects of increasing PEEP-levels on ventilation, lung perfusion, oxygenation, and hemodynamics in an animal model with unilateral lung injury.

Methods: In 8 pigs (25–36 kg) unilateral lung injury was induced by bronchoscopic application of HCl 0.1 m into the left lung (total: 20–35 ml). Twenty-four hours after injury the pigs were anesthetized, endotracheally intubated with a double-lumen tube and mechanically ventilated. Catheters for hemodynamic monitoring were inserted. Volume controlled ventilation (12 ml/kg body weight, FiO_2 1.0) with ZEEP, PEEP 5 cmH_2O and PEEP 10 cmH_2O was performed in random order in each animal. Measurements after 45 min of hemodynamic stability in each phase included differential lung perfusion using colored microspheres and differential lung ventilation using the double lumen tube. In 6 pigs (control group) the study was performed without preceding lung injury. ANOVA was used for statistical analysis.

Results and conclusion: After lung injury and in comparison to the control group, left side lung compliance and left side tidal volumes were significantly lower (data not shown). With increasing PEEP, MAP, CO and shunt fraction decreased in both groups.

Compared to the control group, perfusion of the left lung decreased after lung damage, but was not changed by PEEP. Our study shows that PEEP depresses the circulation but does not alter the perfusion of the injured lung during unilateral lung injury.

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Table

	Lung injury with HCl ($n=8$)			Control ($n=6$)		
	ZEEP	PEEP5	PEEP10	ZEEP	PEEP5	PEEP10
PaO_2 (mmHg)	407 ± 17*	471 ± 11*	468 ± 22*	470 ± 22	488 ± 12	525 ± 14
MAP (mmHg)	75 ± 8**	65 ± 5**	45 ± 8**	67 ± 11**	61 ± 11**	53 ± 9**
CO (l/min)	3.6 ± 0.2**	2.9 ± 0.2**	2.0 ± 0.1**	3.8 ± 0.4**	3.2 ± 0.2**	2.6 ± 0.2**
Left lung perfusion (% of total)	30 ± 3*	30 ± 4*	30 ± 3*	50 ± 1.6	47 ± 1.1	57 ± 1.8
Left lung TV (% of total)	29 ± 1.6*	32 ± 1.2*	33 ± 1.2*	45 ± 0.8*	47 ± 1*	46 ± 0.6*

Mean ± SEM; CO = cardiac output, MAP = mean arterial pressure, TV = tidal volume. * $P < 0.05$ for effects of group. ** $P < 0.05$ for effects of PEEP.

P10 The blood shifts during the pressure volume curve

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Background and goals: The pressure volume (PV) curve of the respiratory system is drawn assuming that the gas volume displacements (ΔV_{gas}) are equals to the lung and chest wall changes (ΔV_{cw}). In this study we compared ΔV_{gas} and ΔV_{cw} during static PV curve obtained by supersyringe (PV_{gas}) and by OEP (PV_{cw}) [1].

Materials and methods: In eight sedated and paralyzed ALI/ARDS patients (5 M/3 F, age 75 ± 13 years, BMI 25.6 ± 3 kg/m^2, PaO_2/FiO_2 222 ± 67 mmHg), the PV curves were obtained by the supersyringe method. A mathematical correction was applied to the gas volume injected or withdrawn by the syringe to avoid mistakes due to temperature, humidity, pressure and gas exchange [2]. To study the deflation phase, avoiding the inflation effects, for each PV curve the difference between the total static compliance (TSC) of PV_{gas} and TSC of PV_{cw}, was added to the deflation limb of PV_{cw}.

Results: (1) Inflation phase: the ΔV_{gas} was always higher than the ΔV_{cw}, the discrepancy between ΔV_{gas} and ΔV_{cw} was at TSC −193.72 ± 145.56 ml, which was correlated to airway pressure product time of inflation ($P<0.001$, $r^2=0.87$) and to the ratio between esophageal and airway pressure variations ($\Delta Pes/\Delta Paw$) ($P<0.01$, $r^2=0.91$).

(2) Deflation phase: the ΔV_{gas} was equal, lower or higher than the ΔV_{cw}, this discrepancy was correlated to central venous pressure ($P<0.01$, $r^2=0.7$) and time to deflation ($P<0.05$, $r^2=0.8$).

Conclusions: The discrepancy between ΔV_{gas} and ΔV_{cw} was correlated to time to perform the PV curve, airway pressure reached, mechanical property of the respiratory system and hemodynamic conditions. We think that the discrepancy can be due to the blood shifts (OUT and INTO the thorax).

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P11 Clinical study of sustained inflation on patients with acute respiratory distress syndrome

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Objective: To evaluate the therapeutic effects of sustained inflation (SI) combined with lung protective strategy in patients with acute respiratory distress syndrome (ARDS).

Design: Prospective study.

Setting: Medical intensive care unit, university hospital.

Patients: Twenty mechanically ventilated ARDS patients.

Interventions: SI (30 cmH_2O, 20 s) was combined with lung protective strategy in 20 ARDS patients. Hemodynamics, pulmonary mechanics and gas exchange were monitored continuously.

Measurements and results: SI was well tolerated by every patient. Four patients were lack of beneficial effects. Arterial oxygen tension and saturation, mixed venous oxygen tension and saturation increased after SI, while venous admixture decreased ($P<0.05$). Dynamic pulmonary compliance and lung volume improved markedly. The effects were maintained in 16 patients for 4 hours. Mean arterial pressure, central venous pressure, pulmonary capillary wedge pressure, mean pulmonary arterial pressure, pulmonary vascular resistance index and right ventricular stroke work index significantly increased during the 20 s inflation ($P<0.05$), but reversed rapidly after the inflation was terminated.

Conclusions: Using with lung protective strategy, SI is able to improve pulmonary compliance, lung volume and oxygenation. It is a safe and valid lung recruitment maneuver.

P12 The optimal pressure of sustained inflation for alveolar recruitment

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Objective: To determine the optimal recruitment pressure of sustained inflation (SI) in treatment of rabbits with acute respiratory distress syndrome (ARDS).

Materials and methods: SI was applied at pressures of 1 ~ 6 times of mean airway pressure (P_m) for 20 s to saline-lavaged adult New Zealand rabbits. Hemodynamics, pulmonary mechanics and gas exchange were observed before SI, during, and 2 min, 5 min after applying SI. Lung histology was observed after experiment.

Results: When the pressure of SI was higher than 3 P_m, arterial oxygen tension (PaO_2) and arterial oxygen saturation were improved. The difference of PaO_2 before and during SI were (75 ± 39) mmHg and (52 ± 25) mmHg respectively in the 5 P_m and 6 P_m group, which were higher than 1 P_m group significantly ([−5 ± 4] mmHg, $P<0.05$). The difference of dynamic pulmonary compliance before and during SI in 5 P_m group was increased markedly ([1.90 ± 0.20] ml/cmH_2O in 5 P_m group, [−0.02 ± 0.04] ml/cmH_2O in 1 P_m group, $P<0.05$). 5 P_m resulted in immediate increased significantly in lung volume ([3.1 ± 2.1] ml/kg in the 5 P_m group, [8.3 ± 0.7] ml/kg in the 1 P_m group). Histologically, Smith lung injury score was 4.03 ± 1.79 in the 5 P_m group, which was less than the score in the group of ARDS model (6.10 ± 0.77). SI with 6 P_m led to alveolar overdistention. With the increasing of SI pressure, mean arterial pressure decreased markedly.

Conclusions: 5 P_m (25 ~ 35 cmH_2O) may be the optimal recruitment pressure of SI in rabbits with ARDS.

P13 Expiratory pressure–volume curves in pulmonary and extrapulmonary ARDS

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Objective: To assess the differences in lung mechanics during expiration between acute respiratory distress syndrome from pulmonary (ARDSp) and extrapulmonary (ARDSe) origin.

Methods: The expiratory pressure–volume (PV) curve was recorded after standardisation of volume history. The ventilator was switched to CPAP of 35 cmH_2O and was then reduced in 5 cmH_2O steps. Volume corresponding to static conditions was recorded. Esophagic pressure was recorded with a fluid-filled catheter [1]. The PV curves were fitted to a sigmoid model [2] for comparing volumes (absolute and percentage to estimated total lung capacity) at the same pleural and transpulmonary pressures. All data are expressed as mean ± SD. Differences between groups were performed using a Mann–Whitney U test.

Results: *Patients*: Ten patients with early ARDS (5 ARDSp/5 ARDSe). Mean age was 59 ± 15.5 years. APACHE-II score: 22.8 ± 6.8. Lung injury score: 2.9 ± 0.3. PaO_2/FiO_2: 124 ± 50.7. No differences were found between ARDSp and ARDSe in these results.

Compliance (C): ARDSp and ARDSe show similar respiratory system C (30 ± 8.7 ml/cmH_2O vs 45 ± 18.1 ml/cmH_2O respectively, n.s.), but ARDSp has lower lung C (35.9 ± 11.3 ml/cmH_2O vs 77.2 ± 50.6 ml/cmH_2O, $P = 0.05$) and higher chest wall C (199.6 ± 44.4 ml/cmH_2O vs 125.5 ± 16.5 ml/cmH_2O, $P < 0.05$).

PV curves (see Fig.): Respiratory system PV curve from ARDSp is shifted down and right with respect to ARDSe. When fractional volumes are considered these differences are also significative. The lung PV curve of ARDSp is shifted in a similar way. However, when considering fractional volumes, the differences are only significative in the low pressure range (0–10 cmH_2O). The chest wall PV curve in the ARDSp group is, as expected, shifted to the left.

Conclusions: The ARDSp has a respiratory system PV curve displaced downwards when compared with ARDSe, which suggests a small amount of reclutable tissue. When the lung PV curve is considered, these differences are higher. The fractional PV curves show similar differences for the respiratory system, but not for the lung. The difference in the latest affects only to the low pressure range, which suggest a greater airway closure in ARDSe.

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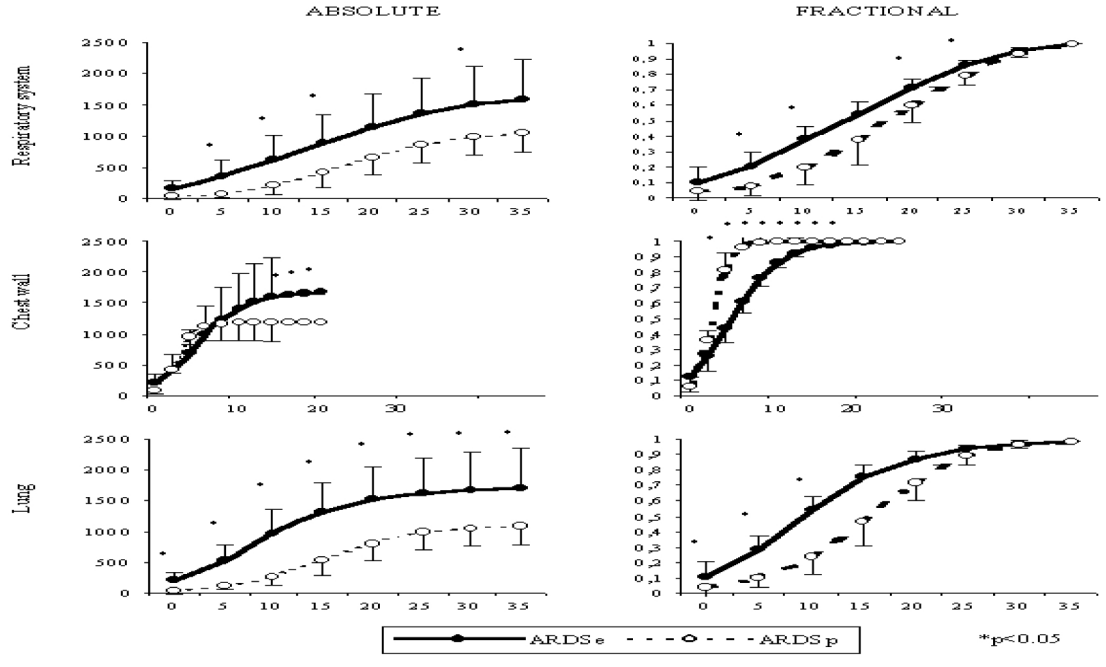
Figure



P14 Influence of positive end-expiratory pressure (PEEP) on left ventricular regional wall motion in patients with acute respiratory distress syndrome (ARDS)

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Regional left ventricular wall motion abnormalities have been described at a positive end-expiratory pressure (PEEP) level of 20 cm H_2O [1]. However, no PEEP level has yet been defined, above which RWMA may occur.

Objective: To assess global and regional LV performance in response to PEEP by transoesophageal echocardiography (TOE) in patients with ARDS.

Setting: Surgical ICU in a university hospital.

Patients: Eight critically ill patients with normal systolic LV function requiring mechanical ventilation (tidal volume 6–8 ml/kg, PEEP 12 ± 2 cmH_2O) due to ARDS.

Measurements: Regional and global LV performance were assessed at PEEP levels of 5, 10, 15, 20 and 25 cmH_2O by means of TOE by the centerline method on the transgastric short-axis view.

Results: PEEP ≥ 15 cmH_2O produced a significant reduction in systolic septal wall motion (hypokinesia) and a significant augmentation of lateral systolic wall motion (hyperkinesia). Global LV performance – measured as fractional area change – was not significantly affected.

Conclusion and discussion: PEEP levels ≥ 15 cmH_2O may be associated with an inhomogeneity of regional wall motion. Most likely, this phenomenon is related to a nonuniform transmission of the increased intrathoracic pressure on the left ventricular wall because of its different relation to the pleural space.

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P15 Does the use of large ventilator tidal volume increase the incidence of postoperative complications?

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The use of large tidal volumes (LTV) (10–15 ml/kg) for mechanical ventilation (MV) of patients with ARDS has been shown to be detrimental. Whether or not the use of LTV for postoperative mechanical ventilation increases the risk of pulmonary complications, pneumonia, and consequent mortality from pulmonary causes is unknown. We performed this study with the hypothesis that postoperative patients receiving MV with large tidal volume would have an increased incidence of pulmonary complications and mortality. Postoperative abdominal and thoracic surgical patients receiving either 9 ml/kg or 14 ml/kg tidal volumes for mechanical ventilation were studied. Those with pre-existing atelectasis, pneumonia or ARDS were excluded. The patients were managed in the SICU and were weaned and extubated according to standard practice. Extubated patients who later required reintubation were not placed on study tidal volumes. Data collection included patient demographics, surgical diagnoses, operations, preoperative chest X-ray results, the size of tidal volume, duration of MV, incidence of pulmonary complications, and patient outcome. The data was analyzed using SPSS statistical soft ware. One hundred and two patients were studied: 52 males and 50 females. Their mean age was 55.4 years. The operative procedures included major elective abdominal surgery, aortic reconstruction, emergency abdominal surgery, and esophageal resections. Eighty patients had normal preoperative chest X-ray. Twenty-two patients had COPD or other chronic pulmonary conditions. Sixty-nine patients had no postoperative pulmonary complications. Pneumonia developed in 31 (30.4%) patients, pulmonary edema in one, and pleural effusion in another. Thirteen of 102 patients (12.7%) died. Fifty-eight patients received 9 ml/kg and 44 received 14 ml/kg tidal volume. Their characteristics are shown in the Table.

Two patients in the 9 ml/kg group and one patient in the 14 ml/kg group died from pneumonia. One of eight patients in the 9 ml/kg group and four of seven patients in the 14 ml/kg group died from septic shock due to gangrene or perforation of the GI tract with peritonitis.

Conclusion: The use of large tidal volume for postoperative mechanical ventilation does not increase postoperative complications or mortality.

Table

	Males	Females	Age	ICU stay (hours)	MV (hours)	Pneumonia	Death
9 ml	24	34	54	178	100	17 (29%)	6/58 (10.3%)
14 ml	28	14	57	171	98	14 (32%)	7/44 (16%)

P16 Lung recruitment manoeuvres decrease gastric mucosal blood flow in ICU patients

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Introduction: The use of recruitment manoeuvres (RM) has recently been introduced into clinical practice for treatment of atelectasis during mechanical ventilation. Transient high airway pressures, such as those employed in RM, may lead to adverse general or regional circulatory effects. The aim of this study was to evaluate effects of RM on gastric mucosal blood flow, systemic oxygenation and respiratory mechanics.

Methods: Nine ICU patients with acute lung injury, age 60 ± 5, APACHE II 22 ± 3, were studied. Gastric mucosal blood flow was measured continuously with laser Doppler flowmetry (LDF). Mean arterial (MAP), central venous (CVP), oesophageal, abdominal and airway pressures were also measured continuously. Cardiac output was measured by arterial pulse contour analysis (PICCO). Three consecutive RMs separated by a 15 min pause were studied, the two first were performed with inspiratory pressure (P_{insp}) 40 cmH_2O, inspiratory time (T_{insp}) 8 s, expiratory pressure (P_{exp}) 20 cmH_2O and expiratory time (T_{exp}) 2 s for 2 min. The third RM was performed with P_{insp} 50 cmH_2O, T_{insp} 4 s, P_{exp} 20 cmH_2O, T_{exp} 1 s for 2 min. Blood gas measurements were performed before, at the end of, and 3 min after each RM.

Results: When comparing values before RM1 with values obtained after RM3 preliminary data indicate that three consecutive RMs did not significantly change MAP, HR, PaO_2 or dynamic compliance. There was a significant decrease in LDF, CI and a significant increase in SVRI. Three patients demonstrated a drastic increase in PaO_2 during all RMs, but this increase was not sustained after the RMs were terminated.

Table

	Before RM1	After RM3
MAP (mmHg)	86 ± 5	88 ± 4
CI (l/min/m²) (n = 4)	4.2 ± 0.2	3.8 ± 0.2*
LDF (PU) (n = 8)	504 ± 49	387 ± 28*
PaO_2 (kPa)	10.5 ± 0.5	11.4 ± 0.9

n = 9. Mean ± SEM. * P < 0.05.

Conclusion: Three consecutive recruitment manoeuvres decreased gastric mucosal perfusion and cardiac index without any beneficial effect on oxygenation.

P17 Asymmetry in lung pathology and short-term effects of independent lung ventilation (ILV) on pulmonary mechanics and gas exchange in patients with blunt chest trauma

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Independent lung ventilation has been used in patients with asymmetric lung pathology. In this study we applied ILV in 17 consecutive ventilated patients with blunt chest trauma with inclusion criteria $PO_2/FiO_2 < 200$ without physical or roentgenographic evidence of unilateral pulmonary disease. Eight of the patients (53%) demonstrated paradoxical PEEP/CPAP effect (worsening of pulmonary mechanics, gas exchange and increase in shunt with PEEP application) before institution of ILV. After application of ILV 10 of the patients (59%) demonstrated pulmonary mechanics asymmetry between left and right lung. In this group of patients we continued with ILV and applied differential PEEP levels (3.4 ± 2.2 cmH_2O for normal lung and 12 ± 3.7 for diseased lung, optimized with constant flow technique) with different tidal volumes for both lungs and level of Pplat < 30 cmH_2O. Pulmonary mechanics, gas exchange and total body oxygen delivery were determined on 1, 6 and 48 hours after ILV application. In patients who did not demonstrate pulmonary asymmetry we replaced ILV with conventional mechanical ventilation. Patients with continued ILV demonstrated significant improvement in oxygenation parameters and total body oxygen delivery and gradually decreasing asymmetry in pulmonary mechanics. In this study we found high incidence (59% of patients) of lung pathology asymmetry in patients with blunt chest trauma without roentgenographic or physical evidence of such asymmetry. Our data suggest that ILV can be used in patients with blunt chest trauma as lung protective ventilatory strategy with maximal favourable effect on diseased lung and minimal adverse effect on normal lung.

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P18 Alveolar recruitment improves arterial oxygenation in responders to prone position

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Introduction: Although prone position is known as a simple method to improve arterial oxygenation in patients with acute respiratory distress syndrome (ARDS), the underlying physiological mechanisms remain poorly understood. This study was performed to show the effect of prone position on alveolar recruitment.

Methods: After approval by the local ethics committee of the medical faculty 12 patients with ARDS diagnosed according to the criteria of the American–European Consensus Conference were included. Patients were ventilated in volume controlled mode and the ventilatory settings were kept unchanged throughout the whole

period of measurements. Patients were kept in prone position for 8 hours. Arterial partial pressure of oxygen (PaO_2), airway pressure, gas flow and functional residual capacity (FRC) were measured (AMIS 2001 Intensive Care Monitoring System; INNOVISION, Odense Denmark) and intrapulmonary shunt (Qs/Qt) was calculated from arterial and mixed venous blood gas analyses. Measurements were performed in supine position (Ts0), immediately after turning to prone position (Tp0), after 1, 2, 4 and 8 hours in prone position (Tp1, Tp2, Tp4, Tp8) and immediately after turning back to supine (Ts1). Patients were defined as responders to prone position if the oxygenation quotient (PaO_2/FiO_2) increased more than 30%. Individual pressure–volume curves (pv-curves) of the respiratory system were constructed by means of FRC measurements and dynamic compliances which were calculated from gas flow and airway pressure measurements. Then alveolar recruitment during prone position was identified as volume increase between pv-curves at a predefined airway pressure of 20 cmH_2O.

Results: Seven of 12 patients showed a sustained increase of oxygenation quotient greater than 30% after prone therapy and were defined as responders (+100% vs +10% in nonresponders). There was no statistical difference in biometric data and severity of ARDS between the two groups. Responders showed a continuous increase of recruited lung volume during prone position. Total alveolar recruitment was significantly greater in responders than in nonresponders ($+800 \pm 200$ ml vs -40 ± 180 ml; $P < 0.0001$). Time course of the alveolar recruitment and time of maximal recruitment differs in all patients. A good correlation was found between total recruited volume and decrease of intrapulmonary shunt ($R^2 = 0.72$).

Conclusion: The present results show that alveolar recruitment increases in responders to prone therapy. An individual time course of alveolar recruitment was found, indicating that the duration of prone position has to be selected according to the specific requirements of each patient. The good correlation between increased lung volume and decrease of intrapulmonary shunt indicates that the recruited lung spaces are capable of participating in gas exchange and are not caused by overdistension or dead space increase.

P19 Rotoprone®: a new and promising way to prone positioning

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Introduction: Prone positioning developed to the most hopeful therapeutical approach in the treatment of severe respiratory failure. Different types of kinetic therapy are practiced, but not every method can be used in any patient. Instable pelvic fractures, aortic rupture, prominent external fixation, obesity, e.g., does sometimes not allow one to turn a patient to the prone position. With a new kind of kinetic bed (Rotoprone®) more patients can treated in prone position. First experiences, benefits and problems will be reported.

Patients and methods: In an open prospective study we observed from July 1999 until June 2000 eight polytraumatized patients in the ICU of the Trauma-Center-Marburg with severe post-traumatic respiratory failure, undergoing prone positioning by using the Rotoprone®. Severity of injury and clinical course were defined through the Injury-Severity-Score (ISS), APACHE-II-Score and the Therapeutic-Intervention-Scoring-System (TISS). The mean ISS was 39.8 (19/52), the APACHE-II-Score on the time of admission was 20.3 (19/23) and the TISS was 28.3 (43/25). All patients were male. The mean age was 39.8 (19/66). The average time of beginning the Rotoprone®-therapy was on the 8.8th day (2/21), the average time of respiratory support was 33.4th day (18/59). The mean time on ICU was 36.6 (22/62) days. Only one patient died on ICU due to multiple organ failure.

Results: Using the SOFA-Score/lung (PaO_2/FiO_2) for measuring the respiratory function we found a value of 170 (93/228) at the beginning of prone positioning with the expected improvement to values of 301 (265/375) at the end of kinetic therapy. Just in one case we had to discontinue the use of Rotoprone® due to a malfunction of the security-mechanism.

Edema of face and neck, pressure induced necrosis, hypotension or arrhythmia never reached such an extent that we had to end kinetic therapy.

Conclusions: This bed is a new and promising tool in treatment of severe respiratory failure. Some patients who require kinetic therapy in the extent of prone positioning who could so far not be turned – due to different reasons – could now be treated. High costs, difficult handling and few available beds are so far limiting factors.

P20 Do we have explanations for the improvement of oxygenation and deterioration of outcome by using prone position in acute respiratory failure?

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In acute respiratory failure (ARF), in particular acute lung injury (ALI) and respiratory distress syndrome (ARDS), change from supine (SP) to prone position (PP) can improve oxygenation. The efficacy of this intervention can be demonstrated by the course of oxygenation index. Nevertheless prone position ventilation (PPV) showed no improvement in survival so far. Endpoint for the assessment of therapeutic effects of an intervention like PPV is generally the mortality rate. The aim of our study is to attempt to analyze the discrepancy between positive effects of prone position ventilation on oxygenation index in ARF and the comparatively high mortality rates despite of this intervention. We studied 110 consecutive patients with ALI ($n = 18$) and ARDS ($n = 92$) at mean age 66 ± 13 [SE] years in a clinical follow-up design at a surgical ICU in a university hospital, who met the criteria of the American European consensus definition. All patients were ventilated intermittent in SP and in PP (135° left/right-side-position) for at least 6 hours/day. Data collection included apart from baseline characteristics individual oxygenation index and underlying diseases of the patients, in particular if of benign or malignant nature. We compared individual oxygenation index (PaO_2/FiO_2) before and after start of prone position (SPSS® T-test) and the data set of each patient with outcome. PPV was well tolerated in all $n = 110$ patients and showed an significant increase of PaO_2/FiO_2 in $n = 106$ within the first 6 hours (SP 149 ± 0.52 vs PP 230 ± 0.73 mmHg [mean ± SEM]). In the remaining four cases

there was a positive effect within the first 24 hours. Sixty-seven (61%) of the patients died in the course of intensive care therapy and 43 (39%) survived. Seven died with an oxygenation index below 100, another 36 with a ratio below 200, 17 below 300 and seven above 300 mmHg. Patients with a malignant underlying disease as cofactor had a 1.8 times higher and those with sepsis a 3.15 times higher risk to die during their ICU-stay despite of PPV. Despite of positive effects of PPV on oxygenation in our patients a considerable part of them died. To our amazement oxygenation index previous to death was not the main problem for most part of the patients in that phase. Malignant diseases in history and sepsis during the ICU-stay seem to increase the risk to die in the course of ALI or ARDS regardless the use of PPV conspicuously. Our results show that for the assessment of a therapeutic intervention in acute respiratory failure not only mortality as an endpoint seems to be suitable, but also important clinical cofactors.

P21 Lung protective strategy for ventilation in acute lung failure with pECLA (pumpless extracorporal lung assist)

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Introduction: The morphological changes in the lungs in acute lung injury (ALI) often lead to high elevated inspiratory pressures and the use of high dosed toxic inspiratory O_2-concentration. This requires an appropriate adaptation of the mechanical ventilation to reduce ventilation associated complications. In our department we use the pumpless extracorporal lung assist (pECLA; Jostra Medizintechnik, Germany) to bridge these ventilation problems till the main lung injuries, which led to the ALI, have been healed.

Methods: In three patients the pECLA-procedure was performed after exhausting all possible ventilation strategies to avoid respirator associated complications. In these patients the femoral vein and artery were cannulated with tubes with diameters between 15 and 19 Fr. Comparable to the continuous arterio-venous dialysis the bloodstream passes a special unit. In this case an oxygenator in which oxygen is inflated with flow of 15 l/min. The high oxygen partial pressure in the oxygenator displaces the carbon dioxide out of its bond to the haemoglobin.

Results: The pECLA-procedure was performed in three patients with a mean age of 55 ± 15 (SD) years. The lung injury score was 3.7 ± 0.4. In two patients the ALI was caused by pneumonia and severe sepsis. In one patient it was caused by a cardiogenic shock. The pECLA-procedure led at the latest after 3 days to lungprotective ventilation (Table). One of the three patients survived and has been discharged from hospital. The two others died. One due to an intracerebral bleeding and the other one due to a prolonged mesenteric ischemia which led to his severe sepsis.

Conclusion: With the usage of the pECLA it seemed to be possible to achieve a lungprotective ventilation also in nearly hopeless cases. To find evidence that morbidity and mortality can be reduced by this approach further trials should be conducted.

Table

	pO_2 (mmHg)		pCO_2 (mmHg)		FiO_2		PaO_2/FiO_2	
Patient	Before pECLA	After pECLA	Before pECLA	After pECLA	Before pECLA	After pECLA	Before pECLA	After pECLA
1	70	60	74	35	1.0	0.35	70	171
2	67	93	33	31	1.0	0.4	67	233
3	57	65	113	40	0.7	0.45	88	144

P22 Does evolution of pre-ECMO conventional therapies affect the use of ECMO over the past decade in the regional ECMO centre in UK?

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Introduction: Extracorporeal membrane oxygenation (ECMO) has been recognised as effective in supporting newborn infants with acute hypoxemic respiratory failure due to pulmonary hypertension. The aim of this retrospective study was to document changing trends in the use of pre-ECMO novel therapies (surfactant, high-frequency oscillatory ventilation and inhaled nitric oxide) over the past decade in one of the regional ECMO centre in UK.

Methods and patients: All neonatal ECMO patients treated between October 1992 and August 2001 were retrospectively reviewed. Pre-ECMO treatments were analysed separately during 1992–1995, 1995–1998 and 1998–2001.

Results: A total of 128 neonates received ECMO. Thirty-two patients were excluded due to major associated congenital anomalies. Of the remaining 96 patients, 64 had meconium aspiration

Table 1

	1992–1995	1995–1998	1998–2001
Numbers of ECMO patients	12	28	24
Surfactant (%)	50	75	83.3
High-frequency oscillatory ventilation (%)	58.3	89.3	95.8
Inhaled nitric oxide (%)	41.7	92.9	100
Time on ECMO (hours)	113.9	151.4	125.2
Survival (%)	91.7	92.9	83.3

syndrome and 32 had other causes. Table 1 shows the distribution of pre-ECMO therapies in meconium aspiration syndrome group and patients' outcome received ECMO.

Conclusion: This data suggests a steady increase in the use of pre-ECMO conventional therapies over the past decade in our regional ECMO centre. However, this has not been associated with a significant reduction in the use of ECMO nationally nor in the ventilated time pre-ECMO, length of time or patient outcome on ECMO.

P23 The effect of lateral positioning on gas exchange and respiratory mechanics in mechanically ventilated patients with unilateral lung disease

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Objective: To study the influence of lateral positioning with the involved side upwards, on gas exchange and respiratory mechanics in intubated patients with unilateral lung disease.

Materials and methods: Mechanically ventilated patients with unilateral lung disease. Of the 15 patients studied, seven had pneumonia and eight atelectasis with no response to routine physicotherapy. All patients were sedated and paralyzed for the study. All patients were ventilated in the A/C mode.

We performed measurements of gas exchange and respiratory system compliance and resistance (interrupter technique) with the patient supine. Immediately afterwards the patient was placed at lateral decubitus position with the involved side upwards. After 10 min at the new position, measurements were repeated. We searched for differences with positioning for the parameters measured. We also tried to correlate changes in oxygenation with a score expressing the radiographic extend of lung disease on the basis of portable anterolateral X-rays. Statistical analysis was performed with *t*-test and Pearson correlation. All measurements are expressed as mean ± SEM.

Results: With lateral positioning there was a statistically significant increase in PaO_2/FiO_2 (from 132.5 ± 19.4 to 162.5 ± 18.9 mmHg, $P<0.000$) and $PaCO_2$ (from 41.7 ± 2.6 to 43.7 ± 2.5 mmHg, $P<0.01$). At the same time a significant decrease in compliance (from 44.9 ± 3.1 to 39.4 ± 2.9 l/cmH_2O, $P<0.000$) and an increase in resistance (from 0.223 ± 0.02 to 0.255 ± 0.02 cmH_2O l^{-1} s, $P<0.000$), were observed. PaO_2/FiO_2 was significantly ($P<0.01$) correlated with the radiographic score ($r=0.76$).

Conclusion: Placement in lateral decubitus positioning with the involved side upwards, results in immediate improvement of oxygenation in the majority of cases of unilateral lung disease. This improvement is correlated with the radiographic extend of disease. At the same time a statistically significant deterioration in respiratory mechanics is observed.

P24 Surfactant phospholipids in the bronchoalveolar lavage fluid (BALF) of children who develop acute lung injury (ALI)

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Introduction: Children with ALI represent 5% of admissions to our Paediatric Intensive Care Unit [1]. Although there has been much research in adults with ALI, little is known about the pathophysiology in children [2]. More specifically there is a paucity of information on the pulmonary phospholipid (PL) changes during ALI children.

Methods: All children without pre-existing lung pathology who developed ALI (defined as $PaO_2/FiO_2<300$ mmHg [39.5 kPa] and bilateral infiltrates seen on frontal chest X-ray [2]) were eligible for the study within 18 hours of the diagnosis. Following parental consent, BALF was collected on days 1–4, then weekly and immediately prior to extubation. BALF was filtered to remove debris, centrifuged at 400 × *g* and 4°C for 10 min to remove cells and the supernatant stored at −80°C prior to analysis. Molecular species compositions of phosphatidylcholine (PC), were determined by electrospray ionisation mass spectrometry of lipid extracts of BALF supernatants. Children without any pulmonary pathology who were intubated following surgical procedures acted as controls. The study was approved by the local research ethics committee.

Results: Over 9 months, 40 (8.8%) children of 452 admissions developed ALI. Ten of 26 eligible children were enrolled in the study; six parents declined consent and 10 children were either too unstable for BALF collection or were not recruited in time. In the study group, the dipalmitoyl PC (DPPC) content in BALF decreased from control values (42.8 ± 6.5% of total PC) to a minimum of 23.1 ± 11.9% ($P<0.01$) between days 2–3, but increased to 37.8 ± 4.8% pre-extubation. These changes were accompanied by reciprocal increases in the concentrations of monounsaturated PC species characteristic of inflammatory cells.

Conclusion: Changes in the PC profile of BALF samples in children with ALI indicate that there is an increase in the cellular breakdown products. We speculate that this alteration in the PC profile with a lowering of DPPC may contribute to the disease process of ALI in children.

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P25 Treatment of status asthmaticus in children: is there a place for sodium bicarbonate?

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Introduction: Status asthmaticus is frequently associated with metabolic acidosis and acidosis reduces the effectiveness of β-agonists. In January 1999 we initiated a new protocol for the treatment of status asthmaticus in which the use of intravenous sodium bicarbonate was added if the pH is below 7.15 in patients with refractory status asthmaticus. This was based upon previous reports in the literature. It was postulated that refractory status asthmaticus could benefit from treating acidosis, although others have pointed out the risk of hypercapnia.

Objective: To investigate the effect of the administration of sodium bicarbonate on carbon dioxide levels in children with status asthmaticus and to evaluate the clinical effect of this treatment modality in reducing the number of ventilated patients.

Methods: We retrospectively studied the children with status asthmaticus admitted to the pediatric intensive care unit (PICU) that received sodium bicarbonate. The following data were collected from the charts: demographic data (age, sex), weight, severity of asthma, duration of admission, treatment of the status asthmaticus and blood gas before and after the administration of sodium bicarbonate.

Measurements and results: During the 2.5-year period reviewed, 42 patients with status asthmaticus were admitted to the PICU. Sodium bicarbonate was given in six patients with a mean total dose of 1.2 mmol/kg (0.57–4 mmol/kg). One patient received two doses of sodium bicarbonate during the same admission. Five of these patients that received sodium bicarbonate, were not mechanically ventilated. It is very likely that all five patients would have been intubated and mechanically ventilated if there had been no improvement of the respiratory distress after the administration of sodium bicarbonate. In the patient who was already mechanically ventilated, sodium bicarbonate was given after intubation. There was a significant decrease of pCO_2 after sodium bicarbonate infusion ($P=0.009$). Also there was a decrease of the respiratory distress. We did not observe adverse effects such as hypokalemia, hypernatremia or aggravation of the altered mental status. Since the initiation of the new protocol four patients were mechanically ventilated, but they were all intubated in the referring hospital prior to admission to the PICU. All patients survived.

Conclusion: Since the initiation of a treatment protocol for status asthmaticus in which sodium bicarbonate was added, sodium bicarbonate was administered in six patients. In these patients there was a significant decrease in pCO_2 and an amelioration of the respiratory distress. No adverse effects were observed. Also since then no patient required intubation after admission to the PICU.

P26 Effect of helium–oxygen mixture on time constant inequalities in COPD patients during controlled ventilation

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The respiratory system of the COPD patients is characterised by regional differences in mechanical properties. When mechanical ventilation is applied, this inhomogeneous lung causes regional dynamic hyperinflation. The aim of the present study was to compare the time constant inequalities obtained with air–oxygen and helium–oxygen mixtures in 14 COPD patients. The local ethic committee approved the protocol and consent was obtained from next of kin. The patients were sedated and paralysed for the duration of the protocol. Controlled mechanical ventilation was performed with constant flow. A Fleisch pneumotachograph calibrated for the use of helium and a differential pressure transducer were inserted between the endotracheal tube and the Y piece. The patients were ventilated successively with air–oxygen and helium–oxygen mixture in a random order. The time constant inequalities at the end of inspiration were calculated by the difference between P_1 and plateau pressure (obtained by an occlusion of 5 s). The time constant inequalities at the end of expiration were calculated by the difference between static intrinsic PEEP (PEEPistat) and dynamic intrinsic PEEP (PEEPidyn). A Wilcoxon test was used to compare the data.

The time constant inequalities at end inspiration and end expiration were reduced (Figs 1 and 2) with the helium-oxygen mixture (15 and 40% respectively).

A modification of the viscoelastic behaviour of the system could explain these results. The inspired volume is distributed more homogeneously to the different unit, with helium–oxygen mixture. During expiration, the regions with long time constant empty faster which could explain the decrease in regional dynamic hyperinflation. In conclusion, helium–oxygen mixture reduces the time constant inequalities of the respiratory system in COPD patient during controlled ventilation.

Figure 1

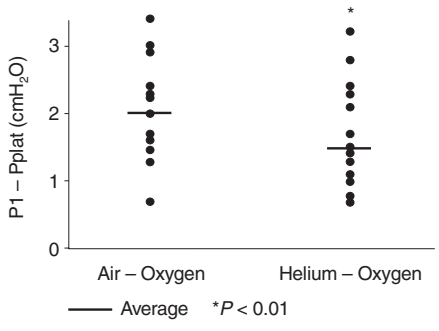
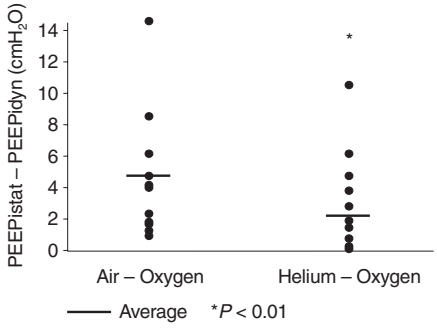


Figure 2



P27 Impact of aerosol particle size on drug deposition during mechanical ventilation: an *in vitro* evaluation

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Aerosol particle size is thought to impact drug deposition in the lung during controlled mechanical ventilation (CMV). The Aeroneb™ Professional Nebulizer System (Aeroneb Pro, in development), designed for continuous aerosolization with mechanical ventilators, utilizes a micro-pump with domed aperture plate that can be modified to generate fine particle, low-velocity aerosols of specific particle sizes. Thus, the effect of a range of aerosol particle sizes on drug deposition can be studied without changing other nebulizer characteristics.

Methods: To better understand the effect of particle size on drug deposition, six Aeroneb Pro nebulizers were modified to generate aerosols ranging from 3.4 to 5.4 μm volume median diameter (VMD), as determined by laser diffraction (Spraytech™; Malvern). Albuterol sulfate (0.5 ml of 0.5% solution) was aerosolized using an Aeroneb Pro placed in the humidified inspiratory limb of a Puritan Bennett 760 Ventilator (tidal volume of 500 ml, peak flow 40 l/min, ramp flow pattern, I:E ratio 1:3, rate 15/min) attached to an intubated adult lung model. The amount of drug deposited on an absolute filter distal to an 8 mm ID endotracheal tube was determined for each aerosol particle size ($n=3$). Drug was eluted from the filter and determined by reverse phase HPLC with isocratic elution and UV detection at 275 nm.

Results: The percent of the total dose administered ± standard deviation (SD) which was deposited in the test lung for each VMD tested is shown in the Table.

Summary: There was an inverse correlation ($P<0.05$, least squares analysis) between deposition of drug and aerosol particle size across the range of particle sizes tested. The efficient deposition (19–40%) of the 0.5 ml dose of albuterol is due, in part, to the low residual volume of the Aeroneb Pro.

Conclusion: Smaller aerosol particles resulted in greater drug delivery *in vitro* when using the modified Aeroneb Pro during CMV. Further studies are warranted to better understand this relationship, and to confirm this relationship *in vivo*.

Table

VMD (μm)	3.4	4.0	4.6	4.9	5.4
Deposition (% ± SD)	39.6 ± 3.9	37.6 ± 4.5	36.0 ± 2.3	26.5 ± 4.5	19.0 ± 4.1

P28 Ultrasound diagnosis of pneumothorax

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Introduction: Diagnosis of pneumothorax needs radiographic confirmation, which has numerous drawbacks in emergency (time-consuming, poor sensitivity, irradiation) or even CT. Can lung ultrasound play a role?

Methods: Eighty-five pneumothoraces were studied in 78 consecutive ICU patients (mean age 43 years, range 17–99, 60 men, 18 women). The diagnosis was radiologic in 71 cases and only scanographic (radioccult cases) in 14. The control group included 254 lungs in 127 consecutive patients (mean age 57 years, range 20–85, 87 men, 40 women) who required CT and were free of pneumothorax. Three signs were assessed: (1) absence of 'lung sliding', (2) absence of pathologic 'comet-tail artifacts', (3) fleeting inspiratory visualization of 'lung sliding' or pathologic 'comet-tails' at the limit of the pathologic area, a sign called 'lung point'. Intensivists trained in emergency ultrasound used a Hitachi-405 with a 5 MHz probe in strictly supine patients.

Results: Ultrasound analysis was prevented in eight cases (parietal emphysema in six cases). In 79 analyzable cases, 'lung sliding' was always absent, at least at the lower anterior half, with complete absence of pathologic 'comet-tails' at the same location. A 'lung point' was present in 53 cases. In 249 controls with anterior aerated pattern, 'lung sliding' was present in 190 cases, pathologic 'comet-tails' in 158 cases, and the 'lung point' was visible in no case.

By considering only absent 'lung sliding', ultrasound had a sensitivity of 100% and a specificity of 78%. By considering absent 'lung sliding' plus absence of pathologic 'comet-tails', sensitivity was 100%, specificity 95%. By considering 'lung sliding' plus absence of pathologic 'comet-tails' plus 'lung point', sensitivity was 67% but specificity 100%. For radioccult cases only, 'lung point' sensitivity was 80% and specificity 100%.

Table

	Pneumothorax		
	Radiologic	Radiooccult	Controls
Lung sliding plus absence of comet-tails	0	0	79
Lung sliding plus comet-tails	0	0	111
Lung sliding absent plus comet-tails	0	0	47
Lung sliding and comet-tails absent	69	10	12
TOTAL	69	10	249
Lung point	45	8	0

Conclusions: Anterior 'lung sliding' or pathologic 'comet-tails' allow pneumothorax to be discounted. The presence of a 'lung

point' indicates pneumothorax. Ultrasound proved more sensitive than bedside radiography. Ultrasound use may therefore obviate the need for CT in a majority of cases.

P29 Bedside fiberoptic bronchoscopy can be safely performed under conscious sedation

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Bedside fiberoptic bronchoscopy aids in the diagnosis and treatment of various respiratory conditions in critically ill patients. Adequate sedation is of paramount importance to ensure the success and safety of the procedure. In our institution, flexible fiberoptic bronchoscopy is done under conscious sedation with a benzodiazepine in the majority of cases in the paediatric intensive care unit.

We retrospectively reviewed 107 procedures performed on 48 patients in the period between March 2000 and November 2001. The median age was 29 months (range 1–306 months). Fifty-five percent ($n=59$) were done via the endotracheal tube, 40% ($n=43$) transnasally while 5% ($n=5$) were done via a tracheostomy. The Olympus fiberoptic bronchoscope (model no. BFXP40) with a 2.8 mm outer diameter was used.

Forty-six percent ($n=49$) of procedures were done with intravenous midazolam sedation with a dose of 0.2–0.4 mg/kg. Twenty-six percent ($n=28$) were performed with no parenteral sedation as these were mostly comatosed intubated patients. Eight percent ($n=8$) of procedures required sedation with a combination of intravenous midazolam, pethidine and chlorpromazine. The remaining patients underwent the procedure with their existing sedative infusions. Topical anaesthesia was used in all procedures. All patients were continuously monitored with cardiorespiratory and pulse oximetry monitors. Only 5.6% ($n=6$) developed transient desaturation. One patient had transient hypotension probably related to sedation, one developed airway bleeding because of underlying thrombocytopenia and one developed transient post-procedure stridor. 3.7% ($n=4$) had their sedation reversed with flumazenil or naloxone.

In conclusion, bedside flexible fiberoptic bronchoscopy under intravenous conscious sedation in children in the paediatric intensive care unit is safe. Proper monitoring and trained personnel are however important to avoid potential complications.

P30 Hypoxaemia during tracheal suctioning; comparison of closed versus open techniques at varying PEEP

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Introduction: Suctioning of artificial airways is a necessary procedure but is not without risk. Hypoxaemia is a recognised complication. Several small studies have suggested that closed suction catheters offer benefits over open suction because disconnection from the ventilator circuit is not required [1], thereby maintaining ventilation, F_IO_2 and PEEP. Other studies have sought to prove the maintenance of lung volume and cardiovascular stability with closed suction [2]. There is little evidence that closed suction systems offer clinical advantage over open suction in terms of arterial oxygenation. No published study had compared changes in PaO_2/F_IO_2 post suction. We performed a study in critically ill adults to identify any differences in PaO_2/F_IO_2 between closed and open suction for a given PEEP.

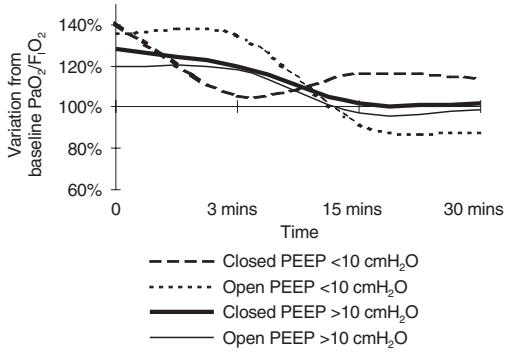
Methodology: We obtained local ethical approval for a prospective, randomised, crossover study. Adult ventilated patients with 6.5 tracheal tubes or larger and arterial catheter were randomised by sealed envelope to receive closed or open suction first, then the converse. Head injured patients were excluded. The two standardised suction episodes were separated by 2 hours. Ventilatory parameters, PEEP and position were unchanged. After baseline ABGs, subjects received F_IO_2 1.0 (hyperoxygenation) for 3 min prior to suctioning. The authors performed suctioning at 100 mmHg negative pressure. 14 F Ballard *Trach-Care* and Indoplas suction catheters were used. Two suction passes were made, timed to less than 30 s total. The patients were re-commenced on pre-suction ventilator settings and F_IO_2. ABGs were drawn at 3, 15 and 30 min post suction and analysed immediately.

Results: Twenty-three patients were recruited. Thirteen subjects were receiving PEEP 10 cmH_2O or greater and 10 less than 10 cmH_2O. Arterial oxygenation data was expressed as PaO_2/F_IO_2 and compared using a paired *t*-test. One high PEEP subject was withdrawn from the study after developing hypoxaemia after open suctioning. No critical incidents were noted. In all patients sedation scores were the same for both episodes.

Hyperoxygenation produced an expected significant increase in PaO_2/F_IO_2 at time zero. At 3 min the sustained increase approached significance. At 15 and 30 min, in both high and low PEEP groups, there were no statistically significant differences from baseline with either closed or open suction ($P=0.140$–0.763). No comparison is therefore possible between the two suction methods.

Discussion: Three minutes of 100% oxygen prior to tracheal suction would seem to prevent hypoxaemia and provide increased oxygenation for up to 3 min after suctioning. This period of hyper-

Figure



Mean change in PaO_2/F_IO_2 from baseline (100%) at PEEP >10 or >10 cmH_2O.

oxygenation is longer than that recommended by the AARC. After 3 min, oxygenation returned to baseline in both high and low PEEP patients and as there was no difference demonstrated, the two methods of suctioning cannot be compared. If hyperoxygenation is performed properly before suctioning, it is unlikely there would be any clinically significant differences between suction methods in terms of hypoxaemia.

References:
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P31 Bacterial filters in breathing circuits: an unnecessary cost?

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Objective: To analyze the utility of bacterial filters (BF) to prevent the incidence of pneumonia (PN), tracheobronchitis (TB) and tracheal colonization (TC) in patients undergoing mechanical ventilation.

Methods: From 1 July 2000 until 31 March 2001 a prospective and randomized study was realized. Included were all patients admitted in ICU and who required mechanical ventilation for 24 hours or more. At admission to the ICU patients were randomized in two groups (one group ventilated with BF, and another one without them). A throat swab on admission and afterwards twice weekly were taken. Infections were diagnosed according to CDC criteria and classified based on throat flora in endogenous and exogenous. The statistical analysis was realized by chi-square test and Student *t*-test, and we took values $P<0.05$ to consider a significant difference.

Results: Included were 230 patients (59.13% male). Mean age was 57.60 ± 17.21 years. APACHE-II was 15.88 ± 5.18. Mortality was 28.26%. Both groups of patients (114 with BF and 116 without BF) were similar in age, sex, mortality and APACHE-II. No significant diferences were found in the percentage of patients who developed PN (24.56% with BF and 21.55% without BF), combined PN or TB (34.21% vs 28.44%), combined PN or TB or TC (42.10% vs 43.96%). Neither in the number of infectious events per 1000 mechanical ventilation-days: PN (17.41 with BF and 16.26 without BF), PN or TB (24.62 vs 20.88), PN or TB or TC (36.63 vs 34.98). Neither in the the percentage of patients who developed infectious events and in the number of infectious events per 1000 mechanical ventilation-days in each group of mechanical ventilation-days. Neither in the number of exogenous events per 1000 mechanical ventilation-days (4.20 with BF and 3.95 without BF).

Conclusions: Bacterial filters in breathing circuits do not reduce the incidence of respiratory infections, neither exogenous events. The employment of bacterial filter may be an unnecessary cost.

P32 Are periodic changes of ventilator circuits necessary?

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Objective: To analyze the utility of periodic change of ventilator circuits (PCVC) to prevent the incidence of pneumonia (PN), tracheobronchitis (TB) and tracheal colonization (TC) in patients undergoing mechanical ventilation.

Methods: From 1 April 2001 until 30 August 2001 a prospective and randomized study was realized. Included were all patients admitted in ICU and who required mechanical ventilation for 72 hours or more. At admission to the ICU patients were randomized in two groups: one group ventilated with PCVC each 48 hours, and another one without change. A throat swab on admission and afterwards twice weekly were taken. Infections were diagnosed according to CDC criteria and classified based on throat flora in endogenous and exogenous. The statistical analysis was realized by chi-square test and Student *t*-test, and we took values $P<0.05$ to consider a significant difference.

Results: Included were 87 patients (62.06% male). Mean age was 59.52 ± 18.23 years. APACHE-II was 16.01 ± 6.24. Mortality was 18.39%. Both groups of patients (39 with PCVC and 48 without change) were similar in age, sex, mortality and APACHE-II. No significant diferences were found in the percentage of patients who developed some infectious events (PN 20.68%, PN or TB 31.03%, PN or TB or TC 48.27%), nor in the number of infectious events per 1000 mechanical ventilation-days (PN 12.42, PN or TB 21.92, PN or TB or TC 37.28). Neither in the the percentage of patients who developed infectious events and in the number of infectious events per 1000 mechanical ventilation-days in each group of mechanical ventilation-days. Neither in the number of exogenous events per 1000 mechanical ventilation-days (PN 2.92, PN or TB 4.38, PN or TB or TC 6.57).

Conclusions: The periodic change of ventilator circuits do not reduce the incidence of respiratory infections, neither exogenous events. This may be an unnecessary practice.

P33 Evaluation of early and late complications of percutaneous dilatational tracheostomy in 86 ICU patients

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Introduction: Due to the prolonged stay of the critically ill under mechanical ventilation in ICU often stomatotracheal intubation should be replaced by tracheostomy. In our ICU for over the last 18 months we are practicing percutaneous dilatational tracheostomy as described by Griggs. The aim of our study is to estimate the safety of the method by evaluating the early and late complications that occurred.

Method: In a retrospective study including 86 patients that have been trachiostomised by the above method we registered all com-

plication that occurred for a period of 40 days after the procedure. In all of the cases the procedure was carried out in the ICU. The average time for the procedure varied between 2–10 min depending mainly on the experience of the performing surgeon.

Results: In all cases per-operative mortality was 0%. The complications registered were grouped in Minor (A): Bleeding up to 20 ml in eight cases, rapture of the cuff in four cases, difficulty in advancing the tube into the trachea in four cases, minor subcutaneous emphysema in the region in two cases, and Major (B): Bleeding 20–150 ml in four cases, prolonged oxygen desaturation to 80% in two cases, extended subcutaneous emphysema in one case.

In group A complications did not request any specific treatment, in contrast with group B that all complication necessitated specific treatment.

Early post-operatively in two cases we had suppuration of the stoma. In two cases we had minor lung atelectasias possibly due to bleeding. Evaluation on the 40th day was possible only in 55 cases that survived. Among these cases we had kelloid formations at the wound site in two cases.

Conclusions: The performance of tracheostomy by the above method is quick and effective in experienced hands in spite of the low possibility of major bleeding. However, the whole procedure should be performed in the presence of surgeon. Post operative scars were minimal.

P34 Comparison of the laryngeal mask airway (LMA) and cuffed oropharyngeal airway (COPA) during percutaneous tracheostomy (PCT) in ICU patients

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Introduction: PCT is frequently used in ICU patients. Recent studies suggest that the use of a LMA has achieved good control of airway during PCT [1]. The COPA is a modification of the Guedel airway which allows manual ventilation by directly connecting to the breathing system [2]. We designed a prospective randomized study to compare the COPA and LMA devices during PCT in ICU patients.

Methods: In this study, a COPA or a LMA device was inserted prior to performing PCT following propofol, fentanyl and mivacurium anaesthesia. A size 9–10 COPA or size 4–5 LMA used in all patients. After oxygenation and ventilation had been adequate, PCT was performed (Sims Portex Ltd, Kent, UK). If patent airway was not provided in COPA or LMA, the devices was removed and endotracheal intubation was performed. All occuring events were documented, such as hypoxia, airway manipulations during this procedure.

Results: Patient's demographic data are in the Table. No procedure-related deaths occurred. The COPA failed in three of 23 patients (13%), the LMA failed in two of 24 patients (8%) to maintain patent airway. The number of airway interventions such as chin lift were higher in COPA group (48%). Three patients in COPA group and four patients in LMA group developed minor bleeding in peristomal area.

Conclusion: Both of COPA and LMA were inserted easily with a high success rate, but airway manipulations in order to maintain patent airway were higher in COPA group. Our data suggest that COPA can be used as an alternative to LMA during PCT.

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Table

	Age	APACHE II	Duration of PCT (min)	Days intubated
COPA ($n=23$)	52.96 ± 17.29	18.70 ± 9.97	4.17 ± 1.11	12.78 ± 6.49
LMA ($n=24$)	48.79 ± 18.14	15.08 ± 7.17	4.71 ± 1.97	10.42 ± 2.95

P35 The percutaneous dilatational tracheostomy, a comparative clinical trial

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Introduction: The dilatational tracheostomy becomes more and more a standard procedure in many ICU. Several systems for the procedure are available. Few clinical experiences are published about this procedure, even less about a comparison of the different kind of systems. On the bases of the experience of 96 self-practiced dilatational tracheostomies we critically report our experiences with two different kind of tracheostomy-sets.

Methods: Between December 1998 to September 2001 we initiated a prospective, comparing observational study on 96 patients on a surgical 12-bed ICU who were undergoing a percutaneous dilatational tracheostomy (PDT). In 36 patients the multi-step-dilatation-procedure, following Ciaglia (Cook®) was used, the Criggs–Method (Portex®), a one-step-dilatation with a certain dilatation-forceps was practiced 59 times. We documented operation-time, costs and complications in the daily practice at a university-teaching-ICU. As complications we considered all transfusion or surgical intervention requiring bleedings, infections which needed surgical treatment or antibiotics or intraoperative lowering of the SpO_2-pressure. The operation teams were classified following their surgical experience: Team 1: senior-resident/resident, Team 2: resident/resident, Team 3: resident/house-man.

Results: The operation-time for the Ciaglia-procedure was 25 (SD ± 14) min, with the Criggs-procedure 20 (SD ± 13) min. Considering the costs was the Criggs-system with 127.– *E* clearly cheaper than the Ciaglia-system with 165.– *E.* We found the Criggs-system easy to learn and to handle, which explains the different durations of operation-times in the different qualified teams: Team 1 needed with a mean operation-time of 36.4 min (n = 11/SD 14 min) significantly longer than Team 2 with a mean operation-time of 27.3 min (n = 24/SD 14.7 min) and Team 3 with a operation-time of 29.2 min (n = 36/SD 18.6). A short-time lowering of the SpO_2-pressure down to 70% occurred in five patients, relevant bleedings were not observed. Dependent on the age of the patients we found fractures of the tracheal cartilage in 25% of the patients but just in one patient further interventions following decannulation were necessary.

Conclusion: The PDT – independent of the used system – became a safe, cheap and fast standard-procedure on our ICU. So far we prefer the Criggs-procedure due to the lower risk of damaging the posterior wall of the trachea, the shorter operation-time and the lower costs. Nevertheless we practice both methods because each surgeon achieves best results with the system of it's own convenience. No difference was found in the incidence of complications.

P36 Evaluation of the mobility of the vocal folds after percutaneous translaryngeal tracheostomy intervention (Fantoni technique) on ICU patients

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The treatment of a critical respiratory insufficiency during a decompensated phase can cause a prolonged period of mechanical ventilation. So a tracheostomic access may be necessary in order to continue the weaning process from the ventilator.

In our study we wanted to evaluate the mobility of the true vocal chords and occurrence of the dyslocation of cricoarytenoid cartilage after the percutaneous tracheostomy with the Fantoni technique, which we applied on 70 patients from 1997 until 2001. All 70 patients were treated with the same tracheal access method in the space between the first and the second tracheal ring.

Our study required an endoscopic evaluation protocol with a direct fibrolaringoscopic access to the patient. So we evaluated the conformation of the upper respiratory-digestive ways and the mobility of the larynx and of the vocal chords (precisely: symmetric movement in adduction and abduction of vocal folds) and occurrence of cricoarytenoid cartilage lesion. We repeated the measurements 7 days after the intervention when we substituted the endotracheal cannule (Time 1) and after 20 days (Time 2).

In the follow up we controlled our patients 2 months after the tracheostomy (Time 3) to find out about eventual anatomic and functional changes of the larynx. Considering the patient's condition we then decided about the possible weaning from the tracheostomic cannule.

Exclusion criteria from patient enrollment were:
1. Patients affected by severe neurologic pathology in which the damage of the central nervous system could eventually interfere with the mobility of the upper respiratory-digestive ways.
2. Patients affected by severe peripheral neuropathy.
3. Patients with previous surgery of the larynx, the thyroid gland and the latero-cervical areas (lymphadenectomy, carotid endarteriectomy, etc.)

Conclusions: We found no change of mobility of the vocal folds in any patient nor dislocation of the cricoarytenoid cartilage at any time.

The complicances we observed were due to the percutaneous technique that consisted in initial lesions like edema (four patients at Time 1, one patient at Time 2) and hematoma (two patients at Time 2) which were not visible anymore after 20 days and cartilage fracture in three patients. On the long run we observed synechie (three patients at Time 2, four patients at Time 3) and cicatric stenosis (three patients at Time 2 and 3).

P37 Over-inflation of the tracheal tube cuff: a case for routine monitoring

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Introduction: Excessive tracheal tube cuff pressure can cause mucosal ischaemia leading to tracheal stenosis or tracheo-oesophageal fistulae [1] and under-inflation of the cuff has been associated with an increased risk of ventilator-associated pneumonia [2]. High-volume low-pressure (HVLP) cuffs were introduced in the early 1970s to enable tracheal wall pressure control. The use of a HVLP cuff does not however guarantee an acceptable mucosal pressure (MP) unless the intra-cuff pressure (CP) is maintained lower than 30 cmH_2O. CP was measured regularly in only 13% of intensive care units (ICU) in one region of England [3]. This prospective observational study examines the CP recorded after induction of anaesthesia and in two critical care facilities.

Method: The CP was measured in 30 sequential anaesthetised patients and 30 critically ill patients in each of two critical care facilities in one region of England. The anaesthetised group had their cuffs inflated by the operating department practitioner (ODP). The cuffs of the critically ill patients were surreptitiously checked once per patient on the ICU. The ODP and ICU nurses were unaware that the audit was taking place. If the CP was high it was reduced to 30 cmH_2O. If a leak was detected after reducing the CP then the cuff was re-inflated to just seal and the patient documented as appropriately high CP.

Results: *Anaesthetised patients*: The mean CP was 62 cmH_2O (range 20–120 cmH_2O, n = 30). There were six (20%) CPs above 100 cmH_2O.

Critically ill patients: The mean CP was 46 cmH_2O (range 13–120 cmH_2O, n = 60). There was no difference in CP between the two ICUs (mean CP was 43 and 48 cmH_2O respectively). There were three (5%) CPs above 100 cmH_2O. Eight patients had appropriately high CPs (mean CP 52 cmH_2O) as reducing the CP caused an audible air leak to occur.

Conclusion: Over-inflation was more frequent than under-inflation and pressures far exceeding the capillary perfusion and even exceeding the systolic arterial pressure were recorded. We recommend that formal protocols of cuff pressure measurement should be implemented or constant pressure cuff inflators used, especially in those who are undergoing prolonged intubation.

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P38 Does the method of humidification within a CPAP circuit affect the work of breathing? A pilot study

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Introduction: It has been shown (for example [1]) that heat and moisture exchange filters (HME) can be as effective in humidification of a breathing circuit as a heated humidification (HH) system. Before considering the replacement of the present HH system with HME filters in the high-flow CPAP circuits, we wished to examine whether they would affect the work of breathing (WOB) through the circuit. We found no evidence in the medical literature that such an investigation had been carried out.

Method: Six healthy male volunteers were studied. They were asked to breathe via a facemask through a high flow CPAP circuit at three different levels of CPAP: 0, 5 and 10 cmH_2O. Either a HH system (MR210; Fisher-Paykel Healthcare, NZ) or a HME (Ventalink; Pennine Healthcare, UK) was used in the circuit. During tidal breathing over a 20 s period, the airflow through the circuit was measured with a Fleisch no. 2 pneumotachograph and the pressure drop across the circuit was simultaneously recorded, both at 200 Hertz. The work of breathing for inspiration and expiration was calculated as the product of volume and pressure. Repeated-measures ANOVA was used for analysis.

Results: The work of breathing per unit tidal volume attributable to the breathing circuit, shown in the Table, was not significantly affected by method of humidification for inspiration ($P=0.058$) or for expiration ($P=0.343$) although it increased for each level of CPAP (inspiration, $P=0.004$ and expiration, $P=0.001$).

Table

	Level of CPAP (cmH_2O)		
WOB mean (SD) (J/l)	0	5	10
Inspiration			
HME	0.20 (0.07)	0.29 (0.09)	0.37 (0.10)
HH	0.19 (0.07)	0.21 (0.06)	0.31 (0.09)
Expiration			
HME	0.14 (0.04)	0.20 (0.10)	0.25 (0.07)
HH	0.12 (0.13)	0.17 (0.04)	0.21 (0.03)

Conclusion: This pilot study suggests a hypothesis that the use of a HME filter, compared to a HH system, may increase the WOB associated with a CPAP circuit. The results are not statistically significant and 25 subjects will be required to test this hypothesis according to power analysis. This study will be carried out on patients on the Intensive Care Unit.

Reference:
1. Martin *et al.*: **Heat and moisture exchange and vaporizing humidifiers in the intensive care unit.** *Chest* 1990, **97**:144-145.

P39 Comfort levels of six CPAP delivery systems

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Objectives: Not all CPAP systems have similar performance characteristics [1]. We aimed to assess comfort levels using six different CPAP delivery systems.

Methods: Six healthy blinded volunteers subjectively ranked each system for ease of breathing and comfort. The CPAP systems were set to 5 cmH_2O CPAP via standardised tubing, mouthpiece and

Table

		Pressure deviation (cmH_2O) from CPAP level at 25 l/min flow		
CPAP delivery system	Subjective ranking	Inspiration	Expiration	Overall
Respironics Vision	1	−0.8	−0.1	0.6
Respironics S/T	2	−0.6	0.1	0.8
Drager Evita 4 (NIV)	3	−1.1	1.3	2.4
Drager Evita 4	4	−1.1	1.3	2.5
Drager CF 800	5	−1.3	0.7	2.0
Siemens Servo 300	6	−1.1	2.3	3.4
Spearman Correlation with ranking *P* value		−0.76 0.084	0.83 0.04	0.89 0.017

NIV, new non-invasive software.

nasal clips. Pressure, flow and volume at the mouthpiece were measured using an Datex AS3 monitor and logged to PC.

Results: The pressure fluctuations between inspiration and expiration at 25 l/min correlated well with the subjective ranking ($P = 0.017$), with differences most evident in the expiratory phase of the cycle ($P = 0.04$).

Conclusions: CPAP systems that minimise pressure fluctuations are more comfortable. Patient comfort can be improved by choosing and setting CPAP systems to minimise pressure fluctuations.

References:
1. Austin PN, *et al.*: **Work of breathing characteristics of seven portable ventilators.** *Resuscitation* 2001, **49**:158-167.

P40 Hypercapnia and respiratory drive in obstructive sleep apnea patients before and after CPAP treatment

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Objective: To investigate the respiratory drive and the response to CPAP treatment in obstructive sleep apnea patients.

Methods: Twenty-one consecutive patients (19 males/2 females) with newly diagnosed disease with polysomnography were enrolled in this study. Blood gases, body mass index measurement (BMI) and spirometry were performed in all patients. Respiratory drive was evaluated by using the $P_{0.1}$ technique and the mean inspiratory flow (V_T/T_I). $P_{0.1}$ was also measured during sub maximal exercise by using the same technique. All parameters of the respiratory cycle were measured during the P0.1 procedure (V_T, f, V_E, T_I, T_{TOT}, T_I/T_{TOT}). We evaluated all the parameters before and 2 days after CPAP treatment.

Results: There was no significant difference in BMI, PO_2, FEV_1, FVC, respiratory cycle indices and $P_{0.1}$ at rest. PCO_2 was significantly reduced (44 ± 5 vs 42 ± 6 mmHg) after treatment. At exercise $P_{0.1}$ and V_T/T_I were significantly reduced (6.6 ± 2.7 vs 4.9 ± 1.6 cmH_2O, $P < 0.01$ and 72 ± 16 vs 64 ± 10, $P < 0.05$, respectively).

Conclusion: The unchanged respiratory drive at rest may not explain the PCO_2 reduction in our population. The significantly reduced respiratory drive and mean inspiratory flow during exercise could possibly explain change of ventilatory control, which may not be detected at rest.

P41 Very early extubation and non invasive ventilation after lung transplantation

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In recent years non invasive mechanical ventilation (NIV), delivered through facial or nose mask, has been successfully used as an effective treatment for acute respiratory failure and as a technique for weaning [1–3]. The aim of this study was to evaluate the use of NIV after very early extubation in lung transplanted patients.

Methods: Twelve patients (two single and 10 bilateral sequential lung transplantation), affected by cystic fibrosis (10) and emphysema (two) were early tracheal extubated, in the operating room. After tracheal extubation, five patients with $PaO_2/FiO_2 < 180$ mmHg and/or $PaCO_2 \geq 70$ mmHg and/or respiratory rate > 30, were assisted with delivery of artificial, non invasive ventilation (NIV). NIV was intermittently applied for a period of 30-40 min, through a full face mask. Pressure support ventilation and ventilatory settings were adjusted based on continuous pulse-oximetry and on measurement of arterial blood gases analysis.

Results: Hemodynamics and oxygenations collected during mechanical ventilation at the end of surgery (FINAL), in spontaneous breathing 30 min after extubation (SB), 30 min after NIV application (NIV) and in spontaneous breathing 120 min after extubation (POST-NIV) are described in the Table.

Discussion: During NIV we observed an improvement in pulmonary gas exchange with a decreasing in respiratory rate and an increasing in tidal volume. No patients were reintubated in ICU.

Table

	FINAL	SB	NIV	POST-NIV
mAP	66 ± 9	81 ± 7	80 ± 6	81 ± 13
mPAP	19 ± 3	22 ± 5	18 ± 5	20 ± 6
CI	3.9 ± 1.2	4.6 ± 0.9	4.3 ± 0.6	4.7 ± 0.3
PaO_2/FiO_2	483 ± 83	155 ± 55	261 ± 88	185 ± 43
$PaCO_2$	47 ± 5	72 ± 13	65 ± 6	63 ± 4
ITBVI	838 ± 93	811 ± 85	784 ± 46	786 ± 61
EVLWI	13.5 ± 4.0	12.5 ± 2.7	11.7 ± 1.5	11.6 ± 1.6

MAP = mean arterial pressure (mmHg), mPAP = mean pulmonary arterial pressure (mmHg), CI = cardiac index ($ml \cdot min^{-1} \cdot m^{-2}$), ITBVI = intrathoracic blood volume index ($ml \cdot m^{-2}$), EVLWI = extra vascular lung water index ($ml \cdot kg^{-1} \cdot m^{-2}$).

Conclusion: NIV permitted very early extubation after lung transplantation avoiding tracheal reintubation.

References:
1. Meduri GU, *et al.*: *Chest* 1996, **109**:179-193.
2. Wysocki M, *et al.*: *Chest* 1995, **107**:761-768.
3. Antonelli M, *et al.*: *JAMA* 2000, **283**:235-241.

P42 Non invasive mechanical ventilation delivered by a new 'helmet' versus a standard face mask

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We compared in six healthy subjects non invasive mechanical ventilation delivered by a new 'helmet' (large [L] and small [S] size) and by a standard face mask (FM). We tested three different ventilatory setting: a continuous flow CPAP ($CPAP_{CF}$), a CPAP delivered by a ventilator ($CPAP_{Vent}$) and a pressure support ventilation (PSV). The level of PEEP and PSV were 5 cmH_2O while F_IO_2 was 21%. Tidal volume V_T, respiratory rate (RR), work of breathing (WOB L), pressure time product (PTP) were measured.

Our results suggest that during CPAP the three systems are equals while during PSV the FM is better.

Table

	V_T (l)	RR (bpm)	WOB L (J/l)	PTP (cmH_2O*s/m)
$CPAP_{CF}$				
Helmet L	0.42 ± 0.05	14.4 ± 4.1	0.36 ± 0.06	81 ± 16
Helmet S	0.44 ± 0.14	14.8 ± 4.3	0.34 ± 0.06	71 ± 14
FM	0.50 ± 0.07	14.9 ± 4.1	0.39 ± 0.09	84 ± 17
$CPAP_{Vent}$				
Helmet L	0.56 ± 0.16	14.8 ± 3.6	0.35 ± 0.12	105 ± 52
Helmet S	0.63 ± 0.12	13.5 ± 2.7	0.31 ± 0.18	85 ± 45
FM	0.55 ± 0.10	14.8 ± 4.3	0.26 ± 0.17	81 ± 49
PSV				
Helmet L	0.68 ± 0.15	12.5 ± 3.3	0.12 ± 0.1	28 ± 24
Helmet S	0.68 ± 0.18	13.1 ± 3.7	0.13 ± 0.1	30 ± 21
FM	0.62 ± 0.15	15.6 ± 3.6	0.01 ± 0.01*	2 ± 1*

* $P < 0.05$ vs helmet L and helmet S.

P43 Comparison of efficacy of different ventilators to administer NIV in healthy subjects

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Background: Patient compliance and efficacy of the ventilator used for non-invasive ventilation (NIV) are important determinants of successful treatment.

Method: In this pilot study, healthy volunteers were requested to breathe normally for 10 min through a close fitting facemask. Each volunteer was ventilated using three ventilators, Galileo (Hamilton Medical, Germany) - pressure support ventilation (PSV), Harmony S/T (Respironics, USA) - pressure ventilation and Breas PV403 (Breas Medical, Germany) - volume control ventilation (VCV), for a duration of 10 min in a random order. The CO_2SMO Plus respiratory profile monitor (Novametrix Medical, USA) linked to a computer was used to measure minute alveolar ventilation (MValv), intrinsic positive end expiratory pressure (PEEPauto), imposed work of breathing (WOBimp), end-tidal Carbon dioxide ($ETCO_2$) in the second 5 min of each episode of ventilation. Visual analogue scale (VAS) for comfort during NIV from seven volunteers was recorded. Repeated measures ANOVA was used to analyse multiple comparisons.

Table 1

Comparison of Harmony, Galileo and Breas (mean [SD], median [interquartile])

	Baseline	Harmony	Breas	Galileo
MValv	7.48 (0.90)	9.42 (2.08)‡	6.72 (1.83) †	7.11(1.74)
PEEPauto	0.00	0.44 (0.13–1.36)*	3.58 (3.06–4.04)*†‡	1.23 (0.73–1.36)*
WOBimp	0.00	0.00	0.25 (0.10-0.37)*†‡	0.00
Vd/Vt	0.30 (0.03)	0.33 (0.05)	0.31 (0.06)	0.32 (0.06)
VCO_2 /kg	2.74 (0.45)	2.28 (0.40)	2.50 (0.55)	2.49 (0.49)
$ETCO_2$	5.19 (0.38)	4.25 (0.62)*	4.55 (0.66) *	4.02 (0.55) *

* $P < 0.05$ compared with baseline. † $P < 0.05$ compared with Harmony. ‡ $P < 0.05$ compared with Galileo.

Results: Thirteen healthy adult volunteers (five male, eight female) aged 22–48 years were studied. Data obtained from the study are displayed in Tables 1 and 2.

Conclusion: In normals, VCV with the Breas was less comfortable than the pressure ventilation modes tested. The increased autoPEEP and WOBimp may reflect this. There is also a suggestion that the auto-track triggering on the harmony may have enhanced comfort in normals when compared to the preset flow triggering on the Galileo.

Table 2

Comfort VAS scores (0–10) for normal ventilation, Galileo, Harmony and Breas

	Baseline	Galileo	Harmony	Breas
Median	7.8	6.9‡	8	2.3*†‡

* $P<0.05$ compared with baseline, † $P<0.05$ compared with Galileo, ‡ $P<0.05$ compared with Harmony.

P44 Non-invasive ventilation (PS-IMV) in patients with acute respiratory failure in common wards away from ICU

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Objective: Trial of non-invasive ventilation (NIV) in two groups of patients (pts) with postoperative acute respiratory failure (ARF) and acute on chronic respiratory failure, in common hospital wards.

Patients and methods: Two groups of pts (age 50–78). *Group A*: Surgical ($n=24$) with ARF, after major abdominal surgery. *Group B*: Medical ($n=11$) with ARF post COPD, sleep apnea syndrome and stroke. The pts fulfilled at least three of the following criteria: (1) dyspnea-tachypnea (RR>28/min), (2) the use of the accessory respiratory muscles, (3) abdominal pattern of breathing, (4) $PaO_2/FiO_2<200$ receiving O_2 (Venturi mask), (5) abnormal 0.25 thorax X-ray findings. NIV was used by using the Bi PAP apparatus with nasal mask, with the following settings: PEEP=5–10 cmH_2O, PS level 10–15 cmH_2O, and IMV breaths 5–12/min, $FiO_2=0.4–0.5$. The application protocol was as follows: first 24 hours – continuous ventilation with short pauses for physical therapy, then with pauses of up to 30 min of spontaneous breathing for the evaluation of the pts respiratory reserve. Pts were monitored with pulse oximeter, BP, CVP, ABG. All the pts were under proper medical treatment (bronchodilators, etc.). The improvement criteria were: sufficient TV, no use of accessory respiratory muscles, $FiO_2<0.4$, $PaO_2>70$ mmHg ($FiO_2\leq0.4$).

Results: *Group A*: 16/24 pts (67%) showed significant improvement of ABG values, SaO_2 and respiratory mechanics. They were all cured and left hospital. 8/24 (33%) failed to respond and were intubated and transferred to ICU, owning to bad compliance due to, nasal mask discomfort ($n=4$), ARDS ($n=3$), acute pulmonary edema ($n=1$). *Group B*: 9/11 pts (82%) were successfully disconnected, 2/11 (18%) failed to be disconnected owning to severe respiratory infection in a COPD, patient ($n=1$) and deterioration of mental status in a stroke pts ($n=1$). NIV duration: approximately 72 hours.

Conclusions: The application of NIV is very attractive and promising with easy use of the BiPAP in common ward pts with ARF. The majority of our pts responded well and had significant benefit avoiding endotracheal intubation, mechanical ventilation and ICU admission.

Reference:

1. Kramer N, Meyer TJ. Mehang J, Cece RD, Hill NS: **Randomized prospective trial of noninvasive positive pressure ventilation in acute respiratory failure.** *Am J Resp Crit Care Med* **151**:1799-1806.

P45 Maintaining ventilatory settings in seven home ventilators during leaks

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Using home ventilators (HV) may be an alternative for non-invasive ventilation in intensive care patients with respiratory failure. Air leaks are frequent in such patients and may be deleterious for the efficacy of ventilation. Few data are available about performances of HV. We analyse the adequacy of ventilatory settings in seven HV during ventilation with increasing leaks on respiratory system.

Study of seven HV on testing bench (SODEREL®): 1: Hélia®(SAIME); 2: Respicaire CV®(DRAGER); 3: O'Nyx®+ (NELLCOR PB); 4: VPAP2 ST® (SULLIVAN); 5: PV 102 (BREAS); 6: Synchrony (RESPIRONICS); 7: Neftis (TAEMA).

Settings: Pep: 6 cm, PS: 15 cm, RR: 12/min, minimal slope, Expiratory Trigger minimal, Inspiratory Trigger maximal (ITmax) and minimal (ITmin).

Three periods have been studied: A: no additional air leak, B: one and C: two calibrated leaks (4 mm diameter each).

Parameters analysed: RR with ITmin, Pep and Paw with ITmax, iFmax, eFmax, I/E with Itmin.

Results: See Table overleaf.

Conclusions: These seven HV are heterogeneous. Only two HV (4 and 6) are able to maintain the major parameters (RR, PEEP level and PS level). Two (1–3) are unable to maintain Pep level with maximum leaks and two (2-7) cannot even reach pressure support level.

Inspiratory time is systematically increased with inverse I/E in two cases. Auto triggering occurs with ITmin in three HV (1–2–5) and is independent of maintaining PEEP level.

It is probably important to consider performances of home ventilators before starting non-invasive ventilation in critically ill patients.

Table

	1A	1C	2A	2C	3A	3C	4A	4C	5A	5C	6A	6C	7A	7C
Pep	**6.27 ± 0.5**	**1.49 ± 0.0**	5.92 ± 0.0	5.79 ± 1.3	5.89 ± 0.1	**4.62 ± 0.2**	5.88 ± 0.0	5.67 ± 0.0	5.84 ± 0.0	5.70 ± 0.1	5.71 ± 0.0	5.73 ± 0.0	4.43 ± 0.0	4.43 ± 0.0
Paw	21.9± 0.1	22 ± 0.05	22.9 ± 0.1	**17.7 ± 6.6**	21.3 ± 0.1	20.2 ± 0.1	20.9 ± 0.0	20.4 ± 0.0	21.7 ± 0.1	20.7 ± 0.0	21.7 ± 0.2	21.8 ± 0.1	22.5 ± 0.2	**18.2 ± 0.4**
RR	**12.1 ± 0.17**	**28.6 ± 0.86**	11.3 ± 2.9	**44 ± 1.2**	12.4 ± 0.7	12.3 ± 0.5	12.1 ± 0.3	12.0 ± 0.1	12.1 ± 0.1	**24.5 ± 1.1**	12.1 ± 0.1	12.1 ± 0.1	12.3 ± 0.3	12.3 ± 0.3
iF	1.57 ± 0.0	1.61 ± 0.0	1.11 ± 0.0	**0.9 ± 0.34**	1.15 ± 0.0	1.24 ± 0.0	1.5 ± 0.05	**1.22 ± 0.0**	1.20 ± 0.0	1.02 ± 0.0	1.28 ± 0.0	1.25 ± 0.0	1.54 ± 0.2	**1.24 ± 0.2**
eF	−1.4 ± 0.1	−1.4 ± 0.0	−1.5 ± 0.0	−1.3 ± 0.5	−1.1 ± 0.0	**−0.7 ± 0.0**	−1.7 ± 0.0	−1.7 ± 0.0	−1.5 ± 0.0	−1.5 ± 0.0	−1.4 ± 0.0	−1.5 ± 0.0	−1.2 ± 0.0	−1 ± 0.1
I/E	0.13 ± 0.1	**0.63 ± 0.1**	0.19 ± 0.1	**1.1 ± 0.0**	0.16 ± 0.2	0.16 ± 0.1	0.26 ± 0.1	0.4 ± 0.0	0.3 ± 0.0	**1.94 ± 0.1**	0.45 ± 0.0	0.46 ± 0.0	**0.29 ± 0.0**	**0.45 ± 0.1**

Triggering level automatically adjusted for 4 and 6.

P46 Effect of noninvasive ventilation on pulmonary gas exchange in chronic obstructive pulmonary disease

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Background: In patients with acute exacerbation of chronic obstructive pulmonary disease, noninvasive ventilation may be used in an attempt to avoid endotracheal intubation and complications associated with mechanical ventilation.

Method: We conducted a prospective, randomized study comparing noninvasive ventilation delivered through a face mask with standard treatment in patients admitted to ICU.

Results: A total of 23 patients were recruited from a large group of 63 patients with chronic obstructive pulmonary disease admitted to critical care department. A total of 12 patients were randomly assigned to noninvasive ventilation (group I) and 11 to standard treatment (group II). The two groups had similar demographic characteristics with (mean age 51.8 ± 10 vs 58.7 ± 8.4, $P = 0.082$ and weight 74.8 ± 13.8 vs 74.9 ± 8.9, $P = 0.97$) and clinical characteristics on admission to the hospital. The use of noninvasive ventilation significantly improved some of the final arterial blood gases and oxygenation parameters in successful cases (Table 1).

However other blood gases and oxygenation parameters showed no improvement or deterioration (Table 2).

Conclusion: In selected cases with acute exacerbation of chronic obstructive pulmonary disease, noninvasive ventilation can reduce the need for endotracheal intubation, and can improve the hypoventilation associated with the disease.

Table 1

	PH	PCO_2	PO_2	Sat	PAO_2
Initial	7.26 ± 0.029	67.1 ± 5.9	50.0 ± 9.5	76.3 ± 12.2	65.9 ± 7.74
Final	7.38 ± 0.028	60.2 ± 5.4	85.8 ± 7.6	93.9 ± 4.7	164.1 ± 28.3
P value	0.000*	0.041*	0.000*	0.004*	0.000*

*significant with improvement.

Table 2

	HCO_3	PaO_2/FIO_2	$P(A\text{-}a)O_2$	PaO_2/PAO_2	Shunt
Initial	31.5± 5.0	238.2± 45.1	15.8±12.9	0.770±0.172	0.93± 0.75
Final	34.3± 6.4	257.7± 31.8	78.3±26.3	0.534±0.089	4.50± 1.40
P value	0.375*	0.368*	0.000**	0.007**	0.000**

*insignificant, **significant with deterioration.

P47 Neuroprotective efficacy of magnesium sulphate in experimental traumatic brain injury

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Objective: Traumatic brain injury (TBI) results in brain damage either by early cell death or by delayed cell death due to secondary injury factors such as blood–brain barrier breakdown, brain edema, and cerebral ischemia. Studies have demonstrated that magnesium (Mg) salts given after traumatic brain injury improve neurological outcome. We aimed to examine the neuroprotective effects of

magnesium on brain edema and blood–brain barrier breakdown after experimental traumatic brain injury in rats.

Method: Experimental closed head trauma was induced on Sprague–Dawley rats by allowing 450 g weight falling from a 2 m height onto a metallic disc fixed to the intact skull. The animals were randomly assigned to receive an intraperitoneal bolus of either 750 μmol/kg magnesium sulphate or 1 ml saline 30 min after the induction of TBI. Brain water content (BWC) and brain tissue specific gravity (SG), as indicators of brain edema, were measured 24 hours after traumatic brain injury. Blood–brain barrier integrity was evaluated quantitatively 24 hours after injury by fluorometric assay of Evans Blue dye (EBD) extravasations.

Results: In magnesium group, brain tissue specific gravity was significantly increased and brain water content was significantly reduced. Evans blue dye content in the brain tissue was significantly decreased in the magnesium group (Table 1).

Conclusion: These experimental results have demonstrated the neuroprotective effects of magnesium sulphate on secondary injury factors like brain edema and blood–brain barrier breakdown after traumatic brain injury.

Table 1

Brain water content, specific gravity and Evans blue dye content in the brain tissue

	BWC (% brain tissue)		SG		EBD (μg/mg brain tissue)	
Groups	Left	Right	Left	Right	Left	Right
Control ($n=6$)	81.7 ± 0.82	81.2 ± 0.49	1.044 ± 0.002	1.044 ± 0.001	0.0053 ± 0.0004	0.0054 ± 0.005
Magnesium ($n=6$)	77.82 ± 0.68	78.02 ± 0.33	1.047 ± 0.0007	1.045 ± 0.001	0.0016 ± 0.0002	0.0017 ± 0.0002
P	< 0.01	< 0.01	< 0.05	< 0.01	< 0.01	< 0.01

P48 Is continued aggressive care justified in patients requiring mechanical ventilation after a stroke following cardiovascular surgery?

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Background and purpose: Ischemic stroke after cardiovascular surgery is a major postoperative event that further complicates ICU care. In many disabled patients who remain ventilated the need for aggressive care is reconsidered. However, the prognosis of patients who survive the acute postoperative phase but require extended ventilatory support due to a stroke is unknown.

Methods: We identified 44 patients with acute ischemic stroke diagnosed after cardiovascular surgery resulting in prolonged endotracheal intubation (>14 days). We collected data on surgical indication, presurgical comorbid conditions, stroke mechanism and location, reason for prolonged intubation, pulmonary complications requiring therapeutic intervention, and duration of ventilatory support and ICU stay. Clinical outcome was defined using the Glasgow outcome scale (GOS). Proportions were compared using the Fisher exact test and continuous variables using the paired *t*-test.

Results: Coronary revascularization, valvular replacement/repair, and aortic surgery accounted for nearly one-third of the interventions each. Sixty-four percent of the strokes had purely embolic features and 29% had a combination of embolic and hemodynamic features. Most patients (75%) remained intubated due to inability to protect the airway, whereas weaning failure was less common (25%). Thirty-seven failed extubation attempts were recorded and 35% of them resulted in serious complications. Pulmonary complications occurred in 59% of patients, including pneumonia in 52% and ARDS in 12%. In-hospital mortality was 46% and only 9% of patients were functionally independent (GOS 4–5) upon discharge. History of lung disease and smoking was associated with poor functional recovery ($P=0.04$). The presence of pulmonary complications was associated with longer ICU stay (34 ± 17 days versus 26 ± 11 days; $P=0.02$) and a trend towards longer duration of mechanical ventilation (38 ± 39 days versus 22 ± 11 days; $P=0.16$).

Conclusion: Prolonged mechanical ventilation is an important poor prognostic factor in patients who suffer a stroke after cardiovascular surgery. Patients with perioperative stroke who cannot be extubated within the first 2 weeks have a very poor outcome, especially those with pre-existing lung disease. Almost half of the patients die in the hospital and less than one in 10 patients achieve meaningful functional recovery.

P49 Pulmonary complications in patients with stroke requiring mechanical ventilation

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Background and purpose: Prior studies have suggested that the outcome of patients with acute stroke who require mechanical ventilation is poor. In most patients swelling of ischemic tissue determines outcome but pulmonary complications may be equally important. Our purpose was to assess the impact of pulmonary complications on the outcome of patients with stroke who need prolonged mechanical ventilatory support.

Methods: We reviewed data on 50 patients with acute stroke who were mechanically ventilated for 5 days or more. We collected

information on stroke type and location, time to intubation, reason for intubation, length of ventilatory support, duration of ICU stay. All pulmonary complications requiring therapeutic intervention were recorded. We defined outcome using the Glasgow outcome scale (GOS). Proportions were compared using the Fisher exact test and continuous variables using the paired *t*-test.

Results: Fifty-two percent of the strokes were ischemic and 58% of them involved the posterior circulation. Sixty-two percent of the hemorrhagic strokes were intraparenchymal hematomas and more than half were infratentorial. The reason for initial intubation was airway protection in 58% of patients, respiratory distress in 24% (usually due to aspiration or pulmonary edema), and respiratory arrest in 18%. Intubation was performed within 48 hours of stroke onset in 88% of cases. All patients received a tracheostomy. The mortality rate was 20% upon discharge and 32% among patients available for follow up at 1 year. Meaningful functional recovery (GOS 4–5) was achieved by 16% of patients both upon discharge and at 1 year. Pulmonary complications occurred in 70% of patients, including 62% of patients with pneumonia and 8% with ARDS. Presence of pulmonary complications was associated with longer duration of ventilatory support (24 ± 26 days versus 14 ± 9 days; $P=0.05$) and ICU stay (27 ± 17 days versus 13 ± 6 days; $P=0.004$), but not with clinical outcome.

Conclusions: Pulmonary complications are very common and serious among patients with stroke who require prolonged mechanical ventilation and need a tracheostomy. Although pulmonary complications lead to prolonged duration of ventilatory support and ICU length of stay and cost, mortality is not increased. Long-term ventilation in patients with stroke is not futile; recovery of functional independence is possible and continuation of full level of care seems warranted.

P50 Stroke treatment and outcome in ICU

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Introduction and methods: There is no general agreement about the opportunity of ICU admission of patients with severe stroke due to high morbidity and mortality. In order to clarify the therapeutic perspective of these patients, is essential to identify some elements that could give early prognostic information. Aim of the present study was to analyze patients with severe stroke admitted to our ICU in order to assess the indications of ICU admission, prognostic value of SAPS II, morbidity and mortality. Clinical sheet of stroke patients admitted to ICU from 15 January 1995 to 31 December 2000 were retrospectively analyzed obtaining the following data: cause of admission, SAPS II, length of stay and mortality in ICU. SAPS II has been related to outcome. (Student's *t*-test).

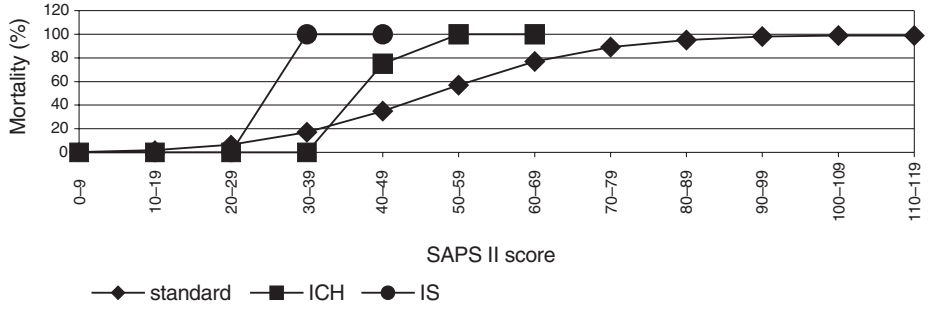
Results and discussion: Twenty-seven patients were studied: 16 (59.3%) had intracerebral hemorrhage (ICH), 5 (18.5%) had subarachnoid hemorrage (SAH), and 6 (22.2%) had an ischemic stroke (IS). The necessity of tracheal intubation and mechanical ventilation was the leading cause of admission in ICU. Mean length of mechanical ventilation was 5 ± 2 days. Mean length of stay in ICU was 7 ± 2 days. Mortality rate was 59.25%. Relationship between mortality, functional outcome and nature of stroke, is shown in Table 1. SAPS II on admission was significantly higher ($P<0.001$) in non survivors. The relationship between expected and observed mortality, in patients with ICH and IS, is shown in Figure 1. We have noted a similar course of observed and expected mortality, although observed mortality was slightly higher than the expected one. We conclude that although high incidence of poor outcome in severe stroke patients admitted to ICU, a good functional outcome is possible in survivors. Moreover the SAPS II may allow a prognostic evaluation of patients on admission.

Table 1

Glasgow Outcome Scale score	ICH ($n=16$)	IS ($n=6$)	SAH ($n=5$)
1 death	10	3	3
2 vegetative state	1	0	1
3 severe disability	3	2	1
4 moderate disability	2	1	0
5 good recovery	0	0	0
5 good recovery	0	0	0

Reference:
1. *Lancet* 1975, **1**:480-484.

Figure 1



P51 Medical specific characteristics of brain dead patients related to etiology

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Introduction: Understanding the progressively changing pathophysiology of brain death (BD) allows expedient diagnosis and implementation of rapid therapeutic measures that maximize successful application of transplantation. The present study investigates whether time course to BD and the incidence of subsequent homeostatic complications differed in patients with traumatic brain injury (TBI) and those with non traumatic intracranial pathology (intracerebral haemorrhage, brain tumor, post cardiac arrest anoxia-IP) and influenced source of organ donation.

Design: Retrospective chart review in a multidisciplinary ICU from January 1992 to November 2001.

Method: Patients were analyzed as to demographics, time to BD, medical complications and their incidence (diabetes insipidus [D.I.], hypotension, hypothermia, hypokalaemia). The patients were divided in two categories, those with TBI and those with IP. Estimation of data was performed using the Mann–Whitney test and χ^2 analysis.

Results: One hundred patients i.e. 2.03% of total admissions ($n = 4150$) developed BD. Solid organ donors represented 24% of brain dead patients and 0.7% of admissions. Patients' demographics, medical complications and their incidence are mentioned in the Table. Incidence of donation was equal in both categories (Table).

Conclusion: Age, previous severity of illness (APACHE II score), GCS and abnormal pupil reactivity, time to BD and hypothermia constitute the most important factors that differentiate the two categories. Early donor recognition, rapid and accurate declaration of BD according to standing law are common practice in our ICU. Nevertheless the percentage of organ donation remains low compared to international standards.

Table

	TBI ($n = 50$)	*IP* ($n = 50$)	*P*
Age* (years)	32.5 ± 20.15	48.73 ± 15.87	< 0.001
APACHE II*	21.13 ± 7.93	18.09 ± 6.35	< 0.005
Admission abnormal pupil reactivity (%)	40	25	< 0.02
GCS* upon admission	5.86 ± 2.9	7 ± 3.79	< 0.05
Time to B.D. (days)*	1.71 ± 1.31	2.69 ± 2.43	< 0.02
Hypothermia (%)	28	16	< 0.03
DI (%)	43	36	n.s
Hypotension (%)	34	32	n.s.
Hypokalaemia (%)	15	13	n.s.

* Mean ± SD

P52 BIS for recognition of brain-death in potential organ donors

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Background and aim of study: BIS is based on EEG monitoring. Although it has been created for assessing depth of sedation or anaesthesia it can give information on damaged brain activity. The aim of study was to check out whether BIS index can indicate brain-death and what kind of BIS record is observed in patients with clinical symptoms of brainstem death.

Methods: Five BIS records of patients with clinically defined symptoms of brain-death were analysed. In all patients' CT scans showed deep and irreversible damage of brain (massive intracerebral haemorrhage). Tests for absence of brainstem reflexes and persistent apnoea had been carried out and patients were qualified for transplantation procedure. BIS was monitored before and during apnoea test and pain stimuli.

Results: In two cases the range of BIS was initially 0 (0–3). BIS monitor alarmed of EEG flat line. No response on pain stimuli nor on apnoea test were observed in one case. In the second patient BIS increased during apnoea test to 90. In the other three cases initially BIS was over 0 (15–45) and during apnoea test increased to over 90. No reaction on pain stimuli was observed. In those cases where reaction on apnoea test was recorded, BIS significantly decreased after apnoea test.

Discussion: The attempts for using BIS in patients with a severely damaged brain as prediction of brain-death have been already described. However there were no investigations on BIS records in patients with diagnosed brain-death. It is underlined in many guidelines for recognition of brain-death that such investigation as EEG must be assessed by highly trained specialists. Therefore the use of a more simple device for recognition of brain-death could be helpful and might increase the number of organ donations. It is especially needed in haemodynamically unstable patients in whom the apnoea test is difficult to perform because it may cause rapid decrease in blood pressure to an unmeasurable level and even circulatory arrest. Although in two cases BIS confirmed diagnosis of

brain-death, in three other patients BIS was significantly higher than 0 and device did not recognise EEG flat line. Probably strong artefacts were the cause of it: the electrical activity of heart, autonomous nervous system impulsation and transmissible trembling of upper half of corps caused by heart work, which can be especially observed in non ventilated patients.

Conclusion: These observations all together make the use of BIS for diagnosis of brain-death in potential organ donors impossible and in our opinion unreliable. Too many factors can influence BIS record and this is unacceptable when used for defining the patient's death.

P53 Apnea test for brain death determination: an alternative approach

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Introduction: Complications that may occur during the 'classical' apnea test include severe respiratoy acidosis causing hemodynamic instability, hypoxemia and an inadequate increase in CO_2 requiring repeat testing. We present our experience administering carbon dioxide (CO_2) during mechanical ventilation as a means of raising arterial CO_2 ($PaCO_2$).

Methods: An arterial blood gas and end-tidal CO_2 ($EtCO_2$) were measured at baseline and hemodynamic monitoring and pulse oximetry were monitored throughout. Using the formula: $PaCO_2$ of 10 mmHg = pH of 0.8, it was predicted what $EtCO_2$ was required to achieve a $PaCO_2$ sufficient to cause a pH 7.20. A gas mixture of 3% CO_2:97% O_2 was then administered through the ventilator adjusting an IMV rate of 2–4 according to the rise in $EtCO_2$. Once the predicted $EtCO_2$ was reached, an blood gas was repeated. The $PaCO_2$–$EtCO_2$ gradient was also calculated pre and post testing. Respiratory movements were monitored by both the respiratory flow loops and by direct visualization by a physician.

Results: Sixteen patients aged 49 ± 15 years were studied. There were no incidences of hemodynamic instability or arterial desaturation during the studies. At the end of the apnea test, the predicted and measured $EtCO_2$ were 52 ± 9 and 56 ± 10 torr, respectively, and the predicted and measured $PaCO_2$ were 60 ± 10 and 67 ± 10 torr, respectively. All patients achieved an adequate arterial pH and there was no change in the $PaCO_2$–$EtCO_2$ gradient during the testing ($P = 0.195$, Student's *t*-test). (Table; mean ± SD).

Table

	Baseline	End of apnea test
pH	7.36 ± 0.05	7.19 ± 0.02
$EtCO_2$ (torr)	32 ± 5	56 ± 10
$PaCO_2$ (torr)	41 ± 5	67 ± 10
$PaCO_2$–$EtCO_2$ gradient	9 ± 4	11 ± 5

Conclusions: Advantages of this technique over the previous method include: 1. allows for continuous measurement of $EtCO_2$ during the apnea test ($EtCO_2$ is predictive of rises in $PaCO_2$); 2. eliminates the likelihood of desaturation episodes; 3. better monitoring for respiratory effort than provided by visual inspection alone.

P54 High serum protein S100B levels in brain-dead patients

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S100B is a protein synthesized in astroglial and Schwann cells in the central nervous system (CNS). Only very low concentrations of this protein are normally present in serum, whereas high levels of S100B have been found in the blood of patients suffering from a variety of CNS disorders, including tumors, cerebrovascular insults or traumatic brain injury (BI). Data on S100B in patients with brain-death are sparse. To clarify this issue, 48 brain-dead (BD) patients (34 men, 14 women) with a mean (± SD) age of 48 ± 21 years (range 14–85 years) were studied. Brain-death was due to trauma ($n = 35$), spontaneous intracerebral hemorrhage ($n = 11$), intracerebral thrombosis ($n = 1$) and intracerebral aneurysm ($n = 1$). For comparison, 36 patients (32 men, 4 women), with severe traumatic BI who did not develop brain-death, having a mean age of 33 ± 15 years (range 17–70 years) were also studied. All patients were intubated and mechanically ventilated. In BD patients, blood samples for S100B determination were obtained after clinical diagnosis of brain-death. In BI patients, blood samples were collected upon admission in the hospital and every 24 hours thereafter, for a maximum of seven consecutive days; in these patients peak and average values of S100B were used for analysis. Protein S100B levels in BD patients (median 7.68 μg/l, interquartile range 4.06–14.10 μg/l) were significantly higher compared to the peak (median 1.30 μg/l, interquartile range 0.60–1.90 μg/l, $P < 0.001$, Mann–Whitney *U* test) or to the average (median 0.60 μg/l, interquartile range 0.36–0.97 μg/l, $P < 0.001$, Mann–Whitney *U* test) values of S100B in BI patients. In conclusion, serum concentrations of protein S100B are high in brain-death victims. Further prospective studies are required to determine the predictive value of S100B levels in the early diagnosis of brain-death.

P55 Quality of life after severe head injury correlates to S100B serum level

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Objective: S100B protein is a new possible indicator of brain damage after severe head injury. Peak values of S100B serum concentrations during the first days after trauma were significantly correlated to survival after severe head injury. In outcome assessment there is an increasing focus on measures of health outcome incorporating the patients own perspective. Therefore the aim of our study was to investigate the correlation of early S100B serum level to the quality of life and outcome after severe head injury.

Methods: We included 51 patients with severe head injury (GCS < 9), who had been admitted between 1 and 6 hours after injury, in a prospective study. Blood samples were taken on admission (mean 2.5 hours). The serum was analyzed for S100B concentrations by using a RIA (Byk-Sangtec). S100B serum values above 0.5 µg/l were defined to be elevated. The outcome was assessed at follow-up (mean 11.9 months after trauma, follow-up rate 100%) using the Glasgow Outcome Scale (GOS 1–3 = unfavourable, GOS 4–5 = favourable) and a questionnaire to assess the quality of life (QOL) according to Blau consisting of 10 items (job, leisure, eating, sleeping, friends, money, family, partnership, health and self assessment). A quality of life index was calculated.

Results: Patients with unfavourable outcome had significantly higher serum concentrations of S100B compared to the patients with favourable outcome (4.9 µg/l versus 1.6 µg/l, $P < 0.0008$). In the evaluation of all patients the QOL concerning all items is significantly lower in the group with S-100B serum concentrations above 2 µg/l on admission (19.6 versus 51.2 points, mean, $P < 0.0007$). The overall rating of QOL was in the same range in these groups (15.2 versus 50.4 points, mean, $P < 0.0002$). Concerning the survivors the quality of life index and the overall quality of life is significantly higher in the group of patients with S100B concentrations ≤ 0.5 µg/l on admission (71.4 versus 55.4 points, mean, $P < 0.05$)

Conclusion: Thus S100B seems not only to be able to predict survival but also to assess the extent of primary brain damage after trauma.

P56 Serum S100B as a biochemical marker of neurological complications in intensive care patients

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Objective: There is growing evidence that S100B protein may be used as a novel biochemical marker of brain cell damage, measured by a simple blood test. Several studies have found increased values in acute neurological diseases such as stroke, head injury, intracerebral haemorrhage or cerebral hypoxia. The objective of our study was to investigate whether measurement of serum S100B is useful to diagnose an acute neurological complication in the analgo-sedated and intubated intensive care patient.

Methods: One hundred and fifty neurointensive care patients with different intracranial diseases were included in our study. Serum S100B protein was measured daily using an immunoluminometric assay (LIAISON®, Byk-Sangtec Diagnostica, Dietzenbach, Germany). The result of the test was usually available at the bedsite within 3 hours. S100B levels and temporal course were investigated for the sensitivity and specificity to diagnose a neurological complication occurring during the intensive care course.

Results: One hundred and twelve patients (75%) showed primarily increased values due to their neurological disease or after surgery. In 22 patients a complication with neurological deterioration was observed such as vasospastic infarction, brain haemorrhage, or contusion/oedema enlargement. In all of these patients, a significant rise of S100B (> 0.5 µg/l) was found. There was no major complication without S100B increase. In three cases, the increase in S100B was the first sign of neurological complication and prompted emergency computed tomography scanning. In two cases, increasing S100B values changed management towards a surgical intervention.

Conclusion: Serial measurement of S100B protein is suitable to diagnose neurological complications with a high sensitivity and specificity and to have an impact on management decisions in intensive care patients.

P57 The influence of ventricular tapping on S100 and NSE serum concentrations: preliminary results

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Objective: Serum markers, e.g. the protein S100 and neuron specific enolase (NSE), are recognized to give additional information about the extension and prognosis of brain damage. In some of these patients, e.g. after SAHs and ICBs, it is necessary to insert a ventricular drainage. Whether the cannulation of the ventricle and the insertion of a ventricular drainage falsifies the serum concentrations of S100 and NSE is not known. The aim of this study was to get further information in this field.

Methods: In this prospective study we included 10 patients (5 women, 5 men, mean age 53.7 years) suffering from SAH ($n = 5$), ICB ($n = 2$), hydrocephalus ($n = 2$) and ischemia ($n = 1$). All patients underwent a ventricular tapping and an insertion of a ventricular drainage. Serum samples for estimation of S100 and NSE were collected before, directly after and 6 hours after insertion of the drainage. In addition we investigated the liquor directly after and 6 hours after insertion for S100 and NSE concentrations. The samples were analyzed by using the Liaison kits (Byk-Sangtec, Dietzenbach, Germany). For statistical work up we used the *t*-test.

Results: None of the patients showed a significantly increased S100 or NSE serum concentration after insertion of the drainage. The mean serum value of S100 before insertion was 0.49 µg/l, directly after 0.42 µg/l and 6 hours later 0.49 µg/l. The mean serum concentration of NSE before insertion was 18 µg/l, directly after 13.9 µg/l and 6 hours later 9.8 µg/l. The concentration of

NSE in the cerebrospinal fluid directly after insertion were significantly higher compared to the serum concentration (85 μg/l versus 13.9 μg/l, mean, $P < 0.05$). The S100 concentration in the liquor was also higher, but failed to be statistically significant (418.8 μg/l versus 0.42 μg/l, mean).

Conclusion: Due to our preliminary results, the serum values of S100 and NSE seem not to be falsified by insertion of a ventricular drainage. So the prognostic value of these serum markers seems to be preserved despite the surgical manipulation. In addition the concentrations of these markers in the cerebrospinal fluid seem to be exceedingly higher compared to the serum concentrations, probably reflecting an intact blood–brain barrier.

P58 Serum S100B as a marker of brain damage in the trauma intensive care unit

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Introduction: Though computer tomography (CT) is a reliable and accurate method of assessing brain damage after trauma, it also exposes the critically ill patient to considerable stress and is thus unsuitable for frequent follow-ups. The intensivist managing severe traumatic brain injury requires a marker which is reliable, repeatable and non-invasive. Our aim was to determine whether S100B could be such a marker in the intensive care setting, both for isolated traumatic brain injury and for traumatic brain injury with additional multiple trauma.

Methods: Ninety-five critically injured patients have been included in this ongoing multi-center prospective study and assigned to one of three groups, according to their pattern of injury:
Group 1: Isolated traumatic brain injury ($n = 50$)
Group 2: Traumatic brain injury in combination with multiple trauma ($n = 35$)
Group 3 (controls): Multiple trauma without traumatic brain injury ($n = 10$).

All patients are examined by CT on admission. S100B values are determined during the first hours after trauma and daily thereafter for a maximum of 3 weeks and compared to clinical, neurological and laboratory findings and to CT.

Results: S100B is elevated during the first hours after trauma, regardless of whether patients are suffering from traumatic brain injury or not, but drops to normal after 48 hours if patients do not have traumatic brain injury. The further course of S100B differs markedly between survivors and non-survivors. In survivors with traumatic brain injury, S100B decreases post-traumatically and remains normal. In non-survivors with traumatic brain injury, S100 remains elevated and/or increases prior to death. This pattern is most clearly visible in patients with isolated traumatic brain injury.

Conclusion: We consider S100B to be a useful marker in the intensive care setting, both for patients with isolated traumatic brain injury and for patients with additional multiple trauma. S100B is a reliable, repeatable and non-invasive marker and does not expose patients to any additional stress. It provides the intensivist with valuable information regarding the effect of therapy on the one hand and regarding prognosis on the other.

P59 Is procalcitonin a new surrogate marker for hypoxic brain damage?

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Objective: Procalcitonin is so far known as a marker of severe sepsis mostly caused by Gram-negative bacteria. But recent literature provided hints for its elevation after mechanic or hypoxic tissue damage, too. In a pilot study we therefore investigated the possibility whether PCT could serve as a neurological outcome marker after out-of-hospital cardiac arrest.

Methods: S100 protein and PCT serum levels were serially analyzed on hospital admission and on the following 3 days in 23 patients resuscitated after out-of-hospital cardiac arrest. At day 14 patients were divided in two groups applying the Glasgow Outcome Scale (GOS): 16 patients in the group with bad neurological outcome (GOS 1–3); seven patients in the group with good neurological outcome (GOS 4–5). If present signs of sepsis or systemic inflammatory response syndrome (SIRS) were documented at the different time points. The diagnostic performance of S100 and PCT levels to differentiate between the both groups was performed with the use of receiver operating characteristics (ROC). Both parameters were measured on the LIA-mat using the assays from Byk-Sangtec and Brahms.

Results: Patients with bad neurological outcome had significantly higher S100 levels than those with a good neurological outcome at all time points and significantly elevated PCT levels at days 1–3. Highest levels for S100 were found immediately after hospitalization and for PCT at day 1. The brain-originated S100 showed best performance immediately after hospitalization with an area under the curve of 0.89 (sensitivity of 62.5% and specificity of 100% at a cut-off value of 1.25 μg/l), while the non-brain-originated PCT was the best predictor for bad neurological outcome at day 1 (AUC = 0.98; sensitivity of 92% and specificity of 100% at a cut-off value of 0.5 μg/l). None of the patients revealed signs of sepsis or SIRS at the investigated time points.

Conclusion: Although we only investigated a small number of patients our results are promising and show that PCT is not only induced in severe bacterial infection, SIRS, septic shock or multi-organ dysfunction syndrome. Further investigations on larger patient populations have to follow. Nevertheless we recommend that S100 and PCT serum levels in the case of patients with out-of hospital cardiac arrest can be used as reliable and, because of their different liberation kinetics, to each other complementary parameters for the prediction of neurological outcome in successfully resuscitated patients.

P60 Cerebral blood flow in critically ill cardiac patients: effects of vasoactive drug therapy

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The introduction of the thermodilution technique (TD) in measuring cardiac output (CO) and coronary sinus blood flow has suggested the application of the same technique into measuring CBF which has been validated by several methods using transcranial Doppler and Xenon inhalation clearance curves.

The present work is intended to assess the effect of two vasoactive drugs on CBF in 20 critically ill patients (12 males, 8 females, mean age: 5.86 ± 9.46) all having CHF due to dilated cardiomyopathy. Following clinical examination all patients were subjected to haemodynamic evaluation including central venous line, arterial cannulation and jugular vein catheterization. The latter was performed using Baim coronary sinus catheter directed towards the right jugular vein under fluroscopic guidance up to the bulb of internal jugular vein. Jugular blood flow (JBF) was measured by constant infusion of ice cold (5%) dextrose solution and recorded digitally on a Baim coronary sinus computer. Haemodynamic measurements including CBF were made at rest and repeated following infusion of noradrenaline (NA) in incremental doses sufficient to raise BP by one third of the basal reading. An average of three readings were taken. NA was discontinued and after 20 min the same method was repeated after dobutamine infusion given in a dose of 10 μg/kg/min for 20 min.

Compared to basic measurements, NA significantly reduced CBF by 22.4 ± 4.79% in 13 patients with simultaneous increase in CVR by 106.73 ± 29.0%, NA increased CBF by 40.46 ± 12.0% in seven patients with simultaneous decrease of CVR by 13.7 ± 6.2%. It also increased systemic vascular resistance by 24.9 ± 2.76%, $P < 0.0001$. On the other hand dobutamine has led to an increase in CBF by 56 ± 12% in 11 patients with simultaneous decrease in CVR by 22 ± 6.31%. It decreased the CBF by 38.1 ± 11.8% in four patients with simultaneous increase in CVR by 130.68 ± 70.01%, and a decrease SVR by 21 ± 5%, $P < 0.0359$.

In conclusion, vasoactive drugs commonly used in critically ill cardiac patients have different effects on cerebral blood flow. Despite the beneficial effects obtained from using NA in increasing perfusion pressure and cardiac output, the adverse effects on CBF are an obvious limitation to its use as a monotherapy, compared to dobutamine which besides augmenting CO improves dramatically CBF.

P61 Validity of cerebral blood flow measurements by the thermodilution technique in critically ill cardiac patients

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Despite the importance of cerebral blood flow (CBF) in determining the natural history and hospital course of critically ill cardiac patients (pts), the qualitative determination of the CBF has been rarely resorted to, because of technical limitations with resultant lack of information about cerebral oxygen consumption and cerebral metabolic rate of oxygen when compared to other organs. The introduction of the thermodilution technique (TD) in measuring cardiac output (CO) and coronary sinus blood flow has led to the suggestion of applying the same technique in measuring CBF. The present work describes the use of TD to measure CBF in a group of critically ill cardiac patients in comparison with the golden standard technique of transcranial Doppler. The group studied included 20 critically ill cardiac pts (12 males, 8 females, mean age 58.6 ± 9.4 years), all having congestive heart failure due to dilated cardiomyopathy, and were candidates for inotropic treatment.

Following clinical examination, all pts were subjected to haemodynamic evaluation including central venous line insertion, arterial cannulation and internal jugular vein catheterization. The latter was performed using Baim coronary sinus catheter directed towards the right jugular vein under fluoroscopic guidance up to the bulb of internal jugular vein. Jugular blood flow (JBF) was measured by constant infusion of ice cold dextrose solution and JBF was recorded digitally on a Baim coronary sinus computer and CBF was calculated from the equation: (JBF × 2 × 100/Brain weight). Following the procedure CBF was measured by application of Doppler technique and expressed as middle cerebral artery flow velocity with the Doppler transducer over the zygomatic arch window. Doppler parameters included: mean velocity, maximum velocity, minimum velocity.. Assessed by TD, CBF averaged 22.32 ± 15.75 ml/min/100 g and was closely correlated in a linear relationship with middle cerebral artery flow velocity measured by the transcranial Doppler technique (45.9 ± 20.25 cm/s, $r = 0.85$, $P < 0.0001$).

In conclusion, CBF can be measured in critically ill cardiac patients by applying the TD principle. Our data have shown the validity of this technique for assessing the course of critical illness and effect of therapeutic interventions with the patient serving as a control for himself.

P62 Correlation of transcranial doppler (TCD) parameters with jugular bulb venous oxygen saturation (SjO_2)

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Introduction: Disturbances of the cerebral circulation play a key role in the pathophysiology of head injury. TCD ultrasonography, a non invasive bedside technique, and SjO_2 monitoring, an invasive technique which has some risk factors, are methods of assessing cerebral hemodynamics. The purpose of the study was to examine the relationships between TCD parameters and SjO_2 measurements in patients with head injury.

Methods and materials: Forty patients (35 ± 18 years) with severe head injury (Glasgow coma scale < 8) were included in the study. All patients were mechanically ventilated, sedated and paralyzed. Continuous monitoring of intracranial pressure (ICP), arterial pressure, pulse oximetry and SjO_2 were performed in every patient. Multiple TCD examinations (total 150) were performed during the first five ICU days. The TCD parameters were: maximum velocity

(V_{max}), minimum velocity (V_{min}), and pulsatility index (PI). The findings from TCD were compared with SjO_2 values using the method of Pearson's product moment coefficient of correlation and linear regression analysis.

Results: Among TCD parameters PI was found to be correlated with SjO_2. There was a leak correlation between PI and SjO_2, for SjO_2 values below 75% ($r = -0.51$, $P < 0.01$). A breakpoint SjO_2 value of 75% was demonstrated above which there was no correlation between PI and SjO_2 ($r = -0.59$, $P > 0.05$). With the same method V_{max} and V_{min} were unable to provide more information.

Conclusion: The pulsatility index (PI) cannot predict changes of SjO_2 values. Therefore a combination of TCD and SjO_2 monitoring can provide better access to cerebral hemodynamics.

P63 Intracranial pressure monitoring in two district general hospital ICUs

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There is a growing consensus that, in selected patients, intracranial pressure (ICP) monitoring is an appropriate intervention in district general hospitals. It improves outcome in patients with traumatic brain injury [1] and is safe [2]. In the Southwest region two district general hospitals without on-site neurosurgical facilities have been inserting Camino™ fibreoptic transducers in their ICUs since 1997.

I conducted a retrospective case note audit of ICP monitored patients at the two centres. Fifty-one patients had monitors inserted between 6 October 1997 and 28 February 2001. Data were collected on: sex, age, initial Glasgow coma score (GCS), diagnosis, duration of ICP monitoring and incidence and nature of complications. Sixty-nine percent of patients were male, with a median age of 29 (range 1–71 years). Median GCS was 6 and 76% had an initial GCS of 8 or less. The most common indication for ICP monitoring was traumatic brain injury (72%). Other diagnoses were anoxic coma (12%), meningitis (8%), subarachnoid haemorrhage (4%), intracerebral bleed (2%) and encephalitis (2%). Median duration of monitoring was 3 days. Only two patients were monitored for more than 5 days; both these patients received two monitors.

The complication rate was low. One (2%) patient had a minor scalp haemorrhage. One (2%) patient had a small intracerebral haemorrhage, detected as an incidental finding on CT scan; it had no clinical sequelae. One (2%) monitor developed a fault and had to be resited. No infectious complications were seen. The data from this audit adds to the weight of evidence that ICP monitoring in selected patient groups is safe in district general hospitals.

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P64 CSF-cytokines (IL-6, IL-12, and IL-13): the right marker for shunt reimplanation after infections?

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Introduction: It is very difficult to determine the optimal time for shunt re-implantation after cerebrospinal fluid (CSF) shunt infection. Total white blood cell count, neutrophil, eosinophil granulocyte and plasma cell counts in CSF do not always provide adequate information for the right decision to re-implant a shunt after an infection. Re-infections have been frequently observed. We therefore decided to examine the contribution the three cytokines IL-6, IL-12 and IL-13 (CSF) could bring in deciding on shunt re-implantation.

Methods: Three patients (2 boys, 1 girl, age: 4 months to 17.5 years) with external CSF drainage and shunt infections due to *Staphylococcus epidermidis* had their CSF examined by ELISA for IL-6, IL-12, and IL-13 over a period of 3–50 days. A simultaneous examination of the cytograms was done and compared with the cytokine results.

Results: The Table shows the similarity in behaviour of the inflammatory cells (IC) and the patients' CSF cytokines.

Conclusion: Whereas the CSF inflammatory cytokines IL-6 and IL-12 decrease in concentration, the anti-inflammatory cytokine IL-13 concentration increases. This means that the cytokines could be a good indicator for the course of CSF infections and hence an

Table

	Patient 1		Patient 2		Patient 3	
Period (days)	1	4	1	3	1	46
IL-6 (pg/ml)	108.3	74.4	184.9	86.0	111.9	12.3
IL-12 (pg/ml)	7.7	6.2	22.5	4.3	8.7	0.7
IL-13 (pg/ml)	39.5	45.5	58.8	78.8	13.0	51.3
IL-12/IL-13	0.19	0.13	0.05	0.05	0.7	0.01
IC (%)	10	3	10	2	65	1

indicator for the optimal timing for shunt re-implantation. CSF leucocyte count and its differentiation depends on the examiner and on the quality of cell preparation. Thus the quantitative determination of the cytokines is more objective. Regrettably, the cytokine values are very variable, meaning that only trends can be estimated. Further studies are needed for reliable information concerning the CSF infection status.

P65 Propofol attenuates the neuroprotective effects of magnesium in experimental traumatic brain injury

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Objectives: Propofol is a popular nonbarbiturate anesthetic agent. Its neuroprotective effects are controversial. The neuroprotective effects of magnesium salts have been documented. We aimed to examine the neuroprotective effects of propofol alone and with magnesium on brain edema and blood–brain barrier (BBB) breakdown after experimental traumatic brain injury (TBI) in rats.

Method: Experimental closed head trauma was induced on Sprague–Dawley rats by allowing 450-g weight falling from a 2-m height onto a metallic disc fixed to the intact skull. Rats were assigned into four groups to receive intraperitoneally 1 ml/kg saline in the control group (C, $n = 10$), 10 mg/kg propofol in the propofol group (P, $n = 10$), 750 μmol/kg magnesium sulphate ($MgSO_4$) in the magnesium group (M, $n = 10$), 10 mg/kg propofol and 750 μmol/kg $MgSO_4$ in the magnesium-propofol group (PM, $n = 10$) 30 min after TBI. Brain water content (BWC) and specific gravity (SG), as indicators of brain edema were measured 24 hours after TBI. BBB breakdown was evaluated quantitatively 24 hours after TBI by fluorometric assay of Evans blue dye (EBD) extravasations.

Results: The increase in BWC, the reduction in SG and EBD content in the group P was statistically significant when compared to the group C. In the group PM, BWC was significantly higher and SG was significantly lower than group M. EBD content in the brain tissue was also significantly increased in the group PM when compared to group M (Table 1).

Conclusions: These experimental data have shown that although propofol has neuroprotective effects on TBI, it is not as effective as magnesium, and it attenuates the neuroprotective effects of magnesium sulphate on secondary injury factors following traumatic brain injury.

Table 1

Statistical significance (*P*) comparison of BWC, SG, and EBD content between the groups

	BWC		SG		EBD	
	Left	Right	Left	Right	Left	Right
C vs M	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**
C vs P	**< 0.01**	**< 0.01**	**< 0.05**	**< 0.05**	**< 0.05**	**< 0.05**
C vs PM	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05
M vs P	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05
M vs PM	**< 0.05**	**< 0.05**	**< 0.05**	**< 0.05**	**< 0.01**	**< 0.01**
P vs PM	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05

P66 Respiratory effects of sufentanil and remifentanil in spontaneously ventilated patients after major abdominal surgery

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Introduction: Opioids as analgosedative agents are commonly used in intensive care units but they are not performed in spontaneously breathing patients because of the potential risks of adverse respiratory events. The aim of this study was to assess the respiratory effects of sufentanil and remifentanil in postsurgical critically ill patients during spontaneous ventilation since the drugs show pharmacokinetic and pharmacodynamic properties which make them attractive for intensive care use.

Patients and methods: Twenty-seven patients requiring mechanical ventilatory support were admitted in the general Intensive Care Unit of the San Giacomo Hospital after major abdominal surgery. They were randomised to receive either sufentanil (group S = 13 patients) or remifentanil (group R = 14 patients) variable continuous infusion in order to obtain pain control and to maintain a Ramsay Sedation Score of 2–3 as the target point. Rescue sedation was provided, when needed, with Midazolam boluses. Respiratory rate (RR), V_E, TV, $EtCO_2$, pH, PaO_2, $PaCO_2$ and SpO_2 were measured in the two groups of patients during the continuous infusion of the opioids before and 1 hour after the beginning of spontaneous ventilation (Pressure Support Ventilation) and then every 6 hours, even after extubation. Statistical differences were scored using the Mann–Whitney U test and ANOVA test for repeated measures.

Results: Adequate analgesia and sedation were achieved with sufentanil and remifentanil administration. Midazolam mean dosage was significantly higher in the remifentanil group. There were no

statistically significant differences between the two groups for RR, TV, T_E, $EtCO_2$, pH, PaO_2, $PaCO_2$, SpO_2 at the different times. No adverse respiratory events were seen during the study.

Discussion: The present results show that sufentanil and remifentanil continuous infusion at the appropriate dosage appear to have no important adverse effects on respiratory drive and gas exchange in spontaneously breathing critically ill patients after surgery.

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P67 Postoperative morphine clonidine analgesia in high-risk patients

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Intramuscular injections of the opiates in some cases cannot provide effective analgesia in patients after traumatic abdominal surgery. The purpose of our research was clinical evaluation of the efficiency of postoperative morphine clonidine epidural analgesia in high-risk patients (ASA III–IV). Epidural analgesia – morphine hydrochloride 4 mg in combination with clonidine 0.05 mg – was applied in 80 patients aged from 44 to 77 during 3 days of the postoperative period, patients with unstable hemodynamics inclusively. The epidural space was identified at the level Th_{5-6} with the following insertion of the catheter by 3–4 cm into the epidural space. Sufficient analgetic effect was observed in 20–30 min after administration of morphine and clonidine and lasted for 10–12 hours. Hemodynamic state remained stable provided sufficient intravenous 'preload' infusion had been performed before the procedure, while the effect of arteriodilatation and hemodilution was observed – CVP went down by 15% ($P > 0.01$), hemoglobin and hematocrit dropping by 7–9% ($P > 0.01$). At the same time slower heart rate and breath rate were observed. Analgetic effect was scored individually in conformity with the rating scale coming from 0 points (the best effect) to 10 points (the worst effect). The average score before the injection was at 7.2 ± 2.1, with the following decrease to 3.1 ± 1.2 one hour after the injection. It is necessary to admit that scores depended on an individual patient.

Advantages of the postoperative morphine clonidine epidural analgesia were that sufficient pain relief was not accompanied by a long lasting sedation effect, which enabled patients to remain active enough to move in bed, breath deeply, and secure effective cough.

Therefore, postoperative morphine clonidine epidural analgesia may be regarded as an alternative method of analgesia in high-risk patients after abdominal surgery.

P68 BIS monitoring in ICU: advantages of the new XP generation

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Background: Bispectral Index (BIS) has been used to measure the level of sedation in critically ill patients [1]. The biggest problems were the artefacts raising from facial muscle or eye movements, and the wide variability of analysed clinical conditions [2]. BIS-XP is a new available device (Aspect, USA), with one more frontal electrode, that should minimise the movement related artefacts. The aim of our study was to compare the new and the old BIS measurement on the same patient in ICU.

Materials and methods: Thirty critically ill patients, admitted to our intensive care unit, were studied. Head-trauma patients were excluded. SAPS II and Ramsay Sedation Scale (RSS) were used to assess physiological impairment and sedation depth. Sedative agents were administered at the following maintenance doses: Propofol (1–3 mg/kg/hour) and Midazolam (0.025–0.033 mg/kg/hour), to achieve a sedation level of 3–4. Sufentanil was administrated (0.01–0.02 μg/kg/min), as needed, to ensure analgesia. Every patient was simultaneously monitored with both the BIS and the BIS-XP, along a period of 3–6 hours. BIS values were continuously recorded and their variations after painful stimuli were relieved.

Results: Both systems well correlated with the level of sedation in every single patient. The BIS-XP was able to eliminate anecdotal rise in BIS value unrelated with depth modifications. Higher variability in BIS monitoring made the range wider than in BIS-XP (coefficient of variation 72% vs 55%). After painful stimuli, BIS-XP was shown to record variations with a mean advance of 42 s (30–67 s), compare to BIS (both BIS and BIS XP have been set with the same smoothing rate). Progress in electrode fixation on the skin were observed with BIS-XP, avoiding repeated installation and allowing long-term monitoring. Sedation level oscillations, undetected by BIS, were revealed by BIS-XP value variations.

Conclusion: The BIS-XP showed sedation monitoring improvement. The added electrode in BIS-XP was likely to improve the number validity, by eliminating patient related artefacts, though the higher sensitivity makes the BIS-XP trend less stable than the BIS one. Moreover the advance in relieving depth variations could be an useful improvement in guiding the administration of sedative-hypnotic agents to titrate adequate sedation.

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P69 'Diprifusor' TCI for sedation of ventilated adult ICU patients: target blood propofol concentration settings

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The principal objective of this multicentre, non-comparative study was to determine the range of target blood propofol concentration settings required when 'Diprifusor' TCI systems are used to administer propofol for sedation in ventilated, adult, ICU patients. Following local ethics approval, data were obtained from 122 patients. Informed consent was obtained from patients or their next of kin. Three categories of ICU patients were studied: 57 post-cardiac surgery, 18 brain injured and 47 general ICU. Mean ages were 60.7, 41.1 and 60.7 years and mean APACHE II scores 9.2, 17.8 and 19 in the three groups respectively. The mean duration of sedation was 15 hours in the post-cardiac surgery patients, 47.6 hours in the brain injured group and 63.3 hours in the general ICU group. All post-cardiac surgery patients had received propofol by Diprifusor TCI for surgery and the same TCI system continued in use for sedation. Patients were excluded if they had received propofol by conventional modes of administration within 4 hours of the start of the study, had an established regimen of sedation with agents other than propofol for more than 24 hours, or a regional anaesthetic block persisting into the period of sedation. Depth of sedation was assessed with a modified Ramsay Score (UK Intensive Care Society National Guideline, 1999) and was also graded as light (L), desired level (D) or excessive (E). The 'Diprifusor' target blood propofol setting was titrated as required to obtain the depth of sedation desired in each patient. A desired level of sedation was obtained, after a mean time of 9.9 min, in all but one patient in whom sedation was 'excessive' throughout. For each patient, the time-weighted average target setting over the entire period of sedation, from the time when a desired level was first obtained, was calculated. Median, 10th and 90th percentile values are presented in Table 1.

Table 1

Time-weighted average Diprifusor target blood propofol settings (μg/ml)

ICU patient category	*n*	Median	10th percentile	90th percentile
Post-cardiac surgery	57	1.33	0.79	1.92
Brain injured	18	0.98	0.58	2.53
General ICU	47	0.41	0.16	1.19
All patients	122	0.99	0.25	1.87

P70 Analgesia and sedation for ventilated newborn infants of low dose remifentanyl infusion

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Introduction: The aim of our study is to verify the usefulness of remifentanyl (R) in ventilated newborn (nw) evaluating the analgesic effect and how variation of R infusion maintains a level of analgesia according to different modality of ventilation (MV).

Materials and methods: Eighteen nw were admitted in ICU for RDS, GA > 32, mean weight 2.250 ± 450 g. A modified scale, according to PIPP and Comfort, was used to evaluate 'comfort'. According to the score (S) all patients were divided in three groups: A < 5; B = 5; C > 5. Data were collected at T0 (basal value), T1 (30 min after start infusion), Tn (every 4 hours), T-est (extubation time), and T post-est (30 min after extubation). R infusion was started at 0.25 μg/kg/min to obtain an 'ideal' S 5 ± 1; and was modified to obtain an adequate analgesia during PCV. After 'critical' phase R was reduced, evaluating the mean *t* to reach an adequate RD (respiratory drive) for weaning. S at this moment was < 5 (max 7). Finally R was stopped and the mean *t* for extubation was calculated. For all parameters median value and SD were calculated. For HR, BP, PSO_2 in A, B, C a Student *t* test was adopted for the significance ($P < 0.005$) through the single value at T0 (T0 vs A, T0 vs B, T0 vs C) and also A, B, C (A vs B, A vs C, B vs C).

Results: The mean *t* of R (T1–Tstop) was 66.94 ± 22 hours, with a mean dose of R 0.146 ± 0.038 μg/kg/min. The mean *t* to reach comfort (5 ± 1) was 20 ± 13.11 hours (T1–T5) with R 0.17 ± 0.14 μg/kg/min. R was 0.18 ± 0.04 μg/kg/min in PCV with a S of 4 ± 0.63.The mean *t*, to obtain a RD to change PCV to PAV, was 2.30 ± 0.56 hours with R 0.09 ± 0.04 μg/kg/min, comfort S 5 ± 0.53 referred to all the period of PAV. Stop-Test was 15 ± 3.4 min. The S at Tpost-est was 5.5 ± 1.03. Statistically significant is the fall of HR at T0 vs A ($P = 0.003$) and T0 vs B ($P = 0.002$) as a confirmation that an adequate level of analgesia brings a stabilization of hemodynamic changes to pain stimuli. SpO_2 increased from T0 vs A ($P = 0.005$) and T0 vs B ($P = 0.001$) due to synchronization of the patients to MV since the good level of analgesia was reached.

Conclusion: No adverse effects were observed: low dose of R maintained an analgesia with an assessment of patients to MV. Infusion *t* did not influence time of extubation. Although the S 5 ± 1 is an hypothetic 'ideal' level of analgesia, we can assess that R could permit, in newborn, to reach a state of comfort during all 'MV therapy' until extubation, when pain stimulus is removed.

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P71 Pain relief in major trauma patients: an Israeli perspective

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Background: The pain of major trauma patients remains often unrelieved while in the Emergency Department. Our objective was to examine pain management in several trauma units, and to evaluate the impact of implementation of a trauma pain management protocol.

Methods: Current status was evaluated from questionnaires filled by trauma unit personnel of nine medical centers. In one, a pain management protocol was introduced. Staff and patients evaluated pain management before and after the protocol was instituted.

Results: About 80% of staff respondents from various centers were not aware of guidelines for pain management in trauma. The belief that pain assists diagnosis was the main reason (78.6%) for withholding analgesia. Large variability existed on what contraindicates analgesia, with the majority withholding analgesia in abdominal and multiple injuries. When administered, analgesia was delayed, and most commonly intramuscular Meperidine was given. After the protocol's implementation, the personnel's awareness of analgesia increased, and consequently it was administered earlier and to more patients, mostly as intravenous morphine.

Patients appreciated the timely analgesia (38% after vs 14% before, $P = 0.01$), with fewer receiving none. Analgesia was considered beneficial by more patients (70% after vs 23% before, $P < 0.001$). This was reflected in increases in overall satisfaction with pain relief during the entire hospitalization.

Conclusion: The importance of pain management protocols in major trauma was demonstrated by the response of personnel and patients. The attitudes of the personnel regarding pain and its relief have changed and this resulted in improved patient perception and cooperation. This suggests that similar protocols should be tested and introduced throughout the country.

P72 Salient beliefs towards the application of an algorithm for pain relief in ICU

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Introduction: The negative effects of pain on ICU patients' recuperation has been reported in many studies, prolonging their length of stay and increasing the cost of hospitalisation. It was demonstrated that the application of an algorithm reduced pain scores.

Objective: The aim of this study was to identify the salient beliefs of ICU nurses toward the application of an algorithm for pain relief.

Methods: This information was assessed using a questionnaire answered by 24 ICU nurses recruited during work, as a convenience sample. Ajzen's theoretical framework was used as a basis for the questionnaire and as a guide for the qualitative analysis of the data.

Results: The respondents found that the application of an algorithm for pain relief increased autonomy and efficacy, ensured a better follow-up and was easy to use. However, it was found to be time consuming and not adapted to all patients, was a rigid framework and did not take into consideration the subjectivity of pain. The main barriers were lack of time, fear of side effects, inaccessibility of the algorithm, the morphine or the pain scale. Also, patients' fear of the drug and refusal of the analgesia offered, physicians' fear of side effects and unwillingness to adhere to the algorithm, the inability of patient to use or understand the pain scale and the chart not adapted were mentioned as barriers.

Conclusion: Although the application of an algorithm seems to be successful in pain relief, this study has identified numerous objectives of intervention to be considered before the official implementation of an algorithm as a protocol for pain relief in ICU. Specific points have been identified to facilitate its integration and reduce workload for nurses already burdened with many aspects of patient care. Information concerning pain is the first steep towards its relief but a more integrated psychosocial approach such as increasing the feeling of self-efficacy of the nursing and medical team needs to be considered in order to improve the quality of care and cut down on health expenses.

P73 Preoperative assessment of carbohydrate-deficient transferrin (CDT) in surgical patients and a prevention of abstinence syndrome

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Complications are much more frequent in chronic alcoholics than in the remaining population after an elective operation or in some other case, like trauma or acute abdomen. In the postoperative period, alcoholics, suffering frequently from a liver disease, malnutrition etc., are threatened with infection, vegetative and metabolic dysregulation, heard ischemia, liver dysfunction and also with a rise of acute abstinence syndrome.

Treatment of the syndrome is mostly based on sedation of the patient to suppress anxiety, agitation or aggressiveness and also to control vegetative manifestations. The drugs, which are mostly used, are able to sedate the patient, on the other hand they make the postoperative care difficult and increase the complication rate. Therefore, improvement of the results demands first of all to identify all risky patients (including secret alcoholics) and to find a suitable medication to suppress the abstinence with minimal sedation of the patient.

It has been known since 1976 that pathological carbohydrate-deficient fraction of transferrin (CDT) occurs in blood plasma of people who are used to consuming more than 60 g of alcohol daily during 14 days, and disappears again after abstinence. The authors have used detection of CDT according to Boehringer–Mann in their hospital since 1998. The results are very precise and reliable.

The test was performed in 228 surgical patients till 30 April 2001, it was positive in 146 patients. In prevention of the abstinence syndrome, the authors obtained the best results by administering clonidine. It reduces the sympathetic reaction to abstinence and surgery. The drug was used in 42 patients with proven preoperative elevation of CDT in dosage 2 × 0.150 mg i.v. Neither abstinence syndrome nor side effects were observed.

The authors suppose the described management, i.e. detection of chronic alcoholics and prevention of the abstinence syndrome in them, to be the most reliable and very effective method.

P74 Accidental withdrawal of catheters in 400 patients in ICU

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Objective: To determine the accidental withdrawal of catheters for an assistance quality control.

Methods: It is a prospective study in a 20-bed medical surgical ICU. Included were all patients admitted from 1 May 2000 to 31 December 2000.

Results: Included were 400 patients (233 males). Mean age was 56.80 ± 17.27 years, APACHE-II was 13.23 ± 5.25. Mortality was 16.50%. Patients distribution was: 185 cardiac surgery, 35 cardiologic, 23 pulmonary, 16 digestive, 51 neurologic, 43 traumathology, 13 intoxication, 32 sepsis and two others. Patients percentage with catheter and the accidental withdrawals per 100 days of catheter were: 86% orotracheal tube (0.70), 98% central venous catheter (0.23), 29% central venous catheter by peripheral access (0.18), 67% jugular vein catheter (0.33), 35% subclavian vein catheter (0.17), 13% femoral vein catheter (0.17), 90% artery catheter (1.26), 82% radial artery catheter (1.35), 13% femoral artery catheter (1.10), 2% pedal artery catheter (0), 2% humeral artery catheter (0), 91% gastric catheter (6.4), 96% Foley catheter (0.02), 7% thoracic drainage tube (0), 7% abdominal drainage tube (0), 3% intracraneal pressure catheter (0.55).

Conclusions: According to the literature we have an acceptable rate of accidental withdrawal of catheters. This is an important aspect, not very studied, of an assistance quality control. More studies are necessary to establish the standards.

P75 Which is worse, a repeated short time ischemia or a continuous long time ischemia? An effect of intermittent reperfusion on tissue damage due to ischemia-reperfusion

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Objective: The aim of this study is to clarify the effect of repeating ischemia-reperfusion on the tissue damage or which is worse, continuous long time ischemia before reperfusion or repeated short time ischemia-reperfusion before definitive reperfusion.

Materials and methods: Small intestinal segments of Wister male rats were clamped with its mesenterial vessels. In group A, the clamped segment was released 60 min after the clamp; in group B, clamped segment was released 30 min after the clamp (for 10 min), re-clamped, and definitively released 60 min after the first clamp; and in group C, the procedure of clamp-intermittent release-definitive release was similar to that of group B and superoxide dismutase and catalase were given during the period of intermittent release. Tissue lipid peroxide (LPO) and the activity to produce oxygen free radicals of neutrophils in the draining vein from involved intestinal segment (chemiluminescence [CL]) were measured 10 min after definitive release.

Results: In group A, LPO and CL were increased from 19 to 43 nmol/g and from 30 to 43 counts per cell (cpc), respectively; in group B, those were increased to 118 nmol/g and 64 cpc, respectively, and in group C, 78 nmol/g and 31 cpc, respectively.

Conclusion: In some condition, tissue damage due to reperfusion injury derived from oxygen free radicals is more severe in repeat of short time ischemia with intermittent release than in long continuous ischemia.

P76 Ischemic preconditioning reduces intestinal apoptosis in rodents

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Recent experimental studies have described the protective effect of ischemic preconditioning (IPC) on ischemia-reperfusion (I/R) injury of the intestine [1,2]. In order to reach a new point of view in the effect of IPC on the intestinal barrier function, the relationship between I/R-induced mucosal injury and apoptosis must be clarified. The present study was undertaken to investigate the relation between IPC and Bcl-2 expression immunohistochemically and apoptosis (by using conventional light microscopy, immunohistochemical staining for cytokeratin 18 [M30 cytodeath Ab], DNA agarose gel electrophoresis) in the intestine. Furthermore, we also investigated the effect of intestinal IPC on serum nitrite/nitrate levels.

With approval of the Ethical Committee, 33 male Wistar rats weighing 250–300 g were randomized into three groups. A control group of rats ($n = 11$) was subjected laparotomy. In an ischemic group ($n = 11$), laparotomy was performed and the superior mesenteric artery (SMA) was occluded by an atraumatic clamp for 30 min. In the preconditioned group ($n = 11$), before the ischemia-reperfusion period, rats were subjected to initial 10 min of intestinal

ischemia and 10 min of reperfusion. Twenty-four hours later, ileum and blood samples were collected. Nitrite/nitrate levels were measured in the blood samples. Serum nitrate level was found to be increased in the I/R group (16.2 ± 0.9 vs 34.3 ± 4.1) but not in the IPC group (11.3 ± 5.9) ($P < 0.05$). The numbers of apoptotic cells at 24 hours after I/R were significantly lower in IPC-treated rats. Diminished Bcl-2 expression observed on the ileal specimens of the I/R group was found to be prevented by IPC.

Our results indicate that IPC provides a significant protective effect on ileum against I/R injury and that its effect is evidenced by a significant increase in the expression of Bcl-2 following the insult. This study shows that intestinal IPC may block the cascade of events that cause apoptosis that can lead to multiorgan failure. In the future, the use of agents causing Bcl-2 upregulation against the spontaneous I/R attacks as a preservative measure in criticial patients could be seriously considered.

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P77 Sepsis: pro-apoptotic and anti-apoptotic signals in liver cells

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Objective: Our aim was to investigate the role of the expression of pro-apoptotic genes: Bax, Cytochrome-C, Caspase-8 and anti-apoptotic gene bcl-2 in liver cells of septic rats.

Materials and methods: Sepsis was induced using the cecal ligation and puncture model in 62 adult Wistar rats. The rats were sacrificed at 6, 12, 24, 36, 48 and 60 hours after the induction of sepsis. A control group of 20 rats was used. Liver tissue was obtained from each rat and the expression of Bax, Cytochrome-C, Caspase-8 and Bcl-2 proteins was detected using the immunohistochemical streptavidin–biotin method.

Results: The expression of both Bcl-2 and Bax proteins was found decreased in liver cells of septic rats (50% and 50.8%, respectively) compared to the controls (80%, $P = 0.02$ and 85%, $P = 0.008$, respectively), while cytochrome-c ($P = 0.9$) and caspase-8 ($P = 0.05$) expression did not differ significantly between septic and control rats. In addition, the expression of all the pro-apoptotic genes: Bax, caspase-8 and cytochrome-c was maximum in liver cells of septic rats in the hyperdynamic phase of sepsis (first 12 hours) and gradually decreased in the hypodynamic phase ($P < 0.05$).

Conclusion: We demonstrate that the expression of regulating of apoptosis genes: bcl-2 and bax, is inhibited in liver cells sepsis and that the expression of executors of programmed cell death in liver cells: caspase-8 and cytochrome-c genes is time dependent in sepsis, with maximum values in the hyperdynamic phase.

P78 Determination of fever in intensive care unit

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Background and goals: Fever is a common problem in intensive care unit (ICU) [1]. Fever is a cardinal feature of both infective and non-infective inflammatory process [2].

Material and methods: We studied 50 patients between July and October 2000 in the ICU. Core temperatures were determined with the use of a rectal thermometer probe. Determination of the APACHE-II score was made of all patients. Blood cultures were obtained on all febrile patients. On each occasion at least two blood cultures from different sites were obtained. Fever was defined as a core temperature of ≥ 38.4°C.

Results: The mean APACHE-II score was (16 ± 0.6). The isolation of *Enterobacter aerogenes*, *Pseudomonas aeroginosa*, coagulase-negative staphylococcus, *pseudomanas* spp. and *Staphylococcus epidermitidis*.

Conclusions: Fever is common and that caused by infective and non-infective processes in approximately equal number. For this reason, in treatment, the empirical coverage of all fevers in the ICU with antibiotics is not necessary [3].

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Table

The patients' cause of admission

		Febrile		Non-febrile
		Blood culture		
Diagnoses	Number	(+)	(–)	
Organophosphate intox.	5	1	1	3
Multiple trauma	9	3	4	2
Myocardial infarction	3	–	2	1
Major abdominal surgery	7	4	2	1
Pneumonia	9	3	3	3
Renal insufficiency	2	–	–	2
Drug intoxications	7	–	3	4
Neurological events	6	2	1	3
HELLP syndrome	2	1	–	1
	50	14	16	20

P79 Leucocytosis in critically ill patients is not always a sign of infection!

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Background: We observed a post-transfusion (PT) leucocytosis in several ICU patients, without showing other signs of sepsis. To prevent unnecessary investigations prompted by leucocytosis, and to understand the phenomenon, a prospective study was conducted.

Methods: Forty-five non-septic patients receiving a non-filtrated packed cells (NFPC) had a complete blood count (CBC) pre, and 2, 4, 6, 12 and 24 hours PT. Eleven patients multiply transfused, were randomly given NFPC or prestorage filtrated packed cells (PFPC), and CBC taken as above. IL-8, a leucocytes-chemoattractant, was measured in NFPC and PFPC stored for 1, 2, 3 and 4 weeks and in 16 NFPC just pre transfusion.

Results: White blood cell count (WBC) ($\times 10^9$/l) significantly increased 2 hours PT (19.5 ± 7.0 vs 14.3 ± 4.8 at baseline) ($P < 0.05$), and returned to baseline in 24 hours. In patients requiring more than one PC, WBC significantly increased 2 hours PT of a NFPC compared to baseline (24.2 ± 7.8 vs 16.8 ± 4.7) ($P < 0.05$), while when the same patients received PFPC, there was no such increase (14.9 ± 5.2 vs 13.9 ± 5.4). There was no change in IL-8 levels in PFPC stored for 1, 2, 3 and 4 weeks (mean 54 pg/ml) while there was a significant increase in IL-8 levels in NFPC (61, 59, 161, and 745 pg/ml, respectively). IL-8 levels were significantly higher in NFPC given to patients developing leucocytosis compared to patients who did not develop leucocytosis (408.4 ± 202 vs 70.4 ± 54.1 pg/ml) ($P < 0.05$).

Conclusions: Transfusion of packed cells may cause an acute and transient leucocytosis in critically ill non-septic patients. Leucocytosis occurred after transfusion of NFPC but not after transfusion of PFPC. We suggest that IL-8 may contribute to this phenomenon.

P80 Transfer in ICU of febrile neutropenic patients: identification of risk factors and prospective validation of a prognostic score

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Objective: Optimal strategy of referral for neutropenic patients from hematology ward to intensive care unit is not yet well defined. Different severity-of-illness scores used in ICU have been recently tested in hematology wards and have failed to predict accurately patients at 'high risk', who could require a pre-emptive transfer in ICU. We performed a case–control study in post-chemotherapy neutropenic patients (for leukaemia or lymphoma), aimed at identifying early risk factors for ICU transfer.

Design: Monocentric, retrospective, case–control (equilibration on age, sex, and type of hemopathy) study comparing febrile neutropenic patients admitted or not in ICU.

Results and measurements: Eighty-two patients have been included (41 cases, 41 controls). Patients included were 51% men, were aged 43 ± 17 years. The majority were hospitalized for an acute myeloblastic leukaemia (56%), the others for acute lymphoblastic leukaemia (30%) or lymphoma (13%). Most of the patients had clinical manifestations of infection (62%) but only 31% a microbiologically demonstration of infection. 61.7% of the patients were not in remission at time of admission in ICU. Mortality in ICU was 65.8%. We compared data between neutropenic patients (referred or not referred in ICU) during their stay in hematology ward. We distinguished an early period (within 72 hours after the onset of febrile neutropenia) and a later period (72 hours before transfer in ICU or before discharge from hospital). Comparing data between these patients during the early period highlighted that urea, creatinin, protein C-reactive, and fibrinogen levels significantly increased whereas hematocrit, platelets and lymphocytes levels were significantly decreased, in patients referred in ICU. Using these 'early' independent risk factors, we define a prognostic score identifying patients who could benefit of an early transfer in ICU. A multicenter, prospective study is now being performed on a second cohort to validate accuracy, adequacy and reliability of this score.

Conclusion: Nowadays, no prognostic score focused on identification of 'high-risk' neutropenic patients has been yet validated. This study allowed the identification of early risk factors independently associated with transfer in ICU. The clinical use in haematology wards of such a prognostic score should allow earlier pre-emptive transfers in ICU, resulting in better management and possibly a better outcome for these patients.

P81 Septic shock etiology in kidney transplant recipients

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Introduction: Septic shock carries a high mortality in kidney transplant recipients. Therefore, early institution of empiric antimicrobial therapy is critical in the management of these patients. There are few data about septic shock etiology in kidney transplant recipients.

Objectives: The aim of this study is to determine the most common septic shock etiologic agents in kidney transplant recipients.

Setting: A kidney transplant specialized ICU in a 90-bed public hospital.

Methods: We prospectively followed (from May 2000 to December 2001) kidney transplant recipients admitted to ICU with diagnosis of septic shock according to SCCM/ACCP criteria. ICU resource utilization, microbiological identification and 28-day mortality were recorded. Apache II score for each patient was calculated within 24 hours of admission.

Results: We studied 14 (10 M/4 F) consecutive patients admitted to ICU with septic shock diagnosis. The mean age was 43 ± 9.5 years and mean Apache II was 23.7 ± 7.3. All patients were receiv-

ing immunosuppression therapy at ICU admission and 11 (78,5%) were in the first year of transplantation. The sources of infection were: lungs ($n = 6$), intra-abdominal ($n = 4$), endocarditis ($n = 2$), central venous catheter ($n = 1$) and central nervous system ($n = 1$). The most common isolated microorganisms were: *Candida* ($n = 5$), cytomegalovirus ($n = 4$), *Staphylococcus aureus* ($n = 3$), *Acinetobacter baumanii* ($n = 2$), *Escherichia coli* ($n = 2$), *Pneumocystis carinii* ($n = 2$), Klebsiella ($n = 1$) and *Mycobacterium tuberculosis* ($n = 1$). In only three (21%) patients just one agent was isolated and in another three (21%) patients we were not able to identify the etiologic agent. The mean length of ICU stay was 15 ± 15.7 days and of mechanical ventilation was 12.5 ± 16 days. In 10 (71%) of these patients a pulmonary artery catheter was inserted and there was need for renal replacement therapy in 13 (93%) patients. The 28-day mortality was 71% and overall ICU mortality was 78.5%.

Conclusions: Although kidney transplant recipients are susceptible to opportunistic infections due to immunosuppressive therapy, bacteria remain a frequent septic shock etiologic agent in these patients.

P82 Colistin in the treatment of infections from multiresistant Gram (–) bacilli

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Objective: To present our experience with i.v. colistin in the treatment of infections with multiresistant Gram (–) bacilli.

Materials and methods: Fourteen patients aged 20–81 years old, with severe infection from multiresistant Gram (–) bacilli, sensitive only to colistin. Of the patients, 11 were critically ill and mechanically ventilated, with an APACHE II score 8–22, and the other three were non-intubated patients with acute respiratory failure, treated in the ward. All patients received intravenous colistin (150,000 U/kg i.v., adjusted for creatinine clearance). A second antibiotic (in 11 cases high-dose b-lactam in continuous intravenous infusion) was added in the regimen. In total 16 courses of i.v. colistin were given, for the following infections: ventilator-associated pneumonia (VAP) (nine cases), nosocomial pneumonia in non-intubated patients (three), sepsis of unknown primary origin (one), urosepsis (one), catheter-related sepsis (two). In all cases, in spite of documented resistance, was included in the therapeutic regimen. The bacteria responsible were *P. Aeruginosa* (14 cases) or *Acinetobacter baumanii* (two cases). All patients had serum creatinine < 2.5 g/dl and none was oliguric.

Results: Clinical response was observed in 12 cases. Thirty day survival was 71.4%. As regards VAP, six of nine cases had a good response. A slight deterioration in renal function was observed in three cases.

Conclusion: The small number of patients and the absence of a control group does not allow any definite conclusions on the clinical effectiveness of colistin. On the other hand we did not notice the daunting complications attributed to colistin in studies from the 1960s. Therefore, pending a definite controlled trial, intravenous colistin use should be considered in severe infections with multiresistant Gram (–) bacilli, when it remains the only sensitive *in vitro* antibiotic.

P83 Clinical outcome in ICU patients with *Enterobacter* bacteremia

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Purpose and methods: To investigate the clinical impact of *Enterobacter* bacteremia in ICU patients, a retrospective (January 1992–December 2000), matched cohort study was performed. All ICU patients with *Enterobacter* bacteremia were defined as cases ($n = 67$). Matching of the controls (1:2-ratio) ($n = 134$) was based on the APACHE II system: an equal APACHE II score (± 1 point) and admission diagnosis.

Results: There was a high rate of appropriate antibiotic therapy in patients with *Enterobacter* bacteremia (96%). The mean delay in the start of antibiotic therapy was short (0.5 ± 0.9 days). Following the matching procedure cases and controls had nearly equal APACHE II scores (23 ± 8.3 vs 23 ± 8.3; $P = 0.890$) and related expected mortality rates (41 ± 24.1% vs 40 ± 24.1%; $P = 0.805$). Patients with *Enterobacter* bacteremia had more hemodynamic instability (78% vs 60%; $P = 0.015$). They also had a longer ICU stay (36 ± 32.1 vs 15 ± 18.7 days; $P < 0.001$) and a longer ventilator dependence (32 ± 26.8 vs 12 ± 17.0 days; $P < 0.001$). There was no difference between cases and controls in age (52 ± 19.8 vs 53 ± 19.3 years; $P = 0.831$), acute respiratory failure (93% vs 84%; $P = 0.079$) and acute renal failure (16.4% vs 15.8%; $P = 0.892$). Hospital mortality was not different between cases and control patients (34.3% vs 38.8%; $P = 0.536$). A multivariate survival analysis showed the APACHE II related expected mortality as the only independent predictor of mortality (HR, 3.7; 95% CI, 2.0–6.7; $P < 0.001$).

Conclusion: After accurate adjustment for severity of underlying disease and acute illness, no difference in mortality was found between ICU patients with *Enterobacter* bacteremia (34.3%) and their matched cohort subjects (38.8%). In the presence of accurate and prompt antibiotic therapy, bacteremia involving *Enterobacter* species does not adversely affect the outcome in ICU patients.

P84 Screening and isolation of methicillin-resistant *Staphylococcus aureus* (MRSA) colonized patients is widely practiced in UK critical care units but little benefit is perceived

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Colonization with MRSA has been shown to be associated with increased length of ICU stay and increased nursing workload in the critically ill patient [1]. Screening and isolation of colonized patients have been recommended [2], but this is becoming

increasingly difficult [3]. Furthermore this practice derives from recommendations of cohort isolation of general ward patients rather than individual isolation of the critically ill [2]. We therefore decided to assess practice in ICU and CCU by postal survey.

Postal surveys were sent to 193 units across England and Wales. Replies were received from 98 units (51%). A follow-up survey was then sent out and replies received from 57 (30%). National guidelines were used alone in 70% (70/98). MRSA colonization was flagged up in 73% (72/98). Colonization was perceived to be increasing in 37% (21/57) and decreasing in 11% (6/57). Routine screening of patients was performed in 54% (53/98). This was performed immediately in 51% (22/43); within 24 hours in 44% (19/43) and on designated days in 5% (2/43). A policy for screening of elective admissions existed in 49% (48/98), however this was felt to help rates of colonization in only 23% (9/38). Routine staff screening was performed in only 2% (2/98). Isolation of MRSA colonized patients occurred in 69% (68/98). This was thought to be effective or to eliminate cross infection in 42% (29/68) and not effective in 15% (14/68). Isolation was not used because it was not felt necessary in 37% (11/30) or because of a lack of resources in 60% (18/30). In units using isolation 19% (11/57) felt this decreased colonization. Increases in inter-hospital transfers were felt to be a cause of increased colonization in 44% (25/57).

National guidelines were widely used, however despite recommended routine screening in certain patients this only occurred in half the units sampled. Despite the frequent use of isolation only 42% of these felt it effective and only 19% had seen a reduction in colonization rates associated with the use of isolation. 37% of those not using isolation did not believe it of value, but 60% did not use isolation due to lack of resources. Overall these figures help suggest that there are considerable resource implications from isolating MRSA colonized patients, but whilst this is common practice its efficacy is not universally perceived and is only rarely associated with reduced colonization.

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P85 Patient-to-patient antibiotic rotation

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Objective: To evaluate ICU-acquired infections, germs responsible and sensibility to antibiotics in an ICU using a patient-to-patient antibiotic rotation. We have compared our dates with EPIC study.

Methods: It is a prospective study in a 20-bed medical-surgical intensive care unit. Included were all patients admitted in ICU during 19 months in two periods of time (first period from 1 January 1999 to 30 July 1999, second period from 1 May 2000 to 30 April 2001), with a length of stay in ICU longer than 24 hours. The infections were diagnosed according to CDC criteria.

Results: Studied were 978 patients (371 and 607 patients in respective periods of time), 601 males and 377 females. Mean age was 57.01 ± 17.80 years. APACHE-II was 13.76 ± 6.31. Mortality was 14.21%. Patients distribution was: 46% cardiac surgery, 11% cardiologic, 10% neurologic, 10% traumathology, 8% pulmonary, 5% digestive, 10% others. We diagnosed 315 UCI-acquired infections in 182 patients. Distribution infections was: respiratory 39%, urinary tract infection 28%, central venous catheter 12%, primary bloodstream 12%, wound surgical 5%, nervous central system 4%. We isolated 322 germs: 47% Gram negative, 43% Gram positive, 10% fungi. We found the following differences between EPIC and our data: (a) rate infections for *Pseudomonas aeruginosa* 28–7.1%, for acinetobacter 9–0.3%, for fungi 17–9.9%; (b) rate resistance of pseudomonas to gentamicin 46–25%, to ureidopenicillin 37–14%, to ceftazidime 27–18%, to ciprofloxacin 26–5%, to imipenem 21–13%; (c) rate resistance of *Staphylococci aureus* to methicillin 60–17%; (d) rate resistance of coagulase-negative staphylococci to vancomycin 3–0%.

Conclusions: In our ICU, with a patient-to-patient antibiotic rotation, we had no serious problems of resistance to antibiotics.

P86 Appropriateness of antibiotic prescribing after transition from an open to a closed intensive care unit

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The main aim of the study was to investigate whether transition from an open to a closed intensive care unit would improve outcome in critically ill patients through more appropriate antibiotic prescribing.

A retrospective chart survey was performed of all sputum and blood cultures taken after more than 48 hours of ICU stay over a 3-month period before (period 1) and a 3-month period after (period 2) transition from an open to a closed intensive care unit. Populations in both periods were compared for age, sex, APACHE scores and the following outcome variables: ICU mortality, average length of stay, percentage appropriate and inappropriate changes in antibiotic therapy, percentage appropriate and inappropriate non-changes in antibiotic therapy, average reporting delays of culture results. Antibiotic therapy was deemed appropriate when the patients showed signs of sepsis, severe sepsis or septic shock according to the ACCP/ACCM criteria and were prescribed antibiotics to which the cultured organisms were fully sensitive. Differences between means of continuous variables were tested by the Student *t*-test and between percentages by the method as described by Armitage [1]. A *P* value of less than 0.05 was considered statistically significant.

There was a trend towards an increased percentage of inappropriate decisions in period 2 vs period 1 (13% vs 9%) although this did not reach statistical significance (see Table).There were no differences in APACHE scores, length of stay or mortality between period 1 and 2.

Statistically significant increased reporting delays prior to inappropriate decisions not to change antibiotic therapy compared to reporting delays prior to appropriate decisions to change antibiotic therapy were found in period 1 but not in period 2 (see Table). Transition from an open to a closed intensive care unit did not lead to better antibiotic prescribing or outcome in ICU patients. Whereas in the open ICU period inappropriate antibiotic therapy was due to a combination of delays in reporting of culture results as well as inappropriate decisions, in the closed period this was solely due to inappropriate decisions not to change antibiotics.

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Table

	Period 1 ($n = 81$)	Period 2 ($n = 37$)	*P* value
% Appropriate decisions	90.10%	87.00%	ns
% Inappropriate decisions not to change antibiotic therapy	9.90%	13.00%	ns
% Antibiotics changed appropriately	30.90%	29.60%	ns
% Appropriate non-change	59.20%	57.40%	ns
Reporting delay prior to appropriate antibiotic change	2.1 days	2.3 days	ns
Reporting delay prior to appropriate non-change of antibiotics	3.66 days	3.9 days	ns
Reporting delay prior to inappropriate non-change of antibiotics	3.63 days	3.2 days	ns

ns, non-significant result.

P87 Audit of therapeutic drug monitoring of dosing of vancomycin on an intensive care unit

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Introduction: Vancomycin is used to treat infections in critically ill patients. Although serum levels are often measured, the relationship between high plasma levels and renal and ototoxicity is not proven [1]. Doses of 1 g achieve peaks of around 25–40 μg/ml and toxicity is unlikely in this range. Troughs of between 5–10 μg/ml are thought to be necessary to ensure efficacy [2]. Due to age and renal function, patients on the general ICU at St George's are routinely prescribed 1 g once a day at 6.00 pm and levels are taken the next morning which permits reporting before the next dose is due. The next dose will only be administered if the level is less than 10 μg/ml. There is no data supporting this practice.

Method: Data was collected over a 6 month period for patients who received once a day dosing of vancomycin for at least 3 days. A pharmacokinetic computer program used the measured plasma vancomycin level at 12 hours post dose to predict the level at 24 hours post dose. Renal function and whether a further dose was administered at 24 hours were recorded.

Results: Twenty-one patients (13 male: 8 female with an average age of 65 years) were audited. Ten patients had some degree of renal impairment (Cr > 110 mmol/l). One hundred and seventy-one doses were audited and results are shown in Table 1.

All levels predicted within 5–10 μg/ml at 24 hours were above 10 μg/ml at 12 hours, resulting in only one of the 23 doses being given. All levels within 5–10 μg/ml at 12 hours were sub-therapeutic at 24 hours.

Conclusion: When monitoring vancomycin levels at 12 hours the target concentration should be above 10 μg/ml to prevent sub-therapeutic plasma level occurring in the later part of the dosing period.

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Table 1

	Measured vancomycin plasma level at 12 hours post dose			Predicted vancomycin plasma level at 24 hours post dose		
Level	> 10 μg/ml	5–10 μg/ml	< 5 μg/ml	> 10 μg/ml	5–10 μg/ml	< 5 μg/ml
Number of samples	63 (37%)	82 (48%)	26 (15%)	12 (7%)	23 (13%)	136 (80%)

P88 Efficacy and safety of sequential IV/PO moxifloxacin for the treatment of severe community-acquired pneumonia

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Background: The oral form of moxifloxacin (MXF) has been used in 9 million patients and has been demonstrated to be an effective and well tolerated treatment for respiratory tract infections in extensive clinical trials. An IV formulation of MXF has been developed and recently was approved in the US for the treatment of community-acquired pneumonia, acute bacterial sinusitis, acute bacterial exacerbations of chronic bronchitis, and uncomplicated skin and skin structure infections. The efficacy and safety of IV/PO MXF compared with IV/PO comparator (CMP) in CAP was examined in two randomized, controlled studies; a pooled analysis of the patients with severe CAP is reported here.

Methods: In both studies, MXF-treated patients received 7–14 days IV/PO MXF 400 mg QD. In study 1, CMP-treated patients received IV/PO alatrofloxacin/trovafloxacin 200 mg QD or IV/PO levofloxacin 500 mg QD; in study 2, CMP-treated patients received IV/PO amoxicillin clavulanate 1200/625 mg TID ± IV/PO clarithromycin 500 mg BID. Severe CAP was defined as the presence of at least one of the following conditions: respiratory rate >30 breaths/min; P_aO_2/FIO_2 ratio <250 mmHg or $PO_2 \leq 8$ kPa (60 mmHg); requirement for mechanical ventilation; chest radiograph indicating bilateral or multilobe involvement; increase in the size of opacity by $\geq 50\%$ within 48 hours of admission; or shock (systolic blood pressure <90 mmHg or diastolic pressure <60 mmHg).

Results: One hundred and ninety MXF-treated and 186 CMP-treated patients comprised the clinically valid population. Treatment groups were similar with respect to demographic and baseline medical characteristics. Bilateral or multilobar involvement was present in 44% of MXF-treated and 54% of CMP-treated patients, and was the most common reason for categorizing CAP as severe. Clinical resolution was achieved in 88% (167/190) of MXF-treated and 83% (155/186) of CMP-treated patients (95% CI = −1.9%, 12.2%). A switch from IV to PO therapy was made by day 5 of therapy for 73% (139/190) of MXF-treated vs 60% (112/186) of CMP-treated patients ($P<0.01$). Similar durations of therapy and time of IV to PO switch were observed for the ITT and microbiologically valid populations. Serious drug-related adverse events occurred in 7% (16/241) of MXF-treated and 6% (14/238) of CMP-treated patients.

Conclusions: Sequential IV/PO MXF is as effective as the standard IV/PO fluoroquinolone or IV/PO beta-lactam/beta-lactamase inhibitor ± macrolide regimens for the treatment of severe CAP. IV/PO MXF is an excellent choice for empiric therapy of severe CAP.

P89 Adult varicella pneumonia requiring intensive care

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Introduction: Varicella pneumonia is the most common severe complication of chickenpox in adults.

Method: In this retrospective case series, we reviewed the clinical presentation and outcomes of all adult varicella pneumonia patients who were admitted to the Medical Intensive Care Unit of a university-affiliated general hospital from 1997 to 2000.

Results: The 10 patients had a mean ± SD age of 44 ± 20 (range: 26–86) years; two patients were above 65 years old (ages 73 and 86). All but one were male. None had previous varicella vaccination. Five patients had direct exposure to persons with chickenpox infection. Four patients had underlying pulmonary pathology: past pulmonary tuberculosis (two), emphysema (one) and recurrent right pleural effusion from autoimmune serositis (one). Two patients had a background history of immunocompromised states (systemic lupus erythematosus and acute myeloid leukaemia). There were four cigarette smokers, two ex-smokers, two non-smokers and two did not have their smoking history documented. The mean respiratory rate was 30 ± 8 breaths per minute (range: 18–42). The mean Acute Physiology and Chronic Health Evaluation II score was 15.7 ± 6.2 (range: 7 to 26). Two patients had acute respiratory distress syndrome and five had acute lung injury. The mean ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen was 261 ± 60 (range: 171–351). The median duration of stay in the ICU was 15 days (range: less than 1 day to 76 days). Eight patients (80%) required mechanical ventilation. The median duration of mechanical ventilation was 16.5 days (range: less than 1 day to 79 days). All patients were started on acyclovir and empirically treated with cloxacillin and ceftriaxone. There were three deaths (30%); two were above 65 years old and the third had acute myeloid leukaemia on chemotherapy. Two patients had acute renal failure and both died.

Conclusion: Varicella pneumonia carries a high mortality. Old age, an immunocompromised state and acute renal failure appear to be associated with increased mortality in our series.

P90 Respiratory Herpes simplex virus at the intensive care unit: a prospective study

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Background: Herpes simplex virus (HSV) can cause a variety of diseases including respiratory infections. A retrospective study performed at our hospital did not clarify the clinical and prognostic significance of HSV in the respiratory tract of critical care patients.

Objectives: A prospective study was conducted between November 1999 and July 2001 in order to evaluate the incidence and significance of respiratory HSV in ICU patients, to identify risk factors for the development of lower respiratory tract (LRT) infections with HSV and to study the origin of the virus.

Methods: Seven hundred and sixty-four patients admitted to our 30 bed ICU in a tertiary care hospital were examined for the presence of HSV in the upper (URT) and lower respiratory tract (LRT).

Results: One hundred and sixty-nine patients (22%) had HSV in the URT. The reactivation of the virus occurred within 10 days for 89% of all positive patients and followed a period of more severe disease as was indicated by SOFA max. In 58 (16.2%) of the 361 patients who had their LRT sampled, the virus was isolated from bronchusaspirate (BA) of broncho-alveolar lavage fluid (BAL). HSV in the throat was a highly significant risk factor (RR 11.6; 95% CI 5.51–23.84) for the development of LRT infections with the virus. Patients with more debilitating disease on admission and during ICU stay were more susceptible for HSV reactivation as was shown by APACHE II and SOFA scores. There was a significant association between HSV reactivation and ARDS (RR 2.94; 95% CI 1.6–5.41). The association between intubation and HSV reactivation was probably due to disease severity although patients with a long intubation (> 7 days) had a RR of 2.77 (95% CI 1.79–4.30) for reactivation of HSV, even when controlled for SOFA max. Patients with HSV reactivation had a longer ICU as compared to those without the virus.

Conclusion: HSV reactivation in ICU patients is more frequent than previously assumed. Reactivation of the virus in the throat is a major risk factor for the development of LRTI with the virus. Patients with HSV reactivation have a longer ICU stay as compared to controls. Further study on the effect of pre-emptive aciclovir therapy in these patients needs to be performed.

P91 The clinical stages and prognostic factors of children with enterovirus type 71 infection developing pulmonary edema and hemorrhage

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Pulmonary edema/hemorrhage was the most severe complications of EV 71 associated hand–foot–mouth disease and usually led to cardiopulmonary failure. The mortality rate was 92% in the 1998 outbreak (11/12). During 2000 and 2001 outbreaks, the mortality rate had been reduced to 33% (8/24). This report was an observation of the clinical stages, risk factors and outcomes. There were 24 children brought to our PICU from May 2000 to June 2001. There were 10 females and 14 males. The age ranged from 5 to 93 months old (mean = 19.8).

The EV 71 infections were confirmed by either positive virus isolation (71%, 17/24) or elevated serum neutralization antibody (> 1:8, 96%, 23/24). We found most of the patients (58%, 14/24) presented five clinical stages: (1) hand–foot–mouth disease; (2) meningoencephalitis; (3) cardiopulmonary failure; and (4) convalescence stage. The third stage was divided into two substages, (3A) hypertension stage and (3B) hypotension stage.

The risk factors associated with mortality/morbidity were age, CSF leukocytosis, increased troponin I, episodes of cardiac arrest, decreased ejection fraction, need of high dosage inotropes support, lack of hypertension stage which might mean delayed hospital visit, initial very high serum glucose and very low worst PaO_2–FiO_2 ratio. Fifty percent of survivors (8/16) had moderate to severe neurological sequelae and needed long-term respiratory care.

P92 Surveillance urine cultures in the ICU: prospective markers for the phenotypic and genotypic drift of emerging yeast pathogens?

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Surveillance for yeast infections in the ICU is essential to define their burden and trends, to provide the infrastructure needed for epidemiological studies, to evaluate therapeutic interventions and to detect new pathogens. The present 12-month prospective observational study was conducted on a defined ICU population including 56 (24%) patients among 240 (100%) ICU admissions with distinct predisposing factors [1], mean age 52 ± 6 years, mean length of ICU stay 9 ± 6 days, APACHE II score 14 ± 5 and SOFA score 5 ± 2. Urine samples were tested by microscopy and culture on selective media. Each isolate was identified to species level, tested for phenotypic characteristics, such as susceptibility to current and novel antifungal agents and studied for genotypic similarities through identifying DNA subtypes with PCR followed by restriction fragment length polymorphism analysis (RFLP) [2] and with minisatellite length polymorphism analysis (MLP), to distinguish epidemic isolates.

Among the patient population, only 18/56 had negative urine cultures, whereas candiduria (> 1000 CFU/ml) was detected in 38/56 patients and two different yeast species were isolated from 7/38 patients. *Candida albicans* was the main aetiology for candiuria (27%), followed by *C. parapsilosis* (20%), *C. tropicalis* and *C. famata* (11.3%) respectively. Emerging yeast pathogens, such as *C. lusitaniae*, *C. dubliniensis*, *Trichosporon asahii* and *T. mucoides* were isolated from 18/38 patients, while *C. krusei* was isolated from only 2/38 patients. All isolates were susceptible to amphotericin B, except *T. asahii*, for which the lowest minimum inhibitory concentrations (MICs) were recorded for itraconazole (Janssen) and voriconazole (Pfizer). Resistance to fluconazole (Pfizer) was only detected in *C. krusei,* in two *C. famata* isolates and in a subpopulation of one *C. lusitaniae* strain, which however were susceptible to both itraconazole and voriconazole. Identical DNA subtypes were identified among *C. albicans*,

C. parapsilosis, *C. famata*, *C. dubliniensis* and *Trichosporon* species, whereas intense genetic heterogeneity was recorded among *C. lusitaniae* isolates.

Additional fixed-time surveillance studies in the ICU, using specific markers linked with phenotypic and genotypic analyses, may be employed to recognize outbreaks, to formulate emerging pathogen case definition and exclusion criteria leading to prevention of further cases, and to evaluate azole-based pre-emptive or targeted treatment when such criteria are fulfilled.

References:
1. Karabinis A, Hill C, Leclerq B, Tancrede C, Baume D, Andremont A: **Risk factors for candidaemia. A case control study.** *Am J Med* 1988, **87**:614-620.
2. Velegraki A, Kambouris M, Skiniotis G, Savala M, Mitroussia-Ziouva A, Legakis NJ: **Identification of medically significant fungal genera by polymerase chain reaction followed by restriction enzyme analysis.** *FEMS Immun Med Microbiol* 1999, **23**:303-312.

P93 5000 days of central venous catheterization: complications

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Objective: To analyze complications of central venous catheterization in Critical Care.

Methods: It is a prospective study in a 20-bed medical surgical ICU. Included were all patients admitted from 1 May 2000 to 31 December 2000.

Results: Included were 400 patients (233 males). Mean age was 56.80 ± 17.27 years, APACHE-II was 13.23 ± 5.25. Mortality was 16.50%. Patients distribution was: 185 cardiac surgery, 35 cardiologic, 23 pulmonary, 16 digestive, 51 neurologic, 43 traumathology, 13 intoxication, 32 sepsis and two others. The number of catheter and length stay of catheter (days) were: global 706 and 4980, peripheral access 145 and 949, jugular 306 and 1806, subclavian 190 and 1694, femoral 65 and 531. Central venous catheter related infections per 100 catheter and per 1000 days of catheterization were: general 3.40 and 4.81, peripheral access 1.64 and 2.52, jugular 3.6 and 6.20, subclavia 1.68 and 1.88, femoral 11.11 and 13.55. Bloodstream infections secondary to central venous catheter per 1000 days of catheterization were: general 1.44, peripheral site 0.84, jugular 0.88, subclavian 1.41, femoral 4.51. Pneumothorax secondary to central venous catheterization: general 1.29% (8/619), subclavian 1.68% (4/237), jugular 1.04% (4/382). The groups of microorganisms found were: 62.4% Gram positives, 25.2% Gram negatives and 12.4% fungi. The microorganisms isolated were: staphylococcus coagulase negative 58.33%, bacillus 4.16%, *Escherichia coli* 8.33%, serratia 4.16%, *Pseudomonas aeruginosa* 4.16%, *Morganella morganii* 4.16%, *Candida albicans* 8.33%, *Candida tropicalis* 4.16%, enterobacter 4.16%.

Conclusions: We have a low rate of central venous catheter complications. Femoral venous catheterization is the site with more catheter related infections.

P94 Central venous catheter-related infection

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Introduction: Central venous catheters (CVCs) account for an estimated 90% of all catheter-related bloodstream infections (CRBSI). The duration of use of CVCs remains controversial and the length of time such devices can safely be left in place has not been fully and objectively addressed in the critically ill ICU patient. As a consequence, scheduled replacement remains widely practiced in many ICUs. Over the past few years, antimicrobial impregnated catheters have been introduced in an attempt to limit catheter-related infection (CRI) and increase the time that CVCs can safely be left in place. A recent meta-analysis concluded that chlorhexidine-silver sulfadiazine (CSS) CVCs appear to be effective in reducing CRI [1].

Materials and methods: This was a prospective randomized double-blind study performed in the adult multidisciplinary ICU at Johannesburg Hospital between 1996 and 1999. The study entailed comparison of a 14-day placement of standard triple-lumen versus antimicrobial impregnated (CSS) CVCs on the rate of CRI. Our aim was to determine whether we could safely increase the duration of catheter insertion time from our standard practice of 7 days to 14 days, to assess the influence of the antimicrobial impregnated catheter on the incidence of CRI, and to elucidate the epidemiology of CRI. One hundred and eighteen critically ill patients were included in the study.

Results: Sixty-two patients received a standard triple-lumen catheter and 56 patients a CSS impregnated triple-lumen catheter. The study spanned 34,951.5 catheter hours (3.99 catheter years). The mean duration of placement for the full sample of 118 CVCs was 12.3 days (range, 1–14). No statistically significant difference in CRI rates between the two types of catheters could be demonstrated. The most common source of primary CRBSI was skin, followed by hub and infusate. The site of CVC insertion (internal jugular vein versus subclavian vein) and the use of parenteral nutrition were not noted to be risk factors for catheter infection.

Conclusions: In this study, we were unable to demonstrate that the CSS catheter provides any significant benefit over standard catheters, which we feel can safely be left in place for up to 12 days and probably 14 days. The most common source of CRI was the skin. The administration of parenteral nutrition and the site of catheter insertion were not noted to be risk factors for CRI.

Reference:
1. Veenstra DL, *et al.*: *JAMA* 1999, **281**:261-267.

P95 Multi-lumen central venous catheters increase the risk of bloodstream infection: evidence from a systematic review

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Background and aim: Infections due to central venous catheters (CVC) contribute to hospital morbidity [1]. There is a controversy as to whether there is a particularly high risk of infection with multiple lumen CVCs. The aim of this systematic review of randomised trials was to test the evidence that multi-lumen CVCs, compared with single-lumen catheters, increase the risk of bloodstream infection, catheter colonisation, and insertion site infection.

Materials and methods: Systematic search (Medline, Embase, Cochrane Library, bibliographies, to 12.2001, any language) for published full reports of randomised comparisons of multi-lumen versus single-lumen CVCs in adults, reporting data on the incidence of infection according to published criteria [2]. Two authors independently screened all retrieved reports and extracted data. Methodological validity of the reports was assessed by all authors using the Oxford scale. Data were combined using a fixed effect model and reported as relative risk (RR) with 95% confidence interval (CI).

Results: Fourteen potentially relevant reports were retrieved; nine were subsequently excluded (not randomised, invalid endpoints). Settings were ICU or surgical ward. In five studies (530 CVCs), bloodstream infection was increased with multi-lumen CVCs compared with single-lumen CVCs (9.5% vs 3.5%, RR 2.62 [95% CI 1.25–5.49]). In four studies (353 CVCs), there was no difference in colonisation (13.1% with multi-lumen vs 14.7% with single-lumen, RR 0.93 [95% CI 0.56–1.55]). In two studies (125 CVCs), there was no difference in insertion site infection (53.1% with multi-lumen vs 39.3% with single-lumen, RR 1.35 [95% CI 0.91–2.01]).

Conclusions: There is evidence from randomised trials that on average one in 17 multi-lumen CVCs will lead to a bloodstream infection which would not have been the case had single-lumen CVCs been used. These data may have clinical implications.

References:
1. Pittet, *et al.*: *JAMA* 1994, **271**:1598-1601.
2. Maki, *et al.*: *N Engl J Med* 1977, **296**:1305-1309.

P96 Dialysis with perfusion lumen catheter in intensive care unit

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Objective: To evaluate dialysis with or without perfusion lumen catheter-related infections, and to compare with central venous catheter in an intensive care unit.

Methods: Catheters inserted and extracted at least 2 days after, in the intensive care unit, are cultured using the quantitative tip cultures technique described by Brun-Buisson. Colonization is defined by a quantitative tip culture yielding $\geq 10^3$ colony-forming units/ml, site infection by catheter colonization with presence of pus at the insertion site, catheter-related bacteremia by catheter colonization and blood culture positive for the same organism.

Findings: Between May 2000 and May 2001, 112 catheters were inserted in 59 patients: 40 central venous catheters, 21 double-lumen dialysis catheters, and 51 three-lumen dialysis catheters with perfusion lumen. The mean disease severity assessed by SAPS II at the ICU admission do not differ for the three groups (48 ± 22, 47 ± 20, and 54 ± 20.9). The mean duration of catheterization was 8.1 days for CVCs, 8.9 for HDCs without perfusion lumen, and 8.9 for HDCs with perfusion lumen (non significant). There was no difference between the two types of DCs and CVCs in catheter colonization and catheter-related bacteremia incidence rates, whatever the insertion site.

Six site infections and three bacteremia happened during the study. As for the local infections, two concern the CVCs (jugular site), four concern the HDCs with perfusion lumen (two jugular sites and two femoral sites). Bacteremia concern one HDC (femoral site) and two HDCs with perfusion lumen (femoral and jugular sites).

Interpretation: The frequency of DC-related infection on CVC-related infection were similar in the ICU patients. There is no increase of the infectious risk due to the use of catheters associating perfusion lumen and dialysis lumen in the ICU patient.

Table

	CVCs	Double-lumen HDCs	Three-lumen HDCs
Rate infections	2	1	6
Rate colonizations	10	10	12
Ratio infections/colonization	0.2	0.1	0.5
Total duration of catheterization	356	154	412
Infection incidence rates per 1000 days of catheter use	28/1000	64/1000	29/1000
Colonization incidence rates per 1000 days of catheter use	5.6/1000	6.49/1000	14.5/1000

P97 Catheter-related infections in a medical cardio-pulmonary ICU: trends after the implementation of a nosocomial infection surveillance system (KISS)

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Background: Central venous catheters are routinely used in critically ill patients and represent a source of nosocomial infections (NI). NI concern 5–15% of hospitalised patients and can lead to complications in 25–50% of those admitted to the ICU [1].

Methods: All patients with devices such as endotracheal tubes (ET), central venous lines (including pulmonary artery catheter) (CV) and/or urinary-tract catheters (UC) were prospectively enrolled during the first quarter of the years 1999 to 2001 according to a standardised protocol (KISS). Device-days, infections and infection rate were recorded. Data were analysed with regard to patients' severity of illness (SAPS II) and length of stay (LOS).

Results: Six hundred and twenty-seven patients with a mortality rate of 12.3% were enrolled in the study. The 31 patients (5%) who acquired a NI had significantly higher SAPS II score (42 ± 17 vs 31 ± 15, $P < 0.001$), hospital (33 ± 37 vs 13 ± 18, $P < 0.001$) and ICU LOS (18 ± 16 vs 4 ± 15, $P < 0.001$), proportion of ventilation (45% vs 12%, $P < 0.001$), and mortality (42% vs 11%, $P < 0.001$). NI occurred after 15 ± 11 days, median 14 days. Despite a significant decrease in device-days and ventilatory-days observed from 1999 to 2001, the absolute number of NI remained unchanged.

Conclusion: Patients at risk to acquire a NI in our ICU are obviously sicker. Whether increased LOS is due to the underlying disease or a result of the NI remains unclear. Implementation of a prospective surveillance protocol of NIs (KISS) led to a significant reduction in device-days and ventilatory-days, but did not reduce the absolute number of NIs. Thus, device-reduction appeared to be most effective in the less severely ill patients only.

Reference:
1. Bates DW, *et al.*: *Arch Intern Med* 1999, **159**:2553.

P98 Nosocomial infection: main cause in development of septic complications during postoperative period

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Objective: To study the frequency of emergence of nosocomial infection in ICU.

Design: Retrospective study of data from case records and flow sheets. One thousand four hundred and fifty-one postoperative patients admitted to ICU during 1999–2000.

Measurements and main results: Of 1451 patients in our ICU during 2 years, we include those 613 (42.2%) who stayed for more than 72 hours. According to results from cultures we divided them to three groups. Group 1 included 355 (57.9%) patients without bacterial growth. Group 2 included patients with proved nosocomial infections (NCI). We obtained samples: 898 from urinary catheters (376 positive – 41.9%), 552 from tracheal tube (457 positive – 82.8%), 597 from blood (282 positive – 47.2%), 64 intradermal segments from central venous lines (34 positive – 53.1%), and 17 from sputum (15 positive – 88.2%). The most common place for development of NCI in our ICU is respiratory tract. On 5th ICU day the tract became infected in almost 56% of the patients. The major role among pathogens played *Acinetobacter* spp. (27.4%), *Citrobacter* spp. (20.3%), *P. aeruginosa* (12% and *Serratia* spp. (10%). The second place for NCI development is reserved for blood-stream infections. Almost the half of the cultures (47.2%) showed bacterial growth. The isolated pathogens were the same: *Acinetobacter* spp. (19%), *Serratia* spp. (16%), but there was substantial rise in emergence of *S. epidermidis* during the last year. Its frequency almost equalized that of *Acinetobacter* spp. The other two main sources for NCI were urine and CV catheters. They remained on 3rd and 4th places. Group 3 included patients with endogenous surgical infections. In this group we obtained samples from surgical wounds and drainages. In 1999 25.6% of cultures showed bacterial growth. During next 2000 this figure rose nearly twice (48.3%). The leading role played the same *Acinetobacter* spp., *Citrobacter* spp., *P. aeruginosa*, *Enterococcus* spp. and *E. coli*. The role *of S. epidermidis* increased greatly during this period.

Conclusions: There was a rise in frequency of nosocomial and secondary endogenous surgical infection in 1999–2000. The frequency of Gram-positive pathogens, namely *S. epidermidis*, nearly equalized that of Gram-negative flora as a cause of nosocomial infection. Nosocomial infection remained the main cause of septic complications in postoperative ICU patients.

Reference:
1. E Gyurov, M Milanov, S Milanov: **Nosocomial infection: main cause in development of septic complications in surgical postoperative patients.** *Crit Care* 1999, **3(suppl 1)**:P54.

P99 Comparative analysis of patients with early-onset versus late-onset nosocomial lower respiratory tract infections in medical ICU

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Objective: To compare risk factors and pathogens between early-onset (occurring 48–96 hours after ICU admission) nosocomial lower respiratory tract infections (NLRTI) and late-onset (occurring after 96 hours of ICU admission) NLRTI.

Patients and methods: From March 1993 to September 1999, all patients admitted in our 30-bed medical ICU were included in this study, their characteristics were prospectively collected. CDC criteria were employed to define nosocomial pneumonia and tracheobronchitis.

Patients with early-onset NLRTI and those with late-onset NLRTI were compared to patients without NLRTI by univariate and multivariate analysis.

Results: Three thousand six hundred and eighty-one patients were hospitalized (age 58 ± 18 years, SAPS II 37 ± 17, length of ICU stay 12 ± 15 days, mechanical ventilation [MV] 85%, duration of MV 11 ± 13 days, ICU mortality 36%, secondary hospitalization 82%, antimicrobial therapy before ICU admission 49%).

Five hundred and seventeen (14%) patients developed at least one episode of NLRTI, late-onset NLRTI were more frequent than early-onset NLRTI (87% and 13% respectively).

Multidrug resistant bacteria were isolated in the major part of NLRTI (respectively for early-onset and late-onset NLRTI): *Pseudomonas aeruginosa* (21%, 24%), *Staphylococcus aureus* (16%, 12%) and *Acinetobacter baumannii* (12%, 30%).

Conclusion: The risk factors associated with either early-onset or late-onset NLRTI are similar to those identified by other studies. In our population, length of ICU stay before NLRTI occurrence does not seem to have an impact on the nature of causing organism; these data could be helpful to improve initial empiric antimicrobial therapy in our ICU.

Table

	Early-onset NLRTI/no NLRTI ($n = 68/3164$)			Late-onset NLRTI/no NLRTI ($n = 449/3164$)		
Multivariate analysis	OR	95% CI	*P*	OR	95% CI	P
Stress ulcer prevention	6.48	3.64–11.55	< 0.001	–	–	–
Digestive failure	3.26	1.33–7.98	0.009	–	–	–
Tracheotomy	2.69	1.22–5.91	0.014	–	–	–
Renal failure	2.17	1.14–4.13	0.018	–	–	–
Corticotherapy	1.81	1.06–3.09	0.028	1.64	1.20–2.25	0.002
Ranitidine	–	–	–	6.36	3.23–12.53	< 0.001
Omeprazole	–	–	–	3.77	1.34–10.58	0.012
Sucralfate	–	–	–	2.11	1.57–2.84	< 0.001
Number of antibiotics	–	–	–	1.45	1.23–1.69	< 0.001
Duration of MV	–	–	–	1.13	1.11–1.14	< 0.001

P100 Compartmentalized cytokine production during mechanical ventilation and ventilator-associated pneumonia

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Introduction: Ventilator associated pneumonia (VAP) is a common and serious complication of mechanical ventilation (MV). In pneumonia, host defense is considered to be dependent upon the expression of pro-inflammatory cytokines (e.g., tumor necrosis factor-α (TNF), and interleukin (IL)-6), anti-inflammatory cytokines (e.g., IL-10), and cytokines with chemotactic abilities (e.g., IL-8).

Aim and methods: We hypothesized that during VAP the inflammatory response is restricted to the side of infection, i.e., to the lung, and may raise before the diagnosis of VAP is clinically made. Non-directed bronchial lavage (NBL) was performed on alternate days in patients expected to require MV for longer than 5 days. Prior to the NBL, blood samples were drawn. The diagnosis of VAP was standardized using a Clinical Pulmonary Infection Score.

Results: VAP occurred in nine patients and the 19 patients who did not develop VAP were considered controls. There were no differences between patients with VAP and controls with respect to age, gender, initial APACHE II score, and primary diagnosis. Levels of TNF, IL-10, IL-6 and IL-8 did not change in control patients in either plasma or NBL-fluid. Furthermore, the diagnosis of VAP was not associated with changes in plasma cytokines. However, serial changes in TNF, IL-10, IL-6 and IL-8 in NBL-fluid strongly correlated with the diagnosis of VAP. A rise of TNF in NBL-fluid above 200 pg/ml predicted a 4.0 (95% CI: 1.1–15.1) times increased risk for developing VAP ($P = 0.04$, time-dependent Cox proportional hazard analysis). An increase of IL-10, IL-6 and IL-8 levels in NBL-fluid above 100 pg/ml, 1 ng/ml, and 15 ng/ml, respectively, was associated with a relative risk of 5.6 (95% CI: 1.5–20.9), 9.0 (95% CI: 1.1–72.1), and 4.6 (95% CI: 0.9–22.6), respectively, for developing VAP.

Conclusion: Local, but not systemic, cytokine levels increase before VAP is clinically diagnosed.

P101 Monocyte normal immune response to LPS stimulation

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Introduction: Monocyte stimulation with LPS has been used to evaluate adequacy of immune response in immunocompromised patients (monocyte deactivation) with severe sepsis. The aim of the study was to investigate the dose response curve of maximum monocyte TNF-α production after LPS stimulation.

Methods: Peripheral blood was obtained from 16 volunteers and the absolute number of monocytes per 100 μl was measured. The same quantity was stimulated by different doses (50, 100, 250, 500, 1000 pg) of LPS for 4 hours. TNF-α levels were measured at baseline and after stimulation and were converted per monocyte. Stimulation with 500 pg of LPS was found to best stimulate monocytes. Then, 100 μl of the same specimens were stimulated with 500 pg of LPS for 4, 8 and 24 hours.

Results: Baseline levels of TNF-a were undetectable. After different doses of LPS stimulation for 4 hours TNF-a levels were as follows:

(a) 50 pg/ml LPS: 995.8 ± 60.6 totally and 9.5 ± 1.6/monocyte,
(b) 100 pg/ml LPS: 1084.6 ± 62.2 totally and 10.8 ± 1.9/monocyte
(c) 250 pg/ml LPS: 1214.7 ± 73.1 totally and 13.9 ± 2.6/monocyte
(d) 500 pg/ml LPS: 1307.1 ± 68.4 totally and 16.6 ± 2.8/monocyte
(e) 1000 pg/ml LPS: 1214.2 ± 67.2 totally and 16.8 ± 2.1/monocyte

Timeframe for TNF-α production after stimulation with 500 pg of LPS is shown in Table 1

Conclusions: Maximum monocyte TNF-α production was observed after stimulation with 500 pg of LPS which was not statistically different compared to 1000 pg. Also, maximum response with 500 pg of LPS was observed after 24 hours of stimulation. These findings are in contrast with the literature which suggests stimulation using 100 pg of LPS for 4 hours for the evaluation of monocyte immune competency.

Table 1

	Baseline	4 hours	8 hours	24 hours	24 hours w/o LPS
Totally	ND	344.3 ± 39.1	414.6 ± 39.6	499.1 ± 60.3	37.6 ± 15.1
Per monocyte	ND	9.8 ± 1.2	11.8 ± 1.3	13.8 ± 1.4	1.9 ± 0.6

P102 Pro-inflammatory cytokines decrease the expression of tight junction proteins in Caco-2 intestinal epithelial cells through a process that is dependent on peroxynitrite formation and PARP activation

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Rationale: We sought to test the hypotheses that cytomix-induced hyperpermeability is mediated by changes in the expression of the tight junction proteins, ZO-1 and occludin, secondary to $ONOO^-$ formation and/or activation of the enzyme, poly (ADP-ribosyl) polymerase (PARP).

Methods: Caco-2 monolayers grown on permeable filters for 21 days in bicameral Transwell chambers were incubated with control medium, medium containing cytomix (CM), a cocktail containing the pro-inflammatory cytokines, IL-1β (1 μg/ml), TNF (10 ng/ml) and IFN-γ (1000 U/ml), or medium containing CM and one of these other pharmacologic agents: ethyl pyruvate (EP; H_2O_2 scavenger; 10 mM): PJ34 (PARP inhibitor; 5 μM): 3-aminobenzamide (3-AB; PARP inhibition; 3 μM): FeTPPS ($ONOO^-$ decomposition catalyst; 50 μM): C-PTIO ($NO^\bullet$ scavenger; 100 μM): PDTC (NF-κB inhibitor; 100 μM) or L-NIL (selective iNOS inhibitor; 20 μM). Permeability was expressed as the apical-to-basolateral clearance ($nL\ cm^{-1}\ h^{-1}$) of fluorescein-labelled dextran (FD4) during the last 48 hours of incubation. Expression of occludin and ZO-1 were assessed by Western blot and immunohistochemistry.

Results: Western blot showed that after 48 hours of incubation with cytomix the intensity of the bands were significantly decreased as compared with the control group. After incubation with the various pharmacological agents with cytomix the intensity of the bands have significantly increased. Immunohistochemistry showed that ZO-1 and occludin were localized to the cell boundaries in control Caco-2 monolayers. Staining was continuous and 48 hours after treatment with CM, ZO-1 and occludin immunostaining was more diffuse. Co-incubating cells with CM and agents that interrupted the NF-κB → iNOS → $NO^\bullet$ → $ONOO^-$ → PARP pathway prevented and these alterations in the immunostaining of ZO-1 and occludin.

Table

Condition	Permeability	Nitrate/nitrite
Control	5.23 ± 0.49	6.6 ± 1.09
CM	99.3 ±7.83*	30.8 ± 1.05*
PDTC + CM	34.1 ± 2.23†	18.3 ± 0.79†
C-PTIO + CM	13.3 ± 1.53†	11.2 ± 0.86†
L-NIL + CM	27.3 ± 2.33†	13.2 ± 0.69†
PJ34 + CM	20.9 ± 2.46†	21.0 ± 0.88†
FeTPPS+ CM	31.0 ± 1.91†	20.7 ± 0.32†
3-AB + CM	19.1 ± 1.73†	21.3 ± 0.90†
EP + CM	22.9 ± 1.64†	17.1 ± 0.82†

*$P < 0.05$ versus control; †$P < 0.05$ versus cytomix.

Conclusion: Taken together, our data support the view that CM increases the permeability of Caco-2 monolayers by activating NF-κB and initiating a chain of events that ultimately leads to PARP activation and decreased expression of the tight junction proteins, ZO-1 and occludin.

P103 The effect of surgery followed by endotoxin on the unspecific cell mediated immunity

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Introduction: It is especially the cell mediated immunity that is affected in the course of sepsis and following surgical stress. The NK cells, the granulocytes and the monocytes constitute the immediate unspecific cells mediated immunity. We therefore investigated the effect on NK cells, granulocytes and monocytes of surgery, endotoxin induced sepsis and a two-hit model composed of surgery followed by administration of endotoxin.

Methods: Three groups of 40 mice. Each group was divided into four groups of 10 in each. All the animals were anaesthetized and subjected to either (1) laparotomy, (2) treatment with *E. coli* endotoxin i.p., (3) subjected to laparotomy followed 20 min later by i.p. endotoxin or (4) left untreated as a control group. In the first 40 mice the NK cell activity in spleens and number of NK cells in livers were measured, in the second the oxidative burst of granulocyte and in the third the antigen presentation capacity of monocytes.

Results: Endotoxin stimulated the NK cell activity and up-regulated the antigen presentation on monocytes. In contrast, surgical stress reduced the NK cell activity, the number of NK cells in tissues and down-regulated the antigen presentation on monocytes. After surgery, followed by administration of endotoxin, the oxidative burst of granulocytes was stimulated while antigen presentation on monocytes was down-regulated. Endotoxin prevented or reverted the postoperative suppression of NK cell activity.

Conclusion: Our two-hit model shows that some cell types of the unspecific immune system exhibit an anti-inflammatory response (monocytes) while others at the same time show an excessive inflammatory response (NK cells, granulocytes). This diversity makes a potential therapeutic immunomodulation very complex, as some cell types would need to be down-regulated while others need to be stimulated.

P104 $p22^{phox}$-containing microparticles from plasma of septic patients are related to reactive oxygen species production and apoptosis of vascular cells in culture

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Reactive oxygen species (ROS) are related to vascular dysfunction in several pathologies and may be related to the pathophysiology of sepsis and multiple organ dysfunction.

To investigate their role and sources we evaluated the effects of plasma of septic patients (SPP) on reactive ROS production and apoptosis of rabbit endothelial (REC) and aortic smooth muscle (RASM) cells in culture through NAD(P)H (0.3 mM)-driven lucigenin (5 μM) luminescence and annexin V assay respectively.

SPP alone showed intrinsic luminescence when compared to plasma from healthy controls (HCP) (51.4 ± 9.5 cpm/min/mg protein vs 7.0 ± 1.2, $n = 5$, $P < 0.05$). After incubation with REC and RASM cells SPP induced a two-fold increase in ROS production ($n = 5$, $P < 0.05$) when compared to incubation with HCP. This enhancement of ROS production by REC and RASM cells were paralleled by increase in apoptosis rates induced by SPP. The fraction responsible for ROS production and apoptosis induction was determined through filtration and ultracentrifugation to be over 50 kD and to contain microparticles (MP), similar to those from activated platelets. MP showed similar luminescence (60.6 ± 4.4 vs 32.9 ± 3.1, $n = 11$), blocked by DPI (60%), a flavoenzyme inhibitor, and by SOD (80%). Addition of MP from SPP to REC and RASM also induced increased luminescence when compared to the effect of MP from HCP; These signals were also inhibitable by SOD and DPI. Incubation of REC and RASM with MP from SPP doubled apoptosis rates when compared to incubation with MP from HCP. Apoptosis was also inhibited by addition of SOD or DPI. After lipid extraction, western-blot analysis of the MP was positive for the $p22^{phox}$ and gp91 subunits of the NAD(P)H oxidase.

Thus, SPP has intrinsic and enhances REC and RASM ROS production, due to NAD(P)H oxidase activity. It causes apoptosis of REC and RASM, also inhibited by SOD and DPI. These effects may be attributable to MP containing the $p22^{phox}$ and gp91 subunits of NAD(P)H oxidase. ROS derived from microparticles may represent a new signaling pathway involved in the pathophysiology of severe sepsis.

P105 LPS activation of leukocytes attenuates adhesion to endothelial cells under shear stress

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Leukocyte adhesion is triggered by upregulation of cell surface adhesion molecules and counteracted by the shear forces of the flowing blood. Since both factors, inflammatory response and flow dynamics are severely altered during endotoxemia, we studied the effects of endotoxin on leukocyte–endothelial interactions under different levels of shear stress *in vitro*. In order to perform the experiments at precisely adjustable levels of shear stress, we used a parallel plate flow chamber as has been employed in a number of adhesion studies previously. Within this chamber, endothelial cells (HUVEC) could be perfused with neutrophils (PMN) at 0.25–3 dynes/cm^2. FACS analysis of adhesion molecules, trypan blue exclusion and PMN migration showed that the cells were not altered during cell separation. To determine the effects of lipopolysaccharide (LPS) on shear-dependent adhesion, we studied HUVEC and PMN in a native state and following activation with LPS at 100 ng/ml and 10 ng/ml. All flow experiments were

videotaped and the results were analysed by the paired *t*-test ($P < 0.05$). The effects of LPS on leukocyte–endothelial interactions strongly depended on the site of activation. Whereas LPS pretreatment of HUVEC increased PMN adhesion by 5–10 fold, pre-activation of the PMN resulted in a 50% reduction of adherent cells. In addition, after pre-activation of PMN, adhesion became increasingly dependent on shear stress and, thus, inhibition by LPS was most pronounced at a normal, postcapillary shear stress of 2–3 dynes/cm^2. As demonstrated by addition of antibodies against selectins, the effect of LPS was due to a functional loss of L-Selectin and P-Selectin mediated interactions. In addition, integrin-mediated adhesion was impaired despite upregulation of CD11b on activated PMN. In summary, our results show that leukocyte–endothelial interactions become increasingly dependent on shear stress as soon as PMN are activated. Once PMN have undergone LPS activation, leukocyte tethering to the endothelium becomes entirely dependent on endothelial E-Selectin. Furthermore, adhesion efficiency decreases despite upregulated expression of CD11b. Since LPS increased the rigidity of PMN, it seems that the increased stiffness attenuated PMN adhesion by hampering PMN flattening and, thereby, reducing the number of available bonds to the endothelium.

P106 Incidence and risk factors of reactive histiocytic hyperplasia with hemophagocytosis in medical intensive care patients

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Introduction: Reactive histiocytic hyperplasia with hemophagocytosis (HHH) is characterised by a systemic proliferation of non-neoplastic histiocytes with phagocytosis of hemopoietic cells. HHH is mainly associated with virus infections, sepsis, hematologic malignancies or carcinomas.

Objective: To determine incidence and risk factors of HHH in patients dying in the intensive care unit (ICU).

Methods: We retrospectively analyzed clinical data and autopsy findings of patients ($n = 107$), who died in our medical ICU. Data included age, sex, medical history, reason for last admission, diagnosis, APACHE II-score, TISS-score and SOFA-score, transfusion requirements, complications, relevant laboratory findings as well as the cause of death. Bone marrow samples obtained at autopsy were histochemically stained with hematoxylin–eosin and prussian blue reaction. Immunohistochemistry with monoclonal antibodies against CD68, CD61 and myeloperoxidase (all DAKO, Hamburg/Germany) was done to identify and quantify the hemopoietic cell lines mainly affected by the HHH. The hemophagocytic activity was graded from mild to severe HHH according to Suster *et al*. [1]. Cases showing moderate to severe hemophagocytic activity were classified as having HHH. Statistical analysis was performed using chi-square-test, correlational and logistic regression analysis.

Results: At autopsy HHH was present in the bone marrow of 69 out of 107 (64.5%) patients: 35/107 (32.7%) had mild, 27/107 (25.2%) moderate, 7/107 (6.5%) severe HHH. The HHH correlates with the iron store and not with the cellularity of the bone marrow. In univariate analysis HHH was associated with higher APACHE II-score, SOFA-score and TISS-score, mechanical ventilation, recent blood transfusion, DIC and sepsis ($P < 0.05$). At autopsy histology of pneumonia and respiratory cause of death were more frequent in patients with HHH ($P < 0.05$).

Conclusions: HHH is frequent in patients dying in the ICU. HHH may contribute to the blood cytopenia often seen in ICU patients. Severity of illness, infections and blood transfusions are predictors of HHH.

Reference:
1. Suster, *et al*.: *Hum Pathol* 1988, **19**:705-712.

P107 Decreased monocyte surface expression of HLA-DQ is associated with prolonged duration of septic shock

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There is increasing evidence for a protective role of Human-Leukocyte-Antigen (HLA)-DQ in response to infection. This study was performed: (1) to investigate the kinetics of monomorphic (m)HLA-II (HLA-DR,-DP,-DQ) and HLA-DQ expression on monocytes during septic shock; (2) to clarify whether maintaining mHLA-II and HLA-DQ expression within normal range (NR) could predict improved recovery and survival. In total, 16 patients (11 males, 5 females) in septic shock have been investigated. mHLA-II and HLA-DQ median fluorescence intensity (MFI) on monocytes have been monitored daily using flow cytometry. Normal range was determined in 19 healthy volunteers. MFI of mHLA-II and HLA-DQ expression throughout septic shock was significantly reduced when compared to control ($P < 0.05$). All patients showed median mHLA-II expression below normal range regardless of duration of septic shock and survival. In contrast, median HLA-DQ expression demonstrated negative correlation with the duration of septic shock (Phi-square = 0.73). Patients with HLA-DQ below normal range showed almost a three-fold prolonged term of septic shock as compared to patients with HLA-DQ expression within normal range (15.2 ± 6.3 days versus 5.5 ± 1.7 days; $P < 0.015$). Although, there was no correlation between median HLA-DQ and survival, all non-survivors showed HLA-DQ expression below normal range. In conclusion, HLA-DQ expression below normal range may predict prolonged duration of septic shock and increased mortality and could be an indicative marker of immune surveillance in critically ill patients.

P108 Complement activation in relation to age in patients with severe sepsis

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Objectives: Severe sepsis is still associated with a mortality of 29% [1]. Sepsis mortality is highest in elderly patients [1]. Another factor, which is related to outcome in sepsis is the extent of complement activation [2]. The aim of this study was to evaluate complement activation in relation to age in severe septic patients.

Methods: This observational study was performed in 20 patients with severe sepsis (SOFA-Score = 9 ± 3) and grouped according to age: ≤ 60 years ('adult', $n = 10$) and > 65 years ('elderly', $n = 10$). Complement proteins Bb, C3a, C4d were performed by ELISA technique. C1-Inhibitor (C1-Inh) activity was measured by Berichrom® C1-Inactivator, and C1-Inh protein concentration by NOR-Partigen®. To compare values at onset of severe sepsis with those on the 8th day Friedman test with *post-hoc* Wilcoxon test was performed. Data are presented as median and range. *$P < 0.05$ was considered significant.

Results: See Table 1.

Conclusions: Activation of the classical pathway of complement was found to be more marked in adult patients than in elderly. Thus, our results suggest age-related differences in the complement activation in severe sepsis.

References:
1. Angus DC, *et al.*: *Crit Care Med* 2001, **29**:1303-1310.
2. Hack CE, *et al.*: *Intensive Care Med* 1993, **19(suppl 1)**:19-28.

Table 1

	Adult		Elderly	
	Sepsis day 1	Sepsis day 8	Sepsis day 1	Sepsis day 8
C4d (μg/ml)	2.4 (2.0–3.3)	1.7* (3.8–8.3)	3.2 (2.5–7.3)	5.4 (3.9–7.0)
C1-Inh activity (%)	105 (72–132)	148* (128–163)	122 (85–133)	132 (107–156)
C1-Inh protein (%)	136 (107–148)	196* (158–211)	123 (100–154)	147 (120–165)
Bb (μg/ml)	0.55 (0.32–2.74)	0.79 (0.41–1.15)	0.90 (0.68–1.05)	1.03 (0.88–1.25)
C3a (ng/ml)	118 (65–370)	524 (212–689)	204 (102–1129)	372 (187–1154)

*$P < 0.05$, sepsis day 1 vs sepsis day 8 (Friedman test with *post-hoc* Wilcoxon).

P109 Comparing C-reactive protein, procalcitonin, and interleukin-6 for the diagnosis of bacterial infection in adult atraumatic patients in a medical center emergency department

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Introduction: Procalcitonin (PCT) has been proposed as a marker of sepsis in the critically ill patients. Its level is related to the severity of sepsis. We investigated the value of PCT, comparing with C-reactive protein (CRP) and interleukin (IL)-6, in the detection of infection in the emergency department (ED).

Methods: Ninety adult atraumatic patients admitted through the ED of a tertiary university hospital in June 2001 were consecutively enrolled. Forty-five were infected, and 31 were not infected. The serum levels of CRP (mg/l), PCT (ng/ml) and IL-6 (pg/ml) were compared between the infected and noninfected groups of patients. Mann–Whitney U test and chi-square test were employed to compare independent and group data, and the receiver operating characteristics (ROC) curve and the respective areas under the curve were calculated.

Results: The best cut-off level for CRP, PCT and IL-6, identified using Youden's Index, was 60 mg/l, 0.6 ng/ml and 24 pg/ml, respectively. Compared with CRP and IL-6, PCT had a comparable sensitivity, a lower specificity, and a lower area under the ROC curve. Bacteremic patients had higher PCT and IL-6 concentrations than those without bacteremia, but similar CRP concentrations. PCT and IL-6 levels were particularly high in septic shock patients.

Table

Parameters	Sens. (%)	Spec. (%)	PPV (%)	NPV (%)	AUC
CRP (cut-off 60 mg/l)	73.3	93.5	94.3	70.7	0.896
PCT (cut-off 0.6 ng/ml)	77.8	64.5	76.1	66.7	0.724
IL-6 (cut-off 24 ng/ml)	89.2	75.0	89.2	75.0	0.829

Sens., sensitivity; Spec., specificity.

Conclusions: PCT is not a better marker of infection than CRP and IL-6 in the adult ED patients, but it is a useful marker of the severity of infection.

P110 Effects of granulocyte-colony stimulating factor (G-CSF) prophylaxis in high risk patients (ASA III and IV) with colorectal cancer on perioperative cytokine levels, complications and global quality of life

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Aim: The effects of a prophylaxis with G-CSF on postoperative outcome was examined in high risk patients with colorectal carcinoma. In a pilot study we examined whether changes in cytokine levels and leukocyte count correlate with the onset of complications and influence global quality of life.

Material and methods: Patients (ASA class III and IV) with colorectal cancer were randomized in a double-blinded pilot study to: prophylaxis with G-CSF (12 hours before surgery, 12 and 36 hours after surgery) versus placebo. Measurements of G-CSF, IL-6, IL-18, Procalcitonin (PCT) in plasma, leukocyte count, percentage of polynuclear granulocytes (PMNs) and their phagocytic activity were started before operation and continued till day 6 after surgery. TNF-α release was determined after LPS *in vitro* stimulation of whole blood. All complications were documented as well as quality of life (QL) at discharge, 2 and 6 months after surgery using the EORTC QLQ 30 questionnaire and for global QL the index-points of the area under the curve (AUC) were calculated.

Results: In one patient of the placebo group surgery was cancelled after randomization (*withdrawal*). In all measurements IL-6 and IL-18 levels and the leukocyte count of the G-CSF group were above placebo and normal values. Only in the placebo group phagocytic activity of granulocytes fell below normal values. There was no difference between the groups regarding IL-8, PCT and TNF-α release. All values were within normal range besides PCT. PCT values were elevated on day 1 after operation on average up to 1.9 and at day 3 on 1.2 ng/ml (normal <0.5 ng/ml). Patient 2 developed fever on day 5 after surgery and leukocytosis on the basis of an anastomotic leakage. Patient 4 had the highest IL-6 levels of all patients on day 6 and on day 8 a duodenal ulcer perforation. Patient 5 developed a bowel atony on day 5 and showed the highest IL-18 levels of all patients on day 6.

Conclusions: The development of postoperative early phase complications is accompanied by changes of cytokine- and bloodcell patterns. Prophylactic treatment with G-CSF elevated IL-6 and IL-18 levels and improved phagocytic activity of granulocytes. The expected influence on global quality of life could not be demonstrated in the pilot study. The correlations found are being further examined in an ongoing randomized, double-blinded trial with 80 patients.

Reference:
1. Lorenz *et al.*: *Inflamm Res* 2001, **50**:115-122.

Table

Patient	Age	Tumor stage	G-CSF	Hospital stay ICU/ward	TISS	QL-AUC Indexpoints	Complications
1	63	pT4pN1 Mx	**Yes**	1/12 days	31	133	Ileus, rezidiv (month 5)
2	58	pT1pN0 M0	**Yes**	1/24 days	21	308	Anastomotic leakage (day 5) Disturbed micturation (day 12)
3	80	pT3pN2 Mx	No	1/14 days	26	92	Nausea/vomiting (day 3) Urinary tract infection (month 2)
4	71	pT2pN0 Mx	**Yes**	45/22 days	582	333	Duodenal ulcer perforation, OP (day 8), pleural effusion, pneumothorax (day 30)
5	47	pT2pN0 M0	No	1/21 days	21	442	Bowel atony (day 5)

P111 Effects of intravenous and intratracheal pentoxifylline on histopathologic changes and wet–dry ratio in HCl acid-induced acute lung injury in rabbits

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Introduction: The aim of this study was to compare the effects of intravenous (IV) and intratracheal (IT) pentoxfylline (PTX) on histopathologic changes and wet/dry ratio in acute lung injury in rabbits.

Methods: Twenty-one New Zealand rabbits were randomly divided into three groups ($n = 7$). After rabbits were sedated with IM ketamine, tracheostomy was performed and endotracheal tube was inserted. Anesthesia was maintained with continuous infusion of ketamine and atracurium. All animals were ventilated with PC mode for 3 hours and the parameters of ventilation were FiO_2: 1.0, PIP: 15 cmH_2O, PEEP: 5 cmH_2O. RR was adjusted to produce initial $PaCO_2$ of 35–40 mmHg. IT HCl (2 ml/kg) was given following tracheostomy in all animals. Five minutes after the application of HCl; Group 1, received IV PTX (20 mg/kg, bolus); Group 2, received IT PTX (20 mg/kg, bolus); Group 3, no treatment. At the end of 3 hours, the rabbits were sacrificed for histopathologic examination to evaluate lung injury and to measure wet/dry ratio. Tissue sections were examined for light microscopy with HE stain. The pathologic lesions were classified ranging from 0 to 4. Right lung was dried at 60°C for 24 hours. These conditions remove virtually all gravimetrically detectable water. The lung wet and dry weights were measured, and wet-to-dry weight ratio was calculated to asses pulmonary edema. Data were compared by Mann–Whitney U test. $P < 0.05$ was considered to indicate statistical significance.

Results: Significant changes in histopathologic findings on bronchial epithelial injury, neutrophil infiltration-density, hemorrhage and hyalen membrane were encountered in group 3 when compared with other groups ($P < 0.01$). There was no significance dif-

ference for septum injury and atelectasia. Wet/dry ratio of group 3 was higher than the other groups ($P < 0.01$).

Conclusion: PTX given after the 5 min of HCl application via IT route might have beneficial effects on histopathologic changes and wet/dry ratio in HCl induced-ALI model.

P112 Correlation between plasma peroxides and procalcitonin levels in patients with severe streptococcal community acquired pneumonia

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Introduction: During lower respiratory tract infection, massive influx and activation of phagocytes and release of reactive oxygen species (ROS) is observed. As a consequence, the lipid peroxidation in plasma may increase. The aim of this study was to estimate the plasma concentration of lipid peroxides in combination with a biochemical indicator of inflammation and to assess a possible correlation between infection and oxidative stress. Plasma procalcitonin (PCT) and peroxides (PEROX) concentrations were measured in 15 patients hospitalised for radiologically confirmed severe streptococcal community acquired pneumonia (CAP). As control values, PCT and PEROX were also measured in 10 healthy subjects.

Methods: Plasma samples for PCT and PEROX were obtained the first day of hospitalisation. PCT was determined by immunolumi-nescence method (LUMITEST PCT, Brahms Diagnostica, Berlin, Germany). PEROX were analysed by a colorimetric assay (OXYSTAT, Biomedica, Wien, Austria).

Results: All control subjects showed a PCT level below 0.5 ng/ml (mean value: 0.32 ± 0.1 ng/ml). Mean patients PCT values was 4.9 ± 2.9 ng/ml ($P < 0.01$ vs control). Plasma peroxides were higher in patients respect to controls (860 ± 130 μmol/l vs 278 ± 46 μmol/l, $P < 0.01$). A good correlation was found between PCT and PEROX values ($r^2 = 0.91$) in patients.

Conclusion: Process of lipid peroxidation seems to correlate with the degree of infection as indicate by PCT levels.

P113 Lipopolysaccharide binding protein: a poor parameter for the differentiation of SIRS and sepsis but useful as determinant of outcome in septic patients

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Lipopolysaccharide binding protein (LBP) is an acute phase hepatic glycoprotein immediately involving in the process of immune response to endotoxin. Elevation of LBP appears to be an important marker associated with release of endotoxin and/or bacteriemia. In our study we investigated serum LBP levels as a prognostic marker for sepsis and Systemic Inflammatory Response Syndrome (SIRS). Also we assessed the correlation of LBP with procalcitonin (PCT), expression HLA-DR on monocytes and the production of TNF-α *ex vivo* by monocytes stimulated by lipopolysaccharide (markers of immunoparalysis).

Methods: The serum levels of lipopolysaccharide binding protein (LBP) and procalcitonin (PCT), the expression of HLA-DR on monocytes and the production of tumor necrotizing factor by monocytes stimulated *ex vivo* by lipopolysaccharide were measured in a group of 68 patients with Systemic Inflammatory Response Syndrome (SIRS), sepsis or septic shock (diagnosed according to ACCP consensus criteria).

Results: We have found that LBP levels:

1. Were elevated in 98% of patients over normal value of 7.3 ng/ml.
2. Were significantly higher in nonsurvivors than in survivors (mean 39.1 ng/ml and 26.1 ng/ml) – the difference being due to group of septic patients – their lethality was significantly increased when LBP levels exceeded 24.1 ng/ml.
3. Were significantly higher in patients with sepsis or septic shock than in patients with SIRS (mean (SD) – 40.5 (18.6) versus 29.8 (17.9) ng/ml).
4. The specificity and sensitivity of LBP levels to differentiate patients with SIRS versus patients with sepsis was low – 50% and 74.3%, respectively.
5. Did not differ between the groups of patients with and without immunoparalysis (37.1 ng/ml to 31.1 ng/ml).
6. Did not correlate with the serum levels of procalcitonin, expression of HLA-DR on monocytes or production of TNF after stimulation by lipopolysaccharide.

Conclusions: Lipopolysaccharide binding protein may be a useful marker for the prediction of outcome in patients with sepsis but its ability to discriminate patients with SIRS to patients with sepsis is low. Further studies are needed to elucidate its possible prognostic significance.

P114 Changes in plasminogen activator inhibitor-1 (PAI-1) in patients with severe sepsis or septic shock

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Introduction: For septic shock, especially that caused by infection with Gram-negative bacteria, endotoxin adsorption (direct hemoperfusion using polymyxin B fixed fiber: PMX-DHP) is regarded as an effective method of treatment in Japan. In 27 patients who were admitted to ICU and underwent PMX-DHP for severe sepsis or septic shock, the kinetics of PAI-1 were determined, and com-

pared between the group with a high endotoxin level of 10 pg/ml or more just before the initiation of PMX-DHP and the group with a normal endotoxin level of less than 10 pg/ml. Furthermore, the relations between PAI-1 and other mediators were examined.

Method: Hemoperfusion using polymyxin B fixed fiber was performed by inserting a double-lumen catheter into the femoral or subclavian vein, at a blood flow rate of 80–100 ml/min. Determinations of PAI-1 and various cytokines including interleukin-6 (IL-6), interleukin-10 (IL-10) and interleukin-1 receptor antagonist (IL-1ra) were performed by enzyme linked immunosorbent assay (ELISA) just before the initiation, just after the completion, and 24 hours after the completion of PMX-DHP.

Subjects' backgrounds and underlying diseases: The number of patients was 12 in the normal level endotoxin group (Group N) and 15 in the high level endotoxin group (Group H). No significant difference was found in age. Regarding sex difference, females were dominant in Group N, while males were dominant in Group H. For other items including the number of pertinent items, septic severity score, APACHE-II score and MOF score, Group H had higher values in general. Most of the patients the underlying disease was sepsis caused by abdominal infection. Concerning the outcome after 4 weeks, nine (75%) out of 12 patients in Group N survived and 11 (73%) out of 15 patients survived in Group H, without significant difference.

Results: *Changes in PAI-1 corresponding to endotoxin level*: PAI-1 before the initiation of PMX-DHP was 416 ± 500 ng/ml in Group H, while that in Group N was 172 ± 141 ng/ml, showing a 2.4-fold higher tendency in Group H than in Group N. However, the correlation between PAI-1 and endotoxin level before the initiation, just after completion, and 24 hours after completion of PMX-DHP was not significant. PAI-1 level just after completion of PMX-DHP was 104 ± 12 and 362 ± 559 ng/ml in Group N and Group H, respectively, showing a decreasing tendency and a greater decrease in Group H after 24 hours.

Relations between PAI-1 and other cytokines: At any period before the initiation, just after completion, and 24 hours after the completion of PMX-DHP, a significant positive correlation was found between PAI-1 and IL-6, indicating the possible role of IL-6 in controlling the kinetics of PAI-1. As in the case of IL-6, a significant positive correlation was also found, at any period, between PAI-1 and IL-10, an anti-inflammatory cytokine. A significant positive correlation was found, at periods before initiation and just at completion of PMX-DHP, but not after 24 hours.

Conclusion: Septic-shock patients who underwent endotoxin adsorption treatment were subjected to examination focusing on the changes in PAI-1. PAI-1 level was apt to be higher in the high endotoxin level group, and had a tendency to decrease in patients with successful PMX treatment.

P115 Antithrombin prevents proinflammatory activation via NFκ and MAPK signaling pathways

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Background: The serpin Antithrombin III (AT) is reported to have anticoagulatory as well as anti-inflammatory properties. AT inhibits cytokine secretion, leukocyte activation and neutrophil migration and it has been shown to be efficacious in treatment of septic disorders.

The molecular mechanism underlying the anti-inflammatory effects of AT III is still unclear. We investigated the influence of AT on NFκB- and MAPK-signaling, both well known proinflammatory signaling pathways in endothelial cells (EC) and monocytes (MO).

Methods: EC or MO were incubated with TNF-α (40 ng/ml) or LPS (10 μg/ml), respectively, in presence or absence of AT (0–30 IU/ml). Activation of the transcription factors NFκB and AP-1 (EMSA), the phosphorylation and degradation of the NFκB inhibitory protein IκBα, JNK/SAPK activation (Western Blot), as well as NFκB regulated protein- and gene expression (Tissue Factor [TF], TNF-α, IL-6) (ELISA, rtPCR) were analysed under influence of AT III, AT III isoforms and binding-modified AT.

Results: AT inhibited activation of NFκB in a dose-dependent manner by preventing phosphorylation and degradation of the inhibitor protein IκBα. AT prevented the activation of the p54 subunit of JNK/SAPK. TF and cytokine production were markedly reduced by AT III (20% of control). The b-isoform of AT, reported to have a higher affinity for glycosaminoglycans (GAGs), was more effective in preventing this proinflammatory activation than the ATα isoform. AT without heparin-binding site had no effect.

Conclusion: AT prevents NFκB- and MAPK-activation in EC and MO when given in therapeutical doses. The anti-inflammatory properties of AT III seem to depend on the interaction of the heparin-binding site of AT with GAGs on cell surface.

P116 Cost effectiveness analysis of drotrecogin alfa (activated) as a treatment for severe sepsis in hospitalised patients

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Introduction: Drotrecogin alfa (activated) significantly reduced severe sepsis (SevSep) mortality at 28 days [1]. According to the French budget environment, it is mandatory to evaluate its cost effectiveness ratio on a pragmatic basis.

Methods: All SevSep patients in the Cub-Réa database (1997–1999 period) defined according to PROWESS [1] and with a hospital length of stay (LOS) ≥ 24 hours ($n = 10,459$) were included. The baseline patients' characteristics are similar to those of the PROWESS criteria study: age (61 years vs 60 years), < 60 years (42% vs 44%), and number of organ failure (2.1 vs 2.4). Key patient data recorded: age, gender, type of admission (medical or surgical), admission mode (direct or transfer), number (1, 2, 3), duration and type of support (respiratory, renal, circulatory) and SAPS II. Stratification according to these criteria and loading of the observed frequencies into a decision-tree for conditional probabilities. Relative risk of death with drotrecogin alfa (activated) estimated according to the observed classification into 11 néoGHM [2] groups (28 days survival represented by the parametric function of Weibull). SevSep impact on long-term mortality estimated

by the McCabe score with three hypotheses for life expectancy (LE): unique LE of 5 years, McCabe > 0 (2 years of survival), McCabe = 0 (4 years LE reduction or half LE reduction versus whole population). Costs estimated by subgroups and by a linear equation (nursing workload, LOS, SAPS II, living or dead status). Calculation of a differential cost effectiveness ratio (drotrecogin alpha (activated) price: 7836.95 € for 4 days treatment and a mean patient's weight of 70 kg) and analysis of Monte Carlo's type.

Results: The expected cost in the model of a SevSep patient treated by standard care is 26,983.3 $€_{FF96}$ vs 26,373.6 $€_{FF96}$ observed from Cub-Réa. The expected cost predicted in the model of a SevSep patient treated by drotrecogin alfa (activated) is 34,605.90 $€_{FF96}$. The survivors LE according to the above hypotheses are 5.0, 10.6, and 6.9 years. Corresponding effectiveness differences in favor of drotrecogin alfa (activated) are 0.33, 0.63, and 0.41 years. The cost per additional year of life saved amounts of 18,446.3 $€_{FF96}$ including all degrees of severity and co-morbidity. The sensitivity analysis model shows that with an expected threshold of 53,357.1 $€_{FF96}$, 96.3% of the bootstrap samples are cost-effective.

Conclusion: The predicted cost effectiveness ratio of drotrecogin alfa (activated) in adult SevSep patients is much lower than the international range considered as acceptable (53,357.10 €). Drotrecogin alfa (activated) is cost-effective when including patients with all degrees of co morbidity.

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P117 Marked reductions of protein C and antithrombin in post-trauma DIC have close relations with MODS and poor outcome

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Objective: Disseminated intravascular coagulation (DIC) associated with marked reductions of protein C and antithrombin in post-trauma patients have close relations with multiple organ dysfunction syndrome (MODS) and their outcome.

Design: Prospective cohort study.

Setting: General intensive care unit of a tertiary care emergency department.

Patients: Seventy-six trauma victims, 26 with DIC and 50 without DIC.

Materials and methods: Protein C antigen concentration (protein C antigen), protein C activity, and antithrombin were measured on the day of the injury, and on the 1st, 3rd, and 5th days after admission. The results of these measurements, demographic data, mortality and incidence of acute respiratory distress syndrome (ARDS), MODS, and sepsis were compared between the patients with and without DIC. DIC patients were further classified into subgroups of survivors and nonsurvivors.

Results: Incidence of ARDS and MODS were significantly high in the DIC patients. The mortality rate of the DIC patients was significantly higher than that of the non-DIC patients. Protein C antigen and activity, and antithrombin decreased significantly in the DIC patients compared with those in the non-DIC patients, which continued to be low up to the 5th day of admission. Clear intergroup differences of the time course were also noted in the levels of protein C antigen and activity, and antithrombin between the survivors and nonsurvivors in the DIC group.

Conclusion: Our findings suggest that DIC involving suppression of the physiologic anticoagulant pathways is an important contributor of MODS and poor outcome in post-trauma patients.

P118 Antithrombin reduces the ischemia/reperfusion-induced hepatic injury by increasing hepatic levels of prostacyclin through activation of capsaicin-sensitive sensory neurons in rats

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We have previously demonstrated that antithrombin (AT) reduces ischemia/reperfusion (I/R)-induced liver injury by inhibiting leukocyte activation through the promotion of hepatic production of prostacyclin (PGI2) [1]. However, AT does not directly promote the endothelial production of PGI_2 in cultured endothelial cells [2]. Capsaicin-sensitive sensory neurons (CSSN) are nociceptive neurons that release calcitonin gene-related peptide (CGRP) upon activation. Since CGRP increases the endothelial production of PGI_2, it is possible that AT may increase the hepatic PGI_2 production in rats subjected to I/R through the activation of CSSN. Recent studies have demonstrated that CGRP increases the endothelial production of nitric oxide (NO). Since NO has been shown to activate endothelial cyclooxygenase-1 (COX-1) activity, we further examined whether AT-induced increase in hepatic level of PGI_2 can be mediated by nitric oxide synthase (NOS) activation. Male Wistar rats were subjected to 60-min ischemia and subsequent reperfusion. Both tissue levels of CGRP and the expression of immunohistochemical CGRP in the liver were significantly increased in rats subjected to I/R 1 hour after reperfusion. AT (250 U/kg, i.v.) significantly enhanced the I/R-induced increase in both hepatic levels of CGRP and the expression of immunohistochemical CGRP. AT-induced increase in hepatic level of CGRP and CGRP expression were completely inhibited by capsazepine (CPZ), a vanilloid receptor-1 antagonist. Furthermore, AT-induced increase in hepatic level of 6-keto-PGF1α, a stable metabolite of PGI_2, were significantly inhibited by CPZ, CGRP (8-37), a CGRP receptor antagonist, and L-nitro-arginine-methyl-ester (L-NAME), a non-selective inhibitor of NOS. AT reduced the I/R-induced liver injury by inhibiting the I/R-induced increase in hepatic tumor necrosis factor (TNF)-α. Pretreatment of rats with CPZ, CGRP (8-37), and L-NAME completely abrogated such preventive effects of AT. Administration of rat α-CGRP produced effects similar to those of AT. These results strongly suggest that AT might reduce the I/R-induced liver injury by increasing the hepatic level of PGI_2 through

the activation of CSSN. Thus, AT might sensitize hepatic CSSN in rats subjected to hepatic I/R, leading to the increase in the hepatic tissue level of PGI_2. In this process, CGRP-induced activation of endothelial NOS and COX-1 could be critically involved.

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P119 Inhibition of proliferation and induction of differentiation of endothelial cells by antithrombin

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Anti-angiogenic and anti-tumor activities of latent and cleaved antithrombin has been described, and *in vitro*, the serpin inhibited proliferation of endothelial cells. We have recently observed that direct cellular effects of antithrombin are mediated by syndecan-4, a heparan sulfate proteoglycan known to bind to the heparin-binding site of antithrombin. Syndecan-4 is known to affect proliferation and differentiation of a variety of cell types. We have, therefore, studied direct effects of intact antithrombin on endothelial cells. Human umbilical vein and calf pulmonary artery endothelial cells were studied in the presence or absence of antithrombin concentrate or monoclonal antibody purified antithrombin with and without concomitant presence of synthetic pentasaccharide. Proliferation was assessed in BrDU incorporation and MTT assays. For testing endothelial cell differentiation, capillary tube formation was investigated in matrigel assays. Proliferation of the two types of endothelial was significantly inhibited by 1–10 U/ml of both antithrombin concentrate and antibody-purified antithrombin. Capillary tube formation induced by matrigel was augmented by the presence of 1–10 U/ml of antithrombin concentrate which was partly reversed with pentasaccharide. Results show that *in vitro* effects of antithrombin on angiogenesis-related endothelial cell functions may be directly exerted by the intact serpine and can be antagonised by pentasaccharide

P120 Syndecan-4 on human peripheral blood lymphocytes and monocytes mediates effects of antithrombin on chemotaxis

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Antithrombin inhibits chemokine-induced migration of neutrophils by activating heparan sulfate proteoglycan-dependent signaling. Whether antithrombin affects migration of other types of leukocytes is unknown. We investigated the effects of antithrombin on spontaneous and chemokine-triggered migration of lymphocytes and monocytes from human peripheral blood in modified Boyden chamber micropore filter assays. Lymphocyte and monocyte populations from human peripheral blood were purified using magnetic antibody cell sorting. Signaling mechanisms in antithrombin-dependent migration were studied by Western blot analyses of protein kinases and Rho activation, or were tested functionally by using signaling enzyme blockers. Expression of heparan sulfate proteoglycan core protein was studied by RT-PCR and flow cytometry. As antithrombins, the concentrate Kybernin®P from human plasma and a monoclonal antibody-purified preparation therefrom were used. Pretreatment of lymphocytes and monocytes with antithrombin inhibited chemotaxis toward optimal concentrations of interleukin-8 or Rantes at concentrations of antithrombin as low as 10 nU/ml; in the absence of the chemokines, direct exposure of cells to gradients of antithrombin stimulated migration. Effects of antithrombin were abolished by pretreating cells with heparinase-1, chondroitinase, sodium chlorate and anti-syndecan-4 antibodies. Expression of syndecan-4 mRNA and protein in monocytes and lymphocytes was demonstrated in RT-PCR and anti-syndecan-4 immunoreactivity assay, respectively. In the presence of pentasaccharide, antithrombin lost its activity on the cells. Antithrombin induced chondroitinase- and heparinase I-dependent phophorylation of protein kinase C-alpha and dissociation of Rho-GTPase. Data indicate that antithrombin directly inhibits chemokine-stimulated migration of monocytes and lymphocytes via effects of its heparin-binding site on cell surface syndecan-4 by activation of protein kinase C and Rho signaling.

P121 Abstract withdrawn

P122 Effect of unfractionated and low molecular weight heparin on microcirculatory antithrombin effects during endotoxemia

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Objective: A recent prospective randomized clinical sepsis trial (Kybersept study) shows a reduction in 90-day mortality by antithrombin (ATIII) only in the prospectively defined subgroup of patients without simultaneous heparin treatment. To investigate whether this clinically observed heparin-ATIII antagonism is caused by a heparin-related reversal of ATIII effects on the microcirculation during endotoxemia, experimental ATIII administration was combined with administration of different heparins at a clinically relevant dose.

Methods: In skin fold preparations of the Syrian hamster, normotensive endotoxemia was induced by i.v. administration of 2 mg/kg endotoxin (LPS, *E. coli*, 2 mg/kg), whereby intravital video fluorescence microscopy allowed determination of venular adherent leukocyte count (VALC) and functional capillary density (FCD), which served as a measure of capillary perfusion. ATIII (ATIII group, $n = 6$, Kybernin, 250 IU/kg i.v.) was substituted 5 min before LPS administration. Another group simultaneously received intravenous unfractionated heparin (ATIII + Hep, $n = 5$, sodium heparin, 100 IE/24 hours, i.v.), whereas additional animals received low molecular weight heparin (ATIII + LMWH, $n = 5$, fraxiparin, 5 µl/kg, 2 hours before LPS, s.c.).

Controls: Saline-treated animals receiving only LPS.

Results: LPS induced a massive increase in VALC with a maximum at 8 hours and a decrease in FCD ($P < 0.01$ vs baseline). Both LPS effects were effectively prevented by ATIII ($P < 0.01$), whereas ATIII + Hep and ATIII + LMWH animals showed microcirculatory disturbances comparable to that observed in endotoxemic controls. In accordance with the clinical finding that beneficial AT III effects during sepsis are antagonized by concomitant heparin administration, our study indicates a relevant *in-vivo* adverse effect of heparins on microcirculatory AT III effects.

P123 Evaluation of anti-inflammatory and anti-adhesive effects of heparins in human endotoxemia

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Introduction: Sepsis results from a generalized inflammatory and pro-coagulant response to an infectious agent. Adhesion molecules and cytokines are of utmost importance for the development of early symptoms as well as the late sequela of endotoxemia.

Heparin is widely known as an antithrombotic agent. But beyond its well-understood anticoagulant activity heparin is able to influence immunologic responses. In addition, *in vitro* experiments and animal studies have shown that heparin inhibits P-selectin and L-selectin mediated adhesion.

Intravenous infusion of LPS into human volunteers provides a standardized model to study activation of inflammatory, pro-coagulant and adhesive cascades in humans.

It was recently demonstrated that heparin blunts endotoxin-induced coagulation activation in a human LPS-model. As pro-coagulant and inflammatory processes are intricately linked in sepsis, we used this LPS-model to elucidate whether clinically applied doses of unfractionated (UFH) or low-molecular weight heparin (LMWH) are able to affect early inflammatory responses in low grade human endotoxemia.

Methods: The trial was a randomized, double-blind, placebo-controlled study in three parallel groups of 30 healthy male subjects. A bolus of LPS 2 ng/kg was given i.v. to all subjects. Ten minutes later, study subjects received either 80 IU/kg heparin followed by a continuous infusion of 18 IU/kg/hour for 6 hours, 40 IU/kg dalteparin, followed by a continuous infusion of 15 IU/kg/hour for 6 hours, or placebo.

Results: Following LPS infusion, TNF-α levels increased > 350-fold in the LMWH and placebo groups but only 150-fold in the UFH group ($P < 0.01$ vs LMWH group). Yet, IL-6, IL-8 and CRP levels were not different between treatment groups.

Plasma levels of sE-selectin increased by approximately 500% and sP-selectin levels doubled 6 hours after LPS infusion in all groups. Similarly, platelet leukocyte aggregates increased in all groups ($P > 0.05$ between treatments).

The changes in differential and absolute blood counts were not modified by any treatment. As expected, CD11b expression increased by 100% while L-selectin decreased by 41% 6 hours after LPS-infusion. Interestingly, both heparins (in particular UFH) decreased L-selectin down-modulation as compared to placebo ($P < 0.01$).

Conclusion: Heparin displayed little anti-inflammatory actions in low grade endotoxemia as measured by cytokine levels or endothelial/platelet activation markers. The heparin induced mitigation of L-selectin down-regulation on neutrophils is in good agreement with the blockade of L-selectin function observed *in vitro* and deserves further investigation.

P124 Measurement of carboxypeptidase R by colorimetric assay

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Carboxypeptidases (CP), carboxypeptidase N (CPN) and carboxypeptidase R (CPR), have been reported as a protease, which can cleave carboxy-terminal arginine or lysine residues from biologically active peptides, such as C3a and C5a, and regulate their activity. CPN is present in the active form in plasma, but CPR is generated from its zymogen during coagulation. CPR (identical to carboxypeptidase U [CPU], plasma carboxypeptidase B [plasma CPB]) has also been described as an inhibitor of fibrinolysis, and termed TAFI (thrombin activatable fibrinolysis inhibitor). ProCPR is activated by thrombin, thrombin–thrombomodulin complex (T-TM), plasmin, and trypsin. Today, the T-TM complex pathway has been taken notice because of effectiveness of Protein C for sepsis. Protein C has been recognized as a mediator between inflammation and coagulation. About CPR, some recent clinical studies have been shown that CPR is an acute phase protein and proCPR have been reduced in DIC. Similar to Protein C, CPR may be a mediator between inflammation and fibrinolysis. Colorimetric assay is one of the methods for measuring CP activity. Although it is convenient for determining CP activity, we noticed that some anticoagulants, such as citrate, interfere with the color development of the reagents used. Therefore, concentration of citrate in samples should be controlled to be constant for background subtraction. If one will pay attention to this point, colorimetric assay will be a good method for measuring CP activity and give us further findings.

P125 The role of natural coagulation inhibitors in correlation with clinic scores in critical patients with obstetric diseases

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Aims: To validate the correlation among the most significant inflammatory cytokines and the coagulation inhibitors system (AT III, Protein C and TFPI), used as markers, and the levels of organ dysfunction in patients with severe pre-eclampsia and HELLP syndrome.

Materials and methods: Patients involved in the study were those admitted (more than 48 hours) in ICU from 1 January 2000 to 30 September 2001). Two groups of patients were studied according with diagnostic and clinic criteria: (NP) normal pregnancy as control group; (SPH) Severe Pre-eclampsia and HELLP syndrome as study group. We have registered inflammatory cytokines plasma levels (IL 6, TNF-α, IL 10) by an ELISA assay; Antithrombin III (ATIII), Protein C (PC) and Tissue Factor Pathway Inhibitor (TFPI) as coagulation inhibitor markers are assessed via functional (activity) and immunological (antigen). We have also monitored the organ dysfunction score with a SOFA modified score (ODS: 0 = no organ dysfunction; 16 = max organ dysfunction).

Table 1

Markers	NP	SPH
IL-6 (pg/ml)	60.4 (18)	127.4* (24)
IL-10 (pg/ml)	10.2 (12)	18.6 (72)
TNF-α (pg/ml)	25.9 (8)	46.9 (6)
AT III (%)	92 (14)	56* (18)
PC (%)	98 (16)	53* (9)
TFPI (u/l)	1.14(0.2)	2.34* (0.6)
ODS	1 (1)	10 (4)

Data are presented as median concentration (SD). * $P < 0.05$ compared with levels at admission (Mann–Witney) *U* test.

Results: We have included 18 patients aged from 17 to 41 years in the SPH group and we have compared these patients with 18 normal pregnancies, aged from 17 to 41 years, before and after the cesarean section. Table 1 shows synthetically our data.

Conclusions: These data confirm our hypothesis about the role of well known markers as IL6 and TNF-α in the inflammatory response associated with severe pre-eclampsia and HELLP syndrome [1]. This is also true for some natural coagulation inhibitors and specially for AT III [2]. Protein C and TFPI show, in these data, a new significant role and contribute to confirm a multiple genesis for the coagulation disorders and the organ dysfunction associated to this obstetric disease. In addition to the well known endothelial dysfunction there is a systemic activation of maternal inflammatory cell responses in association with clotting alterations and this is supported by the correlation between the high levels of the pro-inflammatory cytokines and the low levels of coagulation inhibitors. The inhibitory substitutive treatment with AT III, that we have experienced, and with these natural inhibitors (specially Protein C) could modulate the excessive and altered inflammatory response and might restore a normal coagulation and a good organ function reducing the admission and/or the permanence of these patients in ICU.

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P126 Prophylactic anticoagulation with low dose enoxaparin: is the subcutaneous route appropriate in the critically ill?

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Introduction: Subcutaneously administered LMW heparins are widely used for prophylactic anticoagulation. The appropriateness of the SC route in critically ill patients who require vasopressors and mechanical ventilation has never been established.

Methods: The anti-Xa kinetic (0, 1, 3, 6, 12 hours) following 40 mg of enoxaparin SC was investigated in 16 ICU patients (group 1; age 61.1 ± 16 years; m/f 7/9, APACHE II 20.9 ± 7, mechanical ventilation $n = 15$, vasopressors $n = 13$) and 13 non critically ill patients on the general ward (group 2; age 61.7 ± 9 years, m/f 7/6) requiring prophylactic anticoagulation. Patients with impaired renal function or requiring hemofiltration and those requiring therapeutic anticoagulation were not eligible.

Results: Mean anti-Xa levels were consistently lower in group 1 vs group 2 on ANOVA ($P = 0.001$ between groups and over time) as was the $AUC_{0-12\ hours}$ (2.6 ± 1 vs 4.2 ± 1.7 U/ml*h, group 1 vs 2, $P = 0.008$). BMI (25.7 ± 5 vs 24 ± 6 kg/m^2) and creatinine clearance (67.5 ± 31 vs 67.7 ± 27 mg/dl) were comparable in both groups (P = ns). The peak anti-Xa level 3 hours after administration was negatively correlated to the BMI ($r = -0.41$, $P < 0.03$) and the norepinephrine dose ($r = -0.36$, $P = 0.056$).

Conclusion: It is cautiously concluded that the SC administration of established doses of prophylactic enoxaparin might not be appropriate in the critically ill patient requiring vasopressor support and mechanical ventilation.

P127 Follow up study in the assessment of rVIIa as a universal haemostatic agent in a model of haemodilution

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Introduction: Large volume fluid replacement to treat haemorrhagic shock can result in haemostatic failure due both to a dilution effect [1] and an intrinsic effect [2,3]. Recombinant factor VIIa (rVIIa) is seen increasingly as a possible universal haemostatic agent that could act to reverse or even prevent the dilution and intrinsic effects of fluids used within the 'golden' hour of haemorrhagic shock. Our preliminary findings demonstrated that rVIIa appeared to improve markers of global haemostasis in a model of large volume fluid replacement. This follow up study assessed what effects rVIIa had on global haemostasis and the electron microscopic appearances of clot formation when haemaccel or sodium chloride were used as diluents to create a model of large volume fluid replacement.

Methods: One hundred whole blood samples from normal donors were tested undiluted, or diluted to 50% and 80% using haemaccel or sodium chloride (NaCl).Each sample was tested with and without addition of 90 μg/kg of rVIIa. Global haemostasis was assessed using thrombelastography (TEG). Parameters measured were: Time to initial fibrin formation (R), Time to 20 mm clot amplitude (K), Rapidity of fibrin build up and cross-linking (α), Maximum clot amplitude (MA), Time to MA (TMA), and Clot firmness (G). Haemostatic testing was terminated when maximum clot amplitude was reached and samples were then examined by electron microscopy.

Results: One hundred samples analysed. Twenty samples for each of five fluid groups. Each sample tested ± rVIIa. Without addition of rVIIa, an intrinsic effect with worsening of TEG parameters was noted with increasing dilution in the fluid groups. Addition of rVIIa produced significant improvement in TEG parameters: $P < 0.05$ R, K, α, TMA for all fluid groups; $P < 0.05$ MA and G for 80% Haem, 50% and 80% NaCl. Moreover with increasing dilution there was a greater relative improvement in TEG parameters in rVIIa added groups. When fluid groups were compared to each other to see if the beneficial effects of rVIIa produced a difference, no significant difference was found between groups except for 50% haemaccel compared with 50% NaCl where K, MA and G were significantly better ($P < 0.05$) in the haemaccel group. Electron microscopy demonstrated a reversal of both the dilution and intrinsic inhibitory effects, with increased fibrin deposition and meshwork with greater cross-linking following addition of rVIIa.

Conclusion: In this *in vitro* model of large volume fluid replacement with associated haemodilution, the addition of rVIIa appeared to improve markers of global haemostasis and caused increased fibrin deposition with a tighter resultant meshwork on electron microscopy. Further work is required to assess the potential value of rVIIa as a universal haemostatic agent in trauma settings involving large volume fluid resuscitation.

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P128 Recombinant activated factor VII (rFVIIa-NovoSeven®-NovoNordisk) treatment of bleeding complications in intensive care unit

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Recombinant activated factor VII (rFVIIa-NovoSeven®-Novordisk) was first developed to treat severe bleeding episodes occurring in patients with haemophilia A or B with inhibitor. Complexed with tissue factor, it activates the factor × and allows transformation of prothrombin into thrombin, independently of factors VIII and IX. The success of rFVIIa in controlling haemophilic bleedings has led to use it, punctually for other serious bleedings in liver transplantation, cardiac surgery or in cirrhotic patients.

We report five cases of patients hospitalised in intensive care unit, with haemorrhagic shock or severe haemostasis disorder. Despite of massive transfusions and usual resuscitation therapeutics, their clinical course was pejorative. Then, they were given a 90 μg/kg rFVIIa intravenous dose. See Table overleaf.

A dramatic improvement occurred in a few hours. The majority of haemorrhages stopped after one or two rFVIIa doses administration. The immediate correction of haemostasis disorders allowed a reduction in blood transfusions amount and a decreasing of amine support requiring. One patient presented a thrombosis of the portal venous system quickly corrected, but no other adverse event could be attributed to rFVIIa.

rFVIIa-NovoSeven® appears to be of great interest in the treatment of uncontrolled haemorrhage in intensive care units. It can be considered as an efficient and safe therapy. Nevertheless, because of its high price and of the very preliminary nature of the data we report, further investigations are necessary before using this product as a routine treatment.

Table

Sex/age	Clinical context	Indication	Haemostasis	rFVIIa	PT after rFVIIa
F/23 years	Cirrhosis, ARF, liver T	Liver T	PT: 30% FV: 36%	90 μg/kg × 3	PT: 100%
M/53 years	PAHT, pulmonary T	Bleeding post lung T	PT: 24% FV: 13%	90 μg/kg	PT: 100%
M/60 years	Liver T, aspirin	Adverse event in a liver biopsy	PT: 35% FV: 37%	90 μg/kg × 2	PT: 75%
M/58 years	Fulminant liver failure	Liver T in emergency	PT: 19% FV: 33%	90 μg/kg	PT: 100%
M/55 years	Cirrhosis, liver T	Bleeding post liver T	PT: 29% FV: 41%	90 μg/kg × 2	PT: 100%

ARF, acute renal failure; T, transplantation; PAHT, pulmonary arterial hypertension; PT, prothrombin time.

P129 Renal effect of dopamine, norepinephrine, epinephrine, or norepinephrine–dobutamine in septic shock

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Objectives: To investigate the renal effect of dopamine, norepinephrine, epinephrine, or norepinephrine-dobutamine in septic shock.

Design: A prospective clinical study in which each patient acted as his/her own control.

Setting: Teaching hospital Intensive Care Unit.

Patients: Twenty-two patients with septic shock completed the study.

Intervention: Fluid loading to an optimal left ventricular stroke work index (LVSWI) whilst treated with dopamine, norepinephrine, epinephrine, or norepinephrine–dobutamine each in a randomized order, which was adjusted to maintain mean arterial pressure >80 mmHg for 2 hours. After each 2 hours, a complete hemodynamic parameters and measurement of urine flow rate, creatinine clearance and sodium excretion were performed.

Measurement and results: All patients fulfilled the therapy goals after being treated with all kinds of the drugs. No statistical differences were found for right atrial pressure (CVP), mean pulmonary arterial wedge pressure (PAWP), mean pulmonary arterial pressure (PAP), mean systemic arterial pressure (MAP) during dopamine, norepinephrine, epinephrine and norepinephrine–dobutamine infusions. Epinephrine induced a significant higher cardiac index (CI) compared with norepinephrine alone and norepinephrine–dobutamine ($P<0.05$). Compared with other three groups, cretinine clearance increased significantly in norepinephrine–dobutamine ($P<0.05$), but urine volume increased in dopamine group as compared with epinephrine group ($P<0.05$).

Conclusions: Dopamine, norepinephrine, epinephrine, or norepinephrine–dobutamine could improve systemic hemodynamics in septic shock, but their renal effects were different, dopamine acted as a diuretic and did not improve creatinine clearance, norepinephrine–dobutamine improved creatinine clearance without a significant change in urine output, norepinephrine, epinephrine had no markedly renal effect.

P130 Effects of epinephrine compared to dobutamine–norepinephrine on gastric perfusion in septic shock

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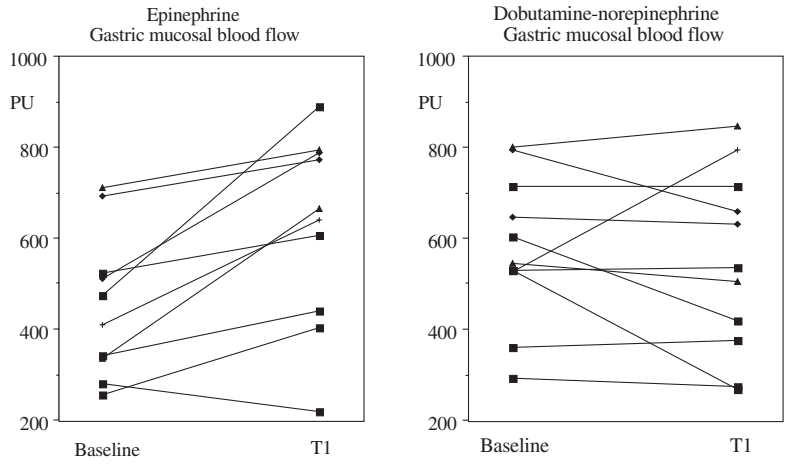
In septic shock, the effects of catecholamines on gastrointestinal blood flow remain controversial. The aim of our study was to compare epinephrine (E) to the combination dobutamine–norepinephrine (D–N) on gastric perfusion in septic shock patients.

Methods: The study was prospective, randomized, on two parallel groups. Systemic and pulmonary hemodynamics, gastric mucosal blood flow (GMBF, laser Doppler), hepatic function (indocyanine green clearance) and blood gases were evaluated just before catecholamines infusion and as soon as mean arterial pressure reached 70–80 mmHg. E or N were titrated (from 0.1 μg/kg/min with 0.2 μg/kg/min increases every 5 min). D was continuously infused at 5 μg/kg/min.

Results: Twenty-two patients were included (11 in each group). At randomization, there was no significant difference between groups. At time of evaluation, mean arterial pressure was 78 ± 3 and 77 ± 5 mmHg in E and D–N groups, respectively. There was no significant difference between groups whichever the systemic and pulmonary hemodynamic or blood gas variable considered. Nevertheless, compared to D–N, E tended to induce greater values of cardiac index (5.0 ± 1.6 vs 4.2 ± 1.5 l/min/m^2, $P=0.078$) and oxygen transport (617 ± 166 vs 481 ± 229 ml/min/m^2, $P=0.068$), induced significantly greater values of GMBF (662 ± 210 vs 546 ± 200 units, $P=0.011$) but did not modify indocyanine green clearance.

Conclusion: In septic shock patients, at the same mean arterial pressure, E enhances more GMBF than the combination of D at 5 μg/kg/min and N (see Fig. overleaf). This effect, which probably results from higher cardiac index, emphasizes the crucial importance of doses in the pharmacodynamic profile of catecholamines.

Figure



P131 Terlipressin in the treatment of catecholamine resistant septic shock

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Introduction: Vasopressin plasma levels are low in advanced septic shock and treatment with low dose vasopressin can reverse catecholamine resistance [1]. Terlipressin, a vasopressin analogue with long half life time, was found to exert less gastrointestinal and myocardial side effects in patients with acute variceal hemorrhage compared with vasopressin. Little is known about effects and side effects of terlipressin administration in patients with septic shock.

Methods: Retrospective study of 14 patients with acute liver failure and septic shock treated with terlipressin for norepinephrine resistant shock. Seven patients were monitored with gastric tonometry during terlipressin therapy. Hemodynamic and metabolic parameters as well as liver function tests were measured sequentially over a 72 hour period and compared to base line levels with ANOVA for repeated measurements.

Results: One to 3 mg of terlipressin were administered in divided doses over 24 hours. There was an increase in blood pressure (MAP) accompanied by a significant decrease in norepinephrine (NE) requirements over time. Nine patients were weaned off catecholamine support. Cardiac index, stroke volume (SVI) and metabolic parameters as well as liver function tests remained unchanged. The mucosal-arterial Pco_2 gap increased significantly over time indicating impaired gastric mucosal perfusion. There was no improvement in the severity of organ failure (SOFA) during terlipressin treatment (Table).

Conclusion: Terlipressin can reverse vasopressor resistant septic shock. The increase in mucosal-arterial Pco_2 gradient during terlipressin treatment raises concerns of significant gastrointestinal side effects associated with this novel therapy.

Reference:

1. Landry DW, Levin HR, Gallant EM, *et al.*: **Vasopressin deficiency contributes to the vasodilation of septic shock.** *Circulation* 1997, **95**:1122-1125.

Table

	Pre	1 hour post	4 hours	12 hours	24 hours	48 hours	72 hours
n/n_{Tono}	14/7	14/7	14/7	14/7	12/6	11/6	10/5
MAP	69 ± 5	81 ± 12†	81 ± 15*	73 ± 10	71 ± 7	74 ± 9	73 ± 10
NE‡	0.48 ± 0.41	0.41 ± 0.38	0.34 ± 0.35	0.33 ± 0.33	0.25 ± 0.25	0.20 ± 0.22	0.19 ± 0.31
SVI	63 ± 21	63 ± 26	64 ± 19	55 ± 14	71 ± 26	64 ± 15	65 ± 28
$Pco_{2\ r\text{-}a}$	1 ± 0.4	1.5 ± 0.3	1.7 ± 0.6	1.9 ± 0.5	2.7 ± 0.7	2.8 ± 0.2*	3.3 ± 0.5*
Lactate	2.8 ± 1.4	3.1 ± 1.8	3.1 ± 1.9	2.9 ± 1.2	2.9 ± 2.2	3.3 ± 2.8	3.8 ± 3.1
SOFA	18 ± 4				18 ± 2	18 ± 3	17 ± 3

All values mean and SD. * $P < 0.05$, † $P < 0.01$, ‡ $P < 0.05$ for all time points compared to base line.

P132 Arginine vasopressin compromises gut mucosal microcirculation in septic rats

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Background: Arginine vasopressin (AVP) is increasingly used in the therapy of septic patients with hypotension [1]. In a prospective, controlled laboratory experiment we studied AVP-associated changes in the villus microcirculation of the septic rat ileum.

Methods: Twenty-four hours after caecal ligation and perforation to create sepsis, moderately hypotensive rats (average decrease in mean arterial pressure [MAP] 20% from pre-septic values) were anaesthetized. Next, intravital video-microscopy was performed on 6–10 villi of ileum mucosa (M_0). The treatment group then received a continuous infusion of AVP to increase MAP by 20 mmHg (M_1) and 40 mmHg (M_2) from M0, while the control group received only normal saline. Measurements were repeated at M_1 and M_2. Video recordings were analysed by a blinded investigator. Diameter of terminal arterioles (Art_d) were determined and stopped flow across the villus microcirculation (total arrest of villus blood flow > 1 s) was quantified.

Statistics: ANOVA with *post-hoc* test (Student–Newman–Keuls). Data are mean ± SD.

Results: AVP infusion was associated with a clear increase in stopped flow time at M_1 and M_2, while no change was observed for Art_d (Table).

Conclusion: These preliminary data demonstrate severe abnormalities in gut mucosal blood flow following AVP infusion in septic rats. Because no change occurred in terminal arteriolar diameters, the observed flow abnormalities could be due to either activities of AVP on larger arterioles or to a concomitant reduction in cardiac output [1].

Reference:
1. Holmes CL, *et al.*: *Chest* 2001, **120**:989-1002.

Table

	Control ($n = 5$)			AVP ($n = 5$)		
	M_0	M_1	M_2	M_0	M_1	M_2
MAP (mmHg)	114 ± 7	109 ± 14	104 ± 11	108 ± 4	128 ± 5*	149 ± 4*
Art_d (μm)	8.04 ± 0.78	7.63 ± 1.15	8.1 ± 0.71	7.12 ± 0.38	7.29 ± 0.59	7.42 ± 0.71
Stopped-flow (s min^{-1})	8 ± 3.5	6 ± 5.8	7 ± 5.2	11 ± 4.3	36 ± 11.2*†	41 ± 9.4*†

* $P < 0.001$ vs M_0, † $P < 0.001$ AVP vs control.

P133 Effect of a maldistribution of microvascular blood flow on capillary O_2 extraction in sepsis

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Inherent in remote organ injury caused by sepsis is a profound maldistribution of microvascular blood flow [1]. Using a 24-hour rat cecal ligation and perforation model of sepsis, we studied oxygen transport in individual capillaries of the extensor digitorum longus (EDL) skeletal muscle. We hypothesized that erythrocyte oxygen saturation (SO_2) levels within *normally* flowing capillaries would provide evidence of either a mitochondrial failure (increased SO_2) or an oxygen transport derangement (decreased SO_2). Using a spectrophotometric functional imaging system [2] we found that sepsis caused (1) an increase in stopped flow capillaries (from 10% to 38%, $P < 0.05$); (2) an increase in the proportion of fast flow to normal flow capillaries ($P < 0.05$); and (3) a decrease in capillary venular-end SO_2 levels from 58.4 ± 20.0% to 38.5 ± 21.2%, while capillary arteriolar-end SO_2 levels remained unchanged compared to sham group. Capillary oxygen extraction increased three-fold ($P < 0.05$) and was directly related to the degree of stopped flow in the EDL. Our results support the hypothesis that tissue capacity to increase O_2 extraction in early sepsis is impaired by a maldistribution of O_2 delivery and not a failure to utilize O_2.

References:
1. Bateman RM, *et al.*: **Erythrocyte deformability is a nitric oxide-mediated factor in decreased capillary density during sepsis.** *Am J Physiol Heart Circ Physiol* 2001, **280**:H2848-H2856.
2. Ellis CG, *et al.*: **Determination of red cell oxygenation in vivo by dual video densitometric image analysis.** *Am J Physiol Heart Circ Physiol* 1990, **258**:H1216-H1223.

P134 Changes in complement cascade during continuous hemodiafiltration (CHDF) in patients with sepsis

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Introduction: Sepsis results from activation to complement cascade, an appropriate and necessary response to infection. Some studies have demonstrated that CHDF could be an effective therapy for removing inflammatory cytokines for systemic inflammatory response syndrome (SIRS). The aim of this study is to evaluate the changes in the complement cascade during CHDF and to determine the effect of CHDF on sepsis.

Methods: Ten patients with sepsis underwent CHDF for at least 3 days in our ICU. Patients with chronic renal failure or receiving steroid therapy were excluded. We assessed complement function and concentrations or activities of CH50, C1q, C3a, C3-proactivator, C3, C4, albumin and C-reactive protein (CRP). Blood samples were obtained from an arterial catheter before and 3 days after the start of CHDF. Blood samples from both membrane sites and the CHDF filtrate were obtained at 2, 6 and 12 hours after the start of CHDF. Statistical analysis was performed on the changes during CHDF and both sites of the membrane ($P < 0.05$).

Results: Six patients survived (S-group) and four patients did not survive (N-group). Levels of C3a before CHDF were extremely high and decreased significantly during CHDF in survived group. The levels of CH50 and C3 before CHDF were low, but did not change significantly during CHDF. The levels of C1q, C4, and C3 pro-activator were within their normal ranges, and did not change during this study. CH50 and C3a were detected in CHDF filtrate. Only the levels of C3a increased significantly through the dialysis membrane.

Conclusions: It was thought that high levels of C3a indicated activation of the complement cascade and low levels of CH50 and C3 occurred due to consumption during sepsis. CHDF can be an effective therapy for sepsis because C3a (chemotactic factor) decreased significantly during CHDF. The complement cascade except for C3a did not change during CHDF in this study. However CHDF may have the potential to activate the complement cascade because the levels of C3a increased through the dialysis membrane.

P135 Arterio- and veno-venosus hemofiltration in the treatment of sepsis and septic shock

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Many inflammatory agents are known to be released in huge quantities in septic shock. The level of the agents could be decreased by the continuous arterio-, and veno-venosus hemofiltration (CAVH and CVVH).

Our study was conducted to remove the inflammatory mediators from the circulation by the assistance of the CAVH and the control of the hemodynamic stability.

Method: Forty-eight patients was applied on the study. The hemodynamic parameters were measured with the thermodilution technique. The mean arterial pressure (MAP), the pulse (F), the cardiac output (CO), the pulmonary wedge pressure (PCWP), the systemic vascular resistance (SVR), the left and right ventricule work-index (LVSWI, RVSWI) were measured, The oxygen delivery and consumption (DO_2, VO_2), the serum lactate level were estimated. The inflammatory parameters – C-reactive protein, procalcitonin, white blood cell – were controlled daily. The laboratory tests of fluid balance and inonogram (Na, K in the urine), the clinical signs (temperature, consciousness, APACHE II score) were assessed daily.

Results: The hemodynamic parameters were stable: CO: 9.6–7.8 l/min, SVR: 541–789 dyns cm^{-5}, the tissue oxygenation was improved (DO_2 7.5–16.7 ml/min/kg, VO_2 1.24–3.4 ml/min/kg). The temperature of patients were decreased (39.2–37.4°C), the urine increased (22.4–43.5 ml/kg/die), the APACHE II score decreased (28.4–19.7) and the GCS (7.8–11.4) increased. The inflammatory parameters were on the normal level after 2 days of the CAVH (CRP: 261–61. PCT: 10–0.5 ng/ml).

The hemodynamic effect of the CAVH or CVVH was favourable, the heart function was improved, the fluid-, and ion-balance could have been controlled well.

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2. Bellomo R, *et al.*: **Continous renal replacement therapy.** *Int J Intensive Care* 2000, **7**:22.
3. Rogiers P: **Hemofiltration treatment for sepsis. Is it time for control trial?** *Kidney Int Suppl* 1999, **72**:S99.

P136 Coupled plasmafiltration-adsorption (CPFA) in septic shock with normal renal function

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Multi-organ dysfunction syndrome (MODS) is the most frequent cause of death in patients admitted to intensive care units. Severe sepsis and septic shock are the primary causes of MODS and develop as a result of the host response to infection and to bacterial wall components, such as the lipid-A containing lipopolysaccharide (LPS). The host response involves both the cellular and humoral arms of the immune system and the generation of pro- and anti-inflammatory molecules. The anti-inflammatory response may lead to a state of 'immunoparalysis'. Continuous renal replacement therapies (CRRT) remove several soluble pro- and anti-inflammatory mediators simultaneously, albeit at low rates. However, large pore membranes, such as those used for plasmafiltration, may enhance cytokine removal and clearance. We recently observed that the use of coupled plasma filtration adsorption (CPFA) improved survival in a rabbit model of septic shock [1]. The outcome was not correlated with single cytokines or mediators (such as TNFα, platelet-activating factor or endotoxin), but rather with a global sepsis severity score. The results of this study suggested that a non-selective removal of various septic mediators was beneficial. A pilot, prospective, cross-over study tested the hypothesis that CPFA combined with hemodialysis might exert similar beneficial effects on hemodynamics and leukocyte responsiveness in humans with established septic shock and that it might prove superior to continuous veno-venous hemodiafiltration (CVVHDF) alone [2].

Objective: To assess the effect of continuous plasmafiltration adsorbtion (CPFA) on biochemical markers of inflammation, cytokines, organ dysfunction, haemodynamic and 28-day mortality in human sepsis.

Design: Prospective.

Setting: Intensive care unit.

Patients: Five patients (3 males and 2 female; mean age 52 ± 19.9 years) with clinical evidence of infection and septic shock were enrolled. Three patients had normal renal function.

Interventions: All patients received protocol-driven supportive intensive care, and those randomized to CPFA received intermittent plasma treatment (10 hours a day) for 10 days using a two-step, modular system made of plasma separation and adsorption on a hydrophobic resin, with final reinfusion of the plasmafiltrate into the patient's line before the hemofilter.

Measurements and main results: Illness severity and risk of death were calculated with the Acute Physiology and Chronic Health Evaluation II (adults) scales. Plasma samples were assayed for acute-phase proteins (C-reactive protein and cytokines [interleukin-6, interleukin 10]). The Apache II score before treatments was 26 ± 5.6, after 14 ± 3.5. Statistically significant improvements were recorded about the differences pre/post treatments concerning Mean Arterial Pressure 78 ± 14.9 vs 86 ± 18.3 mmHg ($P < 0.0001$), Cardiac Index 3.88 ± 1.03 vs 3.24 ± 0.86 l/m^2/min ($P < 0.001$), Systemic Vascular Resistances 1423 ± 552 vs 1862 ± 657 dyne × s/cm^5 ($P < 0.001$), PaO_2/FiO_2 ratio 199 ± 70 vs 244 ± 81 ($P < 0.001$). Laboratory data showed a sharp decline of C-reactive protein along the treatment time from 29.7 ± 11.4 to 6.9 ± 4.8 (–77%); data concerning IL-6, IL-10 showed a reduction to 2.8%, 36.6% in respect of starting values. All patients but one were discharged alive from ICU after 36.8 ± 14.1 days (range 18–57).

Conclusions: CPFA caused a significant attenuation of the acute-phase response in sepsis. The procedure induced a sort of immunomodulation process, and showed a reduction of both pro-inflammatory and anti-inflammatory immunoactive mediators. Our data suggest that this procedure might be beneficial in septic shock patients despite the absence of acute renal failure.

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P137 Myocardial efficiency during levosimendan infusion

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Levosimendan (LS) is a novel agent indicated for the treatment of acute decompensated heart failure. It has a dual mechanism of action, increasing cardiac contractility without increasing myocardial oxygen demand as well as demonstrating vasodilator properties.

This double-blind, randomised, cross-over trial was conducted to assess the effects of LS on myocardial energetics in patients ($n = 8$) with New York Heart Association functional class III and IV heart failure. Patients initially received either placebo or intravenous LS (18 μg/kg bolus, followed by a continuous infusion of 0.3 μg/kg/min for 5 hours). The following day, patients who had received LS were given placebo and vice versa. Cardiac loading conditions and cardiac output (CO) were assessed using a Swan–Ganz catheter, thermodilution and echocardiography. Dynamic positron emission tomography (PET) with ^{11}C-acetate and ^{15}O-H_2O was used to measure myocardial oxygen consumption (MVO_2) and myocardial blood flow (MBF), respectively. Myocardial efficiency was calculated as (heart rate × stroke volume × arterial pressure) / ventricular oxygen consumption.

CO increased by 32% ($P = 0.002$) in patients receiving LS, mainly because of an increase in stroke volume. LS significantly reduced pulmonary capillary wedge pressure by 29% ($P = 0.013$), systemic vascular resistance by 26% ($P < 0.001$) and pulmonary vascular resistance by 28% ($P = 0.025$). Mean MBF was 0.76 ml/min/g with placebo and 1.02 ml/min/g with LS ($P = 0.033$). LS did not increase MVO_2 significantly (8%). Left ventricular efficiency was comparable in LS-treated and placebo-treated patients, while right ventricular efficiency was improved by 24% ($P = 0.012$) with LS.

In conclusion, LS as well as having beneficial haemodynamic effects, also has an energetically favourable profile.

P138 Effect of β-blockade on the haemodynamic responses of levosimendan and dobutamine in the treatment of low-output heart failure

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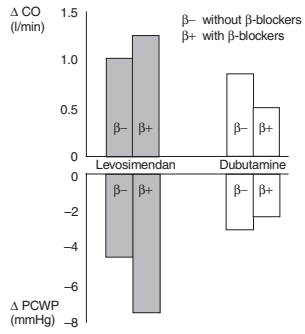
The novel calcium sensitiser, levosimendan (LS), and the β-adrenoceptor agonist dobutamine (DO), both improve cardiac haemodynamics in patients with severe low-output heart failure (HF). However, co-administration of β-blockers may influence the action of these inotropic agents.

In a multicentre, randomised, double-blind trial in patients with severe low output HF ($n = 203$), the haemodynamic effects of LS and DO infusions over 24 hours were compared. The influence of concomitant β-blocker therapy (37% in the LS and 39% in the DO groups) were analysed separately. Patients were given either LS (loading dose of 24 μg/kg over 10 min followed by a continuous infusion of 0.1 μg/kg/min), or DO (continuous infusion of 5 μg/kg/min). The infusion rates were doubled if the cardiac index did not increase by ≥ 30% after 2 hours of treatment.

Figure 1



The use of β-blockers had significant effects on the increase in cardiac output and the decrease in pulmonary wedge pressure ($P = 0.01$ and $P = 0.03$, respectively) (Fig. 1). β-blockade attenuated the effect of DO but did not reduce the effects of LS. There was even a slight trend for improved haemodynamic benefits of LS in patients under β-blockade. These findings suggest that LS may be successfully combined with β-blockers to treat patients with low-output heart failure.

Mean changes in cardiac output (CO) and pulmonary capillary wedge pressure (PCWP) in patients given LS (β– $n = 69$ and β+ $n = 33$) and DO (β– $n = 67$ and β+ $n = 28$).

P139 Effects of levosimendan on cardiac arrhythmia in patients with severe heart failure

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Levosimendan (LS) is a novel calcium sensitiser which enhances cardiac contractility without increasing myocardial oxygen consumption, and induces vasodilation.

The effects of intravenous LS on cardiac arrhythmias in patients with moderate-to-severe heart failure were examined. The results of ambulatory electrocardiograms in 386 patients from 10 randomised, double-blind studies have been pooled (254 patients received LS and 132 patients received placebo).

No significant differences in baseline haemodynamic parameters were observed between the LS and placebo groups. Furthermore, mean 24-hour heart rate did not differ significantly between the two treatment groups (78 beats/min and 74 beats/min in LS and placebo groups, respectively). There were no differences in the occurrence or frequency of new supraventricular tachycardia (SVT), ventricular tachycardia (VT) or an increase in ventricular complexes (Morganroth's criteria) (Table 1). One patient in the placebo group experienced ventricular fibrillation, while no cases of torsades des pointes were observed with either treatment.

Table 1

Percentage of patients with supraventricular tachycardia (SVT), ventricular tachycardia (VT) or increase in premature ventricular complexes (PCV) after receiving levosimendan or placebo

	SVT	VT	Increase in PCV
Levosimendan	5%	12%	8%
Placebo	5%	15%	9%

In conclusion, these data suggest that LS has little potential to induce life-threatening arrhythmias in patients with severe heart failure.

P140 The effects of levosimendan on myocardial oxygen consumption and coronary blood flow early after coronary artery bypass grafting

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Levosimendan (LS) is a myocardial calcium sensitiser indicated for the treatment of acute decompensated heart failure. This randomised, double-blind trial evaluated the haemodynamic effects of LS in low-risk patients ($n = 23$) following coronary artery bypass surgery. The effects of LS on myocardial oxygen (O_2) consumption, coronary blood flow and systemic haemodynamics were measured by thermodilution. Patients received LS, 8 μg/kg ($n = 8$), or LS, 24 μg/kg ($n = 7$), or placebo ($n = 8$) as a 5-min infusion 1 hour after surgery. Measurements of systemic and coronary sinus haemodynamics, myocardial O_2 consumption and cardiac substrate utilisation were made, before and after treatment with LS.

Levosimendan, 8 μg/kg and 24 μg/kg, significantly increased cardiac output (CO) by 0.7 and 1.6 l/min, respectively ($P < 0.05$), compared to baseline. Mean arterial pressure and pulmonary vascular resistance decreased significantly with both doses of LS, as did coronary artery resistance, the latter being indicative of coronary vasodilation ($P < 0.05$). Furthermore, an increase in coronary blood flow of 28 ml/min and 42 ml/min with LS, 8 μg/kg and 24 μg/kg, respectively, was obtained ($P = 0.054$ for both doses combined). Despite the markedly improved cardiac function seen with LS, neither dose significantly increased myocardial O_2 consumption compared with placebo. In addition, no significant differences in myocardial free fatty acid, lactate, pyruvate and glucose utilisation were observed in LS-treated patients compared to placebo controls.

In conclusion, based on the results of this study, LS may be of significant benefit in improving cardiac function in patients with low CO following coronary artery bypass surgery, with no significant increase in O_2 consumption.

P141 Haemodynamic effects of levosimendan in patients during weaning from cardiopulmonary bypass

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Levosimendan (LS) is a calcium sensitiser indicated for the treatment of acute heart failure that possesses a novel dual mechanism of action. It increases both cardiac contractility and induces coronary and systemic vasodilation. In this study the haemodynamic effects of LS were assessed in nine patients (classified as 'high risk') undergoing combined aortic or mitral valve repair/replacement and multiple coronary artery bypass grafting surgery. Immediately after weaning from cardiopulmonary bypass LS, 24 μg/kg,

was given intravenously over 10 min. Haemodynamic data were recorded for up to 60 min post-infusion using thermodilution, 2-D transoesophageal echocardiography and pressure/volume analysis using a Millar 12 pole-conductance catheter with an integrated pressure sensor.

The results (Table 1) show that the LS infusion increased cardiac index (CI), mainly through an increase in stroke index (SI) and a decrease in systemic vascular resistance (SVR). LS treatment improved left ventricular contractility (+d*P*/d*t*) and end-systolic elastance (Ees), without a significant change in the left ventricular isovolumic pressure decline time constant (*Tau*). LS increased coronary graft flow by 32% ($P < 0.05$). No arrhythmias occurred during the 60-min study period.

In conclusion, a 10-min intravenous infusion of LS significantly improved left ventricular function and contractility without impairing the rate of ventricular relaxation.

Table 1

Haemodynamic parameters (mean ± SD) before and after the administration of levosimendan

	CI (l/min/m^2)	SI (ml/m^2)	SVR (dyn/s/cm^5)	+d*P*/d*t* (mmHg/s)	Ees (mmHg/ml)	*Tau* (ms)
Baseline	2.6 ± 0.5	30 ± 7	950 ± 374	766 ± 113	1.1 ± 0.2	42 ± 5
Peak effect	3.9 ± 0.9*	46 ± 10*	669 ± 224*	966 ± 131*	1.5 ± 0.2*	39 ± 5

*$P < 0.05$ compared with baseline; CI, cardiac index; SI, stroke index; SVR, systemic vascular resistance; +d*P*/d*t*, measure of left ventricular contractility; Ees, end-systolic elastance; *Tau*, time constant of isovolumic pressure decay

P142 Levosimendan enhances cardiac performance in patients following cardiac surgery and cardiopulmonary bypass

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This randomised, double-blind, placebo-controlled trial tested the effect of the calcium sensitiser levosimendan (LS) on cardiac performance in patients ($n = 18$) following cardiopulmonary bypass (CPB) and cardiac surgery.

Patients with normal preoperative left ventricular function received either placebo or 'low-dose LS' (18 μg/kg loading dose followed by 0.2 μg/kg/min) or 'high-dose LS' (36 μg/kg loading dose followed by 0.3 μg/kg/min) infusions, starting 15 min prior to separation from CPB ($n = 6$ per group). Treatments were continued for 6 hours. Haemodynamic and cardiac output (CO) measurements were recorded at baseline and following separation from CPB in all groups.

LS significantly ($P < 0.05$) increased CO (from 4.2 to 7.9 l/min) (high-dose) and similarly decreased systemic vascular resistance (from 1150 to 512 dyn/s/cm^5; $P < 0.05$). Arterial and pulmonary artery pressures were significantly reduced by LS. Heart rate was not significantly changed, but stroke volume increased with LS. No differences in arterial oxygenation and perioperative arrhythmias (Holter) were seen between groups.

In conclusion, this study suggests that LS enhances cardiac performance in patients with normal preoperative cardiac function following CPB. The 'low-dose LS' demonstrated equivalent efficacy with the 'high-dose' group but had the advantage of not increasing vasoactive drug requirements.

P143 Ibutilide for pharmacological cardioversion of atrial flutter

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Introduction: Ibutilide an anti-arrhythmic drug (Vaughn Wiliams Classification Type III) is used to support the cardioversion of atrial fibrillation and atrial flutter since some years yet. In some countries ibutilide is also used as an emergency treatment for the pharmacological cardioversion of new arised atrial flutter instead of electroversion. In this prospective study the effectiveness and safety of this emergency treatment were investigated.

Methods: We included all patients with atrial flutter seen in the emergency department. All patients received a treatment with 1.0 mg ibutilide infusion over 10 min. During this period monitoring of heart rate and blood pressure was performed. Later on a telemetric observation of ECG was performed over a period of 24 hours.

Results: The procedure was performed in seven patients with a mean age of 62 ± 12.7 (SD) years. At admission the atrial flutter was persistent meanly for 5 ± 10.1 days (range 1–28 days). The mean size of the left atrium was 44 ± 4.2 mm (range 40–49 mm). In four patients a coronary heart disease was diagnosed. In five patients a stable sinus-rhythm after solitary treatment with ibutilide was recorded. Electroversion after the ibutilide infusion had to be performed in two patients to achieve a stable sinus-rhythm after recurrent atrial flutter. No complications, especially no ventricular tachycardia, occurred during the observation period. In all patients a stable sinus-rhythm could be recorded.

Conclusion: In patients with atrial flutter a pharmacological cardioversion with ibutilide should be performed. Also in patients with chronically atrial flutter and/or dilated left atrium the pharmacological cardioversion is promising a safe and minimally invasive alternative to electroversion.

P144 Ibutilide after unsuccessful electric electroversion of atrial fibrillation

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Introduction: Ibutilide, an anti-arrhythmic drug (Vaughn Wiliams Classification Type III) is used to support the Cardioversion (CV) of atrial fibrillation and atrial flutter since some years yet. Under usage of ibutilide lower energy charges for electroversion and higher rates of success have been reported.

Methods: In this prospective study all patients with atrial fibrillation received, after unsuccessful synchronized electroversion with increased energy charges till 360 J, 1.0 mg ibutilide within 10 min. After that procedure a new electroversion was performed. The success-rates have been reported.

Results: The procedure was performed in 18 patients with a mean age of 62 ± 11.2 (SD) years. At admission the atrial fibrillation was persistent meanly for 333 ± 934.1 days (range 1–4000 days). The mean size of the left atrium was 48 ± 7.4 mm (range 30–60 mm). In four patients a coronary heart disease was diagnosed. In 15 patients a stable sinus-rhythm (SR) could be reported after the ibutilide infusion and further electroversion with 360 J. In two patients SR could be reported after the ibutilide infusion without any further electroversion. In one patient the atrial fibrillation was persistent although he received the therapy with ibutilide. No side-effects, especially no ventricular tachycardia, occurred.

Conclusion: In patients with atrial fibrillation and unsuccessful electroversion a new try should be performed after infusion of 1.0 mg ibutilide. Also in patients with chronically atrial fibrillation for years and/or dilated left atrium this procedure is promising a safe and minimally invasive help for a successful electroversion.

P145 Acute atrial fibrillation (AAF) in cardiac surgery postoperative period (PP): its influence in mortality, intensive care and hospital length of stay (LOS) and costs

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Background: AAF in cardiac surgery postoperative period has been implicated as a complication that leads to longer ICU and hospital stay and to augmented costs. However, it has not been associated with increased mortality rates.

Objective: To determine possible correlation between the occurrence of AAF and length of SICU LOS, total hospital LOS, costs and mortality.

Patients and methods: Three hundred and fifty adult patients consecutively admitted in the immediately postoperative period were prospectively evaluated between June 2000 and November 2001. Those with previously documented atrial flutter or atrial fibrillation were excluded. Patients were included in Group (G) A when AAF did not occur in the PP and in G B when it occurred. Statistical techniques were: *t* Student test, Fischer test and linear regression.

Results: G A included 263 and G B 87 patients (24.8%). The hospital mortality shows no statistically significant difference (15 patients in G A [5.7%] and 6 in G B [6.8%] – $P = 0.7$). The mean SICU LOS was significantly higher in G B (4.47 ± 6.4 days in G A versus 9.74 ± 12.6 days in G B – $P < 0.001$), as well as the hospital LOS (9.26 ± 12.7 days in G A versus 13.69 ± 11.4 days in G B – $P < 0.001$). Hospital costs were increased in 61.9% by AAF occurrence ($P = 0.0025$). G A hospital cost was U$8485.23 ± 9509.54 against U$13,740.34 ± 16,849.1 of G B. Linear regression shows relation between costs and SICU LOS and hospital LOS.

Discussion: AAF was a common complication in these postoperative patients. It was not associated with increased mortality, but it was shown a positive correlation between its occurrence and longer SICU LOS and elevated costs. The longer hospital LOS, as well as the higher cost appear to be related to longer SICU LOS.

Conclusions: It is concluded that AAF in the cardiac surgery postoperative setting is a frequent complication and that it is an important marker of longer SICU LOS and of higher hospital costs. Hospital costs have been increased in AAF patients due to longer SICU LOS. Further studies will be needed to determine whether AAF is the real cause or simply a marker of these findings.

P146 The relationship between plasma urotensin II (hU-II) and pulmonary artery occlusion pressure during cardiac surgery: further evidence that hU-II is influenced by cardiac filling pressures

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Introduction: The (patho-)physiological role of human urotensin II (hU-II) – the most potent endogenous vasoconstrictor yet described – remains to be defined [1]. Preliminary evidence suggests that hU-II levels during cardiac surgery are increased in patients with myocardial dysfunction [2]. However, it is not known, if hU-II plasma concentrations are related to pulmonary capillary wedge pressure (PCWP) as an estimate of left ventricular filling pressure.

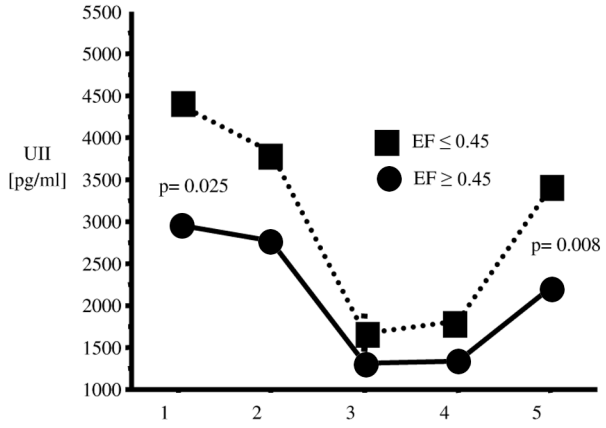
Methods: We investigated 33 consecutive patients during coronary artery bypass (CABG) surgery. Blood was sampled before induction of anesthesia (t1), 20 min after intubation (t2), 10 and 30 min after aortic cross clamping (t3 and t4) during cardiopulmonary bypass (CPB), and 30 min after CPB (t5). Hemodynamic variables (including PCWP) were recorded at t2 and t5. hU-II was determined by a commercially available ELISA.

Results: hU-II concentrations decreased during CPB and returned to baseline thereafter (Fig. 1). Plasma hU-II concentrations were significantly correlated with mean pulmonary artery pressure (MPAP) and PCWP before and after CPB (Spearman's rho: range: 0.52–0.62). Patients with a preoperative ejection fraction (EF)

≤ 0.45 had higher hU-II levels before ($P = 0.02$) and immediately after CPB ($P = 0.008$) than patients with an EF ≥ 0.5 (Fig. 1).

Conclusions: The correlation between hU-II concentrations, MPAP and PCWP during CABG surgery and its relation to the preoperative degree of myocardial dysfunction strongly suggest a role of left ventricular filling pressures in the regulation of plasma hU-II in patients with ischemic heart disease.

Figure 1



The course of plasma urotensin II (U-II) during cardiac surgery. For abbreviations and time points see text.

References:
1. Affolter J, Webb DJ: **Urotensin II: a new mediator in cardiopulmonary regulation?** *Lancet* 2001, **358**:774-775.
2. Heringlake M, *et al.*: **Urotensin II plasma levels during cardiac surgery are related to left ventricular function and pulmonary artery pressure: A new peptide in heart failure?** [abstract]. *Crit Care Med* 2001, **29(suppl)**:A52.

P147 Intrahepatic interleukin-10 synthesis during hypothermic cardioplumonary bypass inhibits TNFα synthesis throughout the STAT-3 pathway

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Background and aim: Hypothermic cardiopulmonary bypass stimulates the synthesis of the anti-inflammatory cytokine IL10 and decreases that of TNFα in the organs. This study was intended to analyze the signaling pathways involved in the suppressive effects of IL10 on intra-hepatic TNFα gene expression

Methods: Twelve young pigs were assigned to a temperature (T°) regimen during standardized CPB: normothermia (T° 37°C; $n = 6$) and moderate hypothermia (T° 28°C; $n = 6$). Six hours after termination of CPB, liver tissue was sampled. Intra-hepatic gene expression and synthesis of TNFα IL10, and of the suppressor of cytokine signalling SOCS-3 were detected and quantified by competitive RT-PCR and by Western blot. DNA binding activity of the transcription factors NF-κB and STAT-3 was detected by eletrophoretic-mobility-shift assay (EMSA) and super shift, and phosphorylation of IκB-α and STAT-3 by Western blot. Cellular origin of TNFα and IL10 was assessed by immunohistochemical staining.

Results: Synthesis of IL10 and SOCS-3 were significantly higher, while that of TNFα was significantly lower, in pigs that were in moderate hypothermia during cardiac surgery than in the others. Hepatocytes themselves produced IL10 but not TNFα after cardiac surgery with CPB. Pigs under moderate hypothermia also showed significantly higher phosphorylation of STAT-3 and DNA binding activity of STAT-3 6 hours after CPB but no lower phosphorylation of IκB-α and DNA binding activity of NF-κB than animals operated on in normothermia.

Conclusion: Suppression of TNFα synthesis during moderate hypothermic CPB by IL10 is dependent on the activation of the transcription factor STAT3- and of the activity of the regulatory SOCS-3, but not on the suppression of the activity of NF-κB.

P148 Methylprednisolone sodium succinate reduces postoperative hyperthermia but does not affect cardiac function after aortic valve replacement

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Objective: Steroids have been used in cardiac surgery for many years to reduce the inflammatory response associated with extracorporeal circulation. However, their clinical benefits have not been well established. The aim of the present study was to evaluate the effect of methylprednisolone on body temperature and cardiac index in the postoperative period of aortic valve replacement with extracorporeal circulation and aortic clamp.

Patients: Twenty-two consecutive patients undergoing aortic valve replacement and extracorporeal circulation. The patients received methylprednisolone (30 mg/kg; $n = 11$, MP group) or received no medication ($n = 11$, no MP group) before cardiopulmonary bypass. Clinical and demographic characteristics of the patients were similar in both groups.

Figure 1

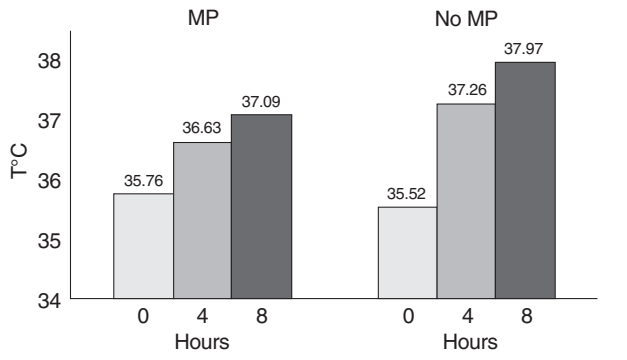
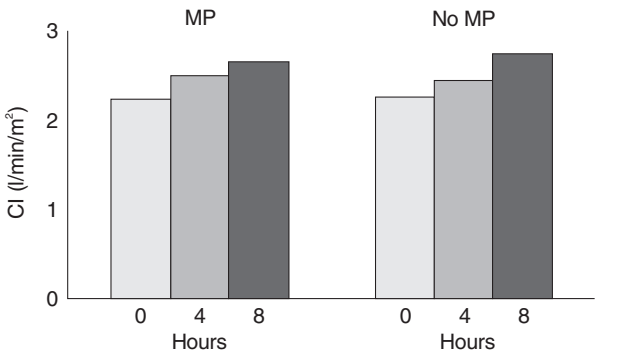


Figure 2



Measurements and main results: Body temperature (T°, °C) and cardiac index (CI, l/min/m²) were measured in the postoperative period on admission in the ICU and at 4 hours and 8 hours after ICU admission. On admission to ICU there were no differences in temperature between groups. Body temperature was significantly lower in group MP at 4, and 8 hours after ICU admission ($P < 0.05$) (Fig. 1).Cardiac index increased during the postoperative period, with no significant differences between groups (Fig. 2).

Conclusion: Methylprednisolone sodium succinate reduces hyperthermia without affecting cardiac function in the postoperative period of aortic valve replacement with extracorporeal circulation and aortic clamp.

P149 Hemostatic and fibrinolysis markers in serum and shed mediastinal blood after elective coronary artery bypass grafting

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Objective: Reduction of homologous blood products in cardiac surgery is mainly achieved by autologous blood salvage. One of the most customary methods consists in autotransfusion of shed mediastinal blood within the first 6 hours after surgery. Aim of this prospective study was to compare serum and shed mediastinal blood qualities of hemostatic and fibrinolysis markers early after elective coronary artery bypass grafting (CABG).

Methods: Forty-seven patients (mean age 68.1 ± 6.9, 15 female/32 male) underwent first-time elective CABG with extracorporal circulation via median sternotomy. Activated partial thromboplastin time (aPTT), prothrombin time (Quick's value), international normalized ratio (INR), thrombin time, and fibrinogen (factor I) in arterial blood and shed mediastinal blood were measured after admission to the ICU and 6 hours after unclamping the aorta.

Results: Mean loss of mediastinal shed blood was 207 ± 127 ml within the first 6 hours after unclamping the aorta. All tests showed that the shed mediastinal blood contained significantly elevated concentrations or activities of all biochemical parameters indicating blood activation or clotting (Table 1).

Conclusions: Mediastinal shed blood is excessively activated regarding coagulation and fibrinolysis. In patients undergoing transfusion of higher quantities of shed blood might cause postoperative excessive bleeding.

Table 1

	After admission to the ICU			6 hours after unclamping the aorta		
	Shed blood	Serum	*P*	Shed blood	Serum	*P*
Quick's value (%)	34	83	< 0.001	22	92	< 0.001
INR	2	1.18	< 0.001	2.12	1.1	< 0.001
APTT (s)	> 120	52	< 0.001	> 120	46	< 0.001
Thrombin time (s)	> 120	18.6	< 0.001	> 120	14.9	< 0.001
Fibrinogen (mg/dl)	121	70.5	< 0.001	40	281	< 0.001

P150 Acute atrial fibrillation (AAF) in cardiac surgery postoperative period: evaluation of preoperative and peroperative factors associated with its higher incidence

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Background: AAF in cardiac surgery postoperative period is implicated in implements in hospital length of stay and costs. Some preoperative and peroperative factors have been associated to a higher incidence of the arrhythmia. Advanced age, longer surgery time, mitral valve surgery (MVS) and stopping beta-blockade have been described.

Objectives: To evaluate some preoperative and peroperative factors in order to identify those patients with higher probability for cardiac surgery postoperative AAF.

Patients and methods: Three hundred and fifty adult patients consecutively admitted in postoperative period of cardiac surgery were prospectively followed. Clinical and surgical variables were collected and then compared between patients who developed AAF in postoperative period and those who did not. Statistical techniques were: Student *t*-test and Fischer test.

Results: In the patients submitted to cardiac arterial by-pass surgery (CABS), the mean age in the two groups were significantly different (69.98 ± 9.67 years old in AAF patients and 62.89 ± 10.65 years old in no AAF patients – $P < 0.0001$). Water retention during surgery was higher in AAF patients ($P = 0.05$) while water retention on the first postoperative day was also higher in AAF patients but P value was 0.07. Left atrial diameter, body mass index, surgery time, extra corporeal circulation time, aortic clamping time, diagnostic of diabetes and chronic obstructive pulmonary disease, lactate and creatinine levels and PaO_2/FiO_2 ratio were not statistically different in the two groups. Postoperative AAF incidence was higher in MVS when compared to non-MVS (43.4% versus 22.6% with $P < 0.01$).

Conclusion: Advanced age, water retention and Mitral Valve Surgery were shown to be predictors for AAF in cardiac postoperative period. The other factors analyzed did not influence the incidence of the arrhythmia but further analyses are needed.

P151 Methemoglobin formation in children with congenital heart disease treated with inhaled nitric oxide after cardiac surgery

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Background: Inhaled nitric oxide is used as a therapy of pulmonary hypertension in children after cardiac surgery. Hemoglobin binds to nitric oxide with great affinity and forms methemoglobin by oxidation in the erythrocyte. Once produced, methemoglobin is unable to transport and unload oxygen in the tissues. The amount of available hemoglobin in the body for oxygen transport is thereby reduced. Anemia, acidosis, respiratory compromise, and cardiac disease may render patients more susceptible than expected for a given methemoglobin level. The goal of the present study was to investigate the effect of inhaled nitric oxide on methemoglobin formation in critical ill children. We therefore measured methemoglobin levels in children with congenital heart disease after cardiac surgery who where treated with inhaled nitric oxide in a range of 5 to 40 ppm.

Methods: We enrolled 38 children with congenital heart disease after cardiac surgery into a retrospective chart review study. We extracted demographic data and physiological measurements at the following time points: (1) T0 = before starting inhaled nitric oxide therapy, (2) T1 = 24 hours after begin of inhaled nitric oxide therapy, (3) T2 = half-time therapy, (4) T3 = end of therapy, (5) T4 = 24 hours after finishing inhaled nitric oxide therapy.

Results: Median duration of inhaled nitric oxide therapy was 5.5 days (quarter percentiles 3/9, range 2–29), nitric oxide concentration at T1 and T2 was 16 ppm (10/20, 5–40) and 12.5 ppm (7.7/20, 2–40) respectively. Median cumulative dose of inhaled nitric oxide was 1699 ppm (809/3122, 193–7018). Methemoglobin levels increased moderately but significantly during therapy (T0 vs T1, $P < 0.05$ and T0 vs T2, $P < 0.001$). Comparing methemoglobin levels during therapy showed a significant difference between: T1 vs T3 ($P < 0.05$), T1 vs T4 ($P < 0.001$) T2 vs T3 and T4 ($P < 0.001$). The highest measured methemoglobin level was 3.9%. Methemoglobin levels correlated positively with the applied inhaled nitric oxide doses at T1 ($r^2 = 0.4086$; $P < 0.01$) and at T2 ($r^2 = 0.5477$; $P < 0.01$). At T1 methemoglobin level was negatively correlated with T1 blood pH value. The overall mortality rate was 13.2% (five of 38 study patients died).

Conclusion: This study extends the findings of previous reports that methemoglobin levels did not cause toxic adverse effects in children with congenital heart disease after cardiac surgery treated with inhaled nitric oxide. We recommend the use of the minimal effective dose of inhaled nitric oxide and continuous monitoring of methemoglobin levels especially in cases of anemia or sepsis.

P152 Fibrinolytic activity in patients with atrial arrhythmias during acute myocardial infarction, treated with streptokinase

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Background: Increased level of plasminogen-activator-inhibitor-1 (PAI-1) reflects impaired fibrinolytic activity and is associated with increased risk for failed fibrinolysis with fibrinolytic agents, including with streptokinase (STK). Atrial arrhythmias (AA) in patients with acute myocardial infarction (AMI) are associated with heart failure and increased mortality. The prognostic role of pre-treatment PAI-1 activity in patients with AA and AMI, treated with STK was evaluated.

Methods: In patients with AMI, treated with streptokinase, pre-treatment PAI-1 levels were estimated by chromogenic method (normal levels 0.5–3.5 U/ml) and the presence or absence of AA assessed. Included were atrial fibrillation and/or flutter and/or tachycardias. We compared pre-treatment variables (PAI-1 included) and in-hospital events in patients with and without AA.

Results: AA were found in 22.4% (26/116) of patients. Among pre-treatment variables, the only statistically significant difference between patients with and without AA was observed in mean pre-treatment PAI-1 levels ($P = 0.0017$). PAI-1 level over 7 U/ml was the most significant independent risk factor for AA ($P < 0.05$, OR 3.5, 95% CI 1.15–10.6). AA were significantly associated with cardiogenic shock, pulmonary edema, cardiopulmonary resuscitation after STK, conduction disturbances and mortality. In-hospital mortality of patient with AA was 23% and 4% without them (OR 6.45, 95% CI 1.66–25.017). Among in-hospital events, cardiogenic shock was the most significant independent predictor of AA.

Conclusions: AA in patients with AMI, treated with streptokinase, were associated with elevated mean pre-treatment PAI-1 levels and increased mortality due to heart failure. Pre-treatment PAI-1 over 7 U/ml was the only independent significant risk for AA during AMI.

P153 Predictive role of plasminogen-activator-inhibitor-1 (PAI-1) in non-ST-segment elevation acute coronary syndrome

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Background: Increased plasma activity of plasminogen-activator-inhibitor-1 (PAI-1) is associated with increased risk for coronary thrombosis, but its role in predicting adverse events in non-ST-segment elevation acute coronary syndrome (ACS) is not yet defined. Therefore, we studied prospectively the role of PAI-1 activity for the 30-days composite endpoint of death and new myocardial infarction (MI) in patients with ACS.

Methods: Fifty-one patients with chest discomfort, but no ST-segment elevation on ECG were admitted to the ICU. PAI-1 levels were estimated at admission and every 12 hours in the first 48 hours by chromogenic method (normal range 0.5–3.5 U/ml), as well as Troponin T (TnT) by electrochemiluminescence immuno method at admission and 8 hours later (normal level up to 0.1 μg/l). After initial medical therapy, in case of recurrent ischemia and/or haemodynamic and/or rhythmic instability, percutaneous interventions (PCI) were performed. Thirty-days mortality and new MI were registered.

Results: The composite 30-days endpoint of mortality and/or new MI was 13.1% (7/51). Between patients with and without composite death and/or new MI statistically significant difference was observed in mean admission PAI-1 levels (5.3 ± 4.2 vs 3.0 ± 2.4 U/ml, $P < 0.05$), highest mean PAI-1 levels in the first 48 hours (5.98 ± 4.1 vs 3.2 ± 2.4 U/ml, $P < 0.05$), mean ICU stay (7.8 ± 7.0 vs 3.1 ± 1.4 days, $P < 0.001$), but nonsignificant difference in mean admission TnT (0.5 ± 0.7 vs 0.4 ± 7.3 μg/l, $P > 0.05$) and highest in-hospital TnT levels (1.4 ± 1.8 vs 0.9 ± 1.5 μg/l, $P > 0.05$). The risk for 30-days mortality and/or new MI was significantly increased only in patients with PAI-1 levels over 5.0 U/ml in the first 48 hours of therapy (OR 17.5, 95% CI 2.05–149.1).

Conclusions: PAI-1 level > 5.0 U/ml during first 48 hours of therapy was the only significant risk for composite 30-days death and/or new MI of patients with non-ST-segment elevation ACS.

P154 Fibrinogen, ejection fraction and Killip classification as mortality prediction factors in acute coronary syndrome

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Background: In patients with acute coronary syndrome, there is a relation between the patient's outcome and multivariate group of coronary risk factors. The aim of this investigation is to develop a predictive equation of mortality in patients with acute coronary disease, taking those factors with mortality risk significantly higher to predict acute coronary disease's outcomes.

Methods: *Patients*: Between April to September 2001, were followed 53 patients with acute coronary disease (18 unstable anginas and 35 acute myocardial infarcts). Ninety-two variables between clinical, laboratory and echocardiography were analyzed. *Statistical analysis*: Database was analyzed using SPSS 9.0 for Windows. Forward stepwise logistic regression model was used to analyze the joint association of multiple covariates with overall mortality. No missing covariate data was found. The result constant and B coefficients was include in the equation (Z function) to predict the patient's outcome. Values of $P < 0.05$ were considered statistically significant.

Results: *Mortality risk*: Logistic regression analysis was used to examine the effects of multiple covariates (92) on the overall mortality risk and we found this major cardiovascular mortality risk factors: age, heart rate, pain duration, blood nitrogen ureic, fibrinogen, Killip and ejection fraction. A new logistic regression analysis was applied to these covariates (8) with the objective to obtain those with prediction power higher to explain the patient's outcome. In this step were included: blood fibrinogen, Killip classification and ejection fraction.

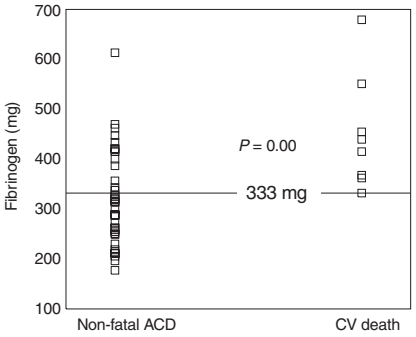
During follow-up, eight of 53 patients died of cardiac causes (15%). The mortality rates of death increased with a fibrinogen ≥ 333 mg/dl (Fig. 1 overleaf; $P = 0.001$, with a mean valor of 405 mg/dl). Likewise the mortality rates increased with Killip classification increases (Fig. 2 overleaf) and with ejection fraction ≤ 48% (Fig. 3 overleaf; $P = 0.001$, with a mean valor of 40.1%).

With these predictors was developed a mortality predictive equation (Z function) using a constant ($K = -11.4997$) and the B coefficients of each covariate (fibrinogen: 0.0268, Killip: 1.947 and ejection fraction: −0.0974). The equation obtained was: death probability (P)= (−11.49) + (0.268 × fibrinogen) + (1.971 × Killip) + (−0.974 × FE%).

The death probability increases when P value increases from 0.5 to 1. The prognostic of patient's outcome was tested and compared with the real patient's outcome. It shows a sensibility 71% and specificity 97%.

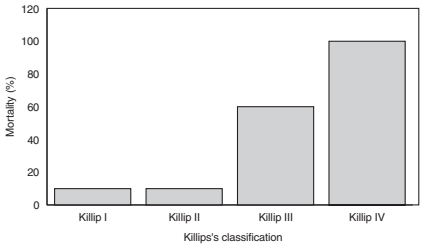
Conclusions: Blood fibrinogen, ejection fraction and Killip classification were major independent covariates that predict patient's outcome in acute coronary disease.

Figure 1



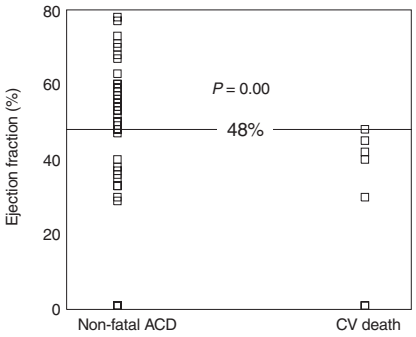
Fibrinogen seric concentrations in patients with non-fatal acute coronary disease (ACD) and cardiovascular (CV) death.

Figure 2



Mortality rates by Killip classification.

Figure 3



Ejection fraction in patients with non-fatal acute coronary disease (ACD) or cardiovascular (CV) death.

P155 Platelet dysfunction in acute coronary syndromes: diagnostic aspects and relation to angiographic patency

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Thrombosis on top of an atheromatus unstable plaque is now accepted as the most common mechanism underlying acute ischemic syndromes (ACS), and in that process platelet dysfunction plays a central pivotal role through interaction with the vessel wall. The present study is an attempt to highlight and re-evaluate the role of platelets in the pathogenesis of ACS via the combined approach of aggregometry and flow cytometry techniques before applying any reperfusion therapy.

Methods: For this purpose we studied 44 individuals who were classified into three groups, group (1): 24 patients (pts) with acute myocardial infarction (AMI) (21 M, 3 F, mean age: 49 ± 11 years), group (2): 10 pts with unstable angina pectoris (UAP) (6 M, 4 F mean age: 49 ± 7 years), and group (3) 10 normal individuals who served as controls (9 M, 1 F, mean age: 27 ± 2 years). All cases were selected in such a way as to be free from gross liver and kidney impairment and were subjected to clinical examination, ECG and echocardiography. Coronary angiography was performed to assess the extent of CAD (the number of lesions in the coronary arteries with more than 50% stenosis as well as the patency of the infarct-related artery according to TIMI flow grading system).

Blood samples were withdrawn from pts on admission to the critical care department of Cairo University before any intervention. Specific lab investigations to assess the platelet activity included measurement of platelet aggregation with ADP, collagen, and ristocetin using the four channels chronolog aggregometer whereas the flow cytometry was employed to assess surface expression of glycoprotein IIb/IIIa receptors.

Results: Compared to healthy control subjects, pts with AMI and UAP had significantly greater aggregatory response to ADP (102%, 105% vs 75%, $P < 0.001$) to collagen (88%, 91% vs 74%, $P < 0.001$) and to ristocetin (77%, 90% vs 71%, $P < 0.001$) and substantially greater number of glycoprotein IIb receptors: (91, 90% vs 73%, $P < 0.001$) and gp IIIa (94, 96% vs 67%, $P < 0.001$) respectively. Platelet aggregatory response to ADP, collagen, and ristocetin had no significant correlation with the number of coronary vessels affected ($P = 0.4$), nor the patency across the culprit vessel ($P = 0.33$).

Conclusion: Compared to the healthy controls and prior to reperfusion therapy, pts with ACS exhibit a significant platelet aggregatory activity. Contrary to our expectations our data clearly show no correlation between platelet activity neither with the number of coronary vessels affected nor with different grades of TIMI flow.

P156 Acute myocardial infarction in patients older than 80 years: 3 years later

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Objective: To analyze the survival and functional capacity 3 years after an acute myocardial infarction in patients older than 80 years.

Methods: It is a retrospective study. We studied all patients admitted from 1 January 1994 to 31 December 1997 with a myocardial infarction who were older than 80 years. The analysis of functional capacity was realized through telephone interview. We analyzed mortality during hospital stay and 3 years after. Used was a daily activity scale (DAS) compounded by five actions (walking, dressing, bathing, cleaning and eating). Each action had a punctuation from 0 to 2 (0 = total dependence, 1 = partial dependence and 2 = independence). The total punctuation had a range from 0 to 10. The statistical analysis was realized by Student *t*-test and values $P < 0.05$ were taken to establish a statistically significant difference.

Results: Studied were 112 patients (48.21% were male). The localization of the myocardial infarction was anterior in 63.39% cases and 77.67% developed Q wave. During hospital stay 41

patients died (36.60%), at the end of the first year 53 patients were dead (50.89% accumulate mortality), and after 3 years 65 patients were dead (the accumulate mortality was 58.03%). The 47 survivors had a mean DAS 8.42 ± 3.01. There were significant differences on comparing the development of Q-wave (8.81 with Q-wave vs 8.22 without Q-wave) and the sex (8.95 males vs 7.86 females). None had significant differences according to the localization of myocardial infarction (8.25 anterior vs 8.69 inferior).

Conclusions: Patients older than 80 years with a myocardial infarction had an acceptable functional capacity 3 years later, although the accumulate mortality was elevated.

P157 Diabetes mellitus worsens the prognosis of an acute myocardial infarction in patients older than 80 years

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Objective: To evaluate the influence of diabetes mellitus in the prognosis of an acute myocardial infarction in patients older than 80 years.

Methods: This was a retrospective analysis. We studied a period of time of 10 years (from 1 July 1989 to 30 June 1999). Analyzed were all patients older than 80 years admitted with an acute myocardial infarction. The statistical analysis was realized by Chi-square test. Values $P < 0.05$ were considered statistically significant.

Results: Analyzed were 235 patients (51.06% males) and 26.38% had diabetes mellitus. They had the following pathological antecedents: arterial hypertension 39.14%, coronary disease 34.04%. Myocardial infarction was anterior in 69.78% cases and 80.85% patients developed Q wave. Patients had several complications: 14.04% supraventricular tachycardia, 5.95% complete atrioventricular block, 59.14% left ventricular failure, 34.89% cardiogenic shock and dead 39.14%. Patients with diabetes mellitus developed more left ventricular failure (67.74% vs 53.17%), cardiogenic shock (46.77% vs 32.36%) and had more incidence of exitus (50% vs 35.26%). We did not find significant differences in the sex, antecedents of arterial hypertension, antecedents of coronary disease, localization of myocardial infarction and development of Q wave. Neither were significant differences noted in the appearance of supraventricular tachycardia and complete atrioventricular block.

Conclusions: Diabetes mellitus had a negative influence in the evolution of an acute myocardial infarction in patients older than 80 years.

P158 Cardiac troponin I and T in patients with impaired renal function after heart surgery

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Objective: Cardiac troponins are specific markers of myocardial injury but the effects of renal dysfunction on postoperative levels remain unclear. In a prospective study postoperative troponin concentrations were evaluated in patients with normal or high serum-creatinine.

Methods: One hundred and ninety-one patients after elective heart surgery without myocardial infraction were divided into two groups according to serum creatinine. Group I included patients with serum creatinine < 1.3 mg/dl ($n = 106$), group II patients with serum creatinine ≥ 1.3 mg/dl ($n = 85$). CTnI and cTnT serum levels were measured before, and 6, 12, 24, 48 and 120 hours after the operation. Serum creatinine and urea concentrations as well as 12-lead electrocardiograms were recorded preoperatively, on the ICU and on day 1, 2 and 5. Levels and variability of troponin concentrations were expressed by median, first and third quartiles and analyzed by non-parametric methods.

Results: Pre-operative concentrations of both troponins were normal, but increased after surgery in all patients. Maximal slope of cTnI in group I ranged between 1.2 and 4.9 μg/l ($X_{med} = 2.1$ μg/l) and in group II between 2.1 and 5.9 μg/l ($X_{med} = 2.9$ μg/l). Maximal slope of cTnT ranged between 0.145 (I) and 0.474 μg/l ($X_{med} = 0.274$ μg/l) and 0.212 and 0.650 μg/l ($X_{med} = 0.406$ μg/l) (II). Serum concentrations of cTnI and cTnT in group II were significantly higher ($P = 0.003$ [cTnI], $P = 0.002$ [cTnT]).

Conclusions: In all patients cardiac troponin concentrations postoperatively increased, but patients with pre-operatively normal creatinine presented lower serum concentrations of both troponins than those with high creatinine values. These results indicate that for postoperative interpretation of troponins the status of renal function must be taken into account.

P159 The use of cardiac troponin I to diagnose myocardial dysfunction in the critically ill

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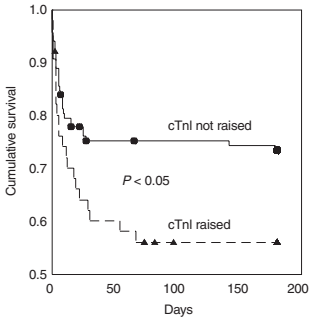
Background: Myocardial dysfunction in the critically ill is characterized by decreased contractility, increased compliance and progressive ventricular dilatation. The phenomenon is global but the clinical consequences are demonstrated predominantly by the left ventricle. The condition is most commonly seen in patients with sepsis and acute neurologic events, but has also been recognized in patients with trauma and other diseases giving rise to systemic inflammatory response syndrome. The pathophysiology is uncertain, but myocyte damage attributed to either micro-ischemia or circulating myocardial depressant substances are prevailing postulations. Electrocardiogram and conventional cardiac markers like CK-MB are modalities of low sensitivity and specificity to diagnose this condition. Cardiac troponin I (cTnI) is a highly tissue specific protein that is detectable in circulation even with minor myocardial injury. Given these properties, it appeared reasonable to use a biochemical assay of cTnI to detect myocardial dysfunction in these patients.

Objective: The purpose of the present study is threefold: to address the incidence of abnormal cTnI levels in critically ill patients; to evaluate the association of cTnI elevation with left ventricular dysfunction; and to assess whether cTnI elevation presages a poorer clinical outcome.

Methods: A prospectively designed study that recruited all admissions to our intensive care unit from June 2000 through September 2000. Patients suffered from myocardial infarction or undergone cardiopulmonary resuscitation was excluded. Blood samples for measurement of cTnI levels were obtained on admission and upon 72 hours. Transthoracic echocardiogram was performed within the first 3 days of admission to assess left ventricular ejection fraction using method described by Simpson. Extensive clinical evaluations and electrocardiograms were also obtained. In-ICU mortality was documented and surviving patients were followed up for a 6-month period.

Results: Fifty-one patients (30%) of 170 admissions in the final cohort had elevated cTnI levels. The median cTnI level on admission was 3.0 ng/ml (1.2–6.0 ng/ml) and the median level at 72 hours was 3.7 ng/ml (1.5–8.8 ng/ml). Patients with elevated cTnI levels had lower systolic arterial pressure, higher creatinine levels, worse oxygenation index, greater APACHE II scores as well as more frequently suffered from sepsis ($P < 0.05$ in all conditions). Multiple logistic regression demonstrated cTnI status to be an independent predictor of left ventricular dysfunction with an adjusted odds ratio of 10.34 (2.31–46.21) and a P value of 0.002. Cumulative survival at 6 months revealed significant difference in mortality rates between cTnI-positive and cTnI-negative patients (log rank 4.55, $P = 0.03$). cTnI status however was not shown to be an independent predictor for in-ICU mortality by multivariate analysis.

Figure



Conclusion: There is a high incidence of cTnI elevation in the intensive care unit setting. cTnI is a surrogate marker for myocardial dysfunction and is also useful for risk stratification in those that are critically ill.

P160 Troponin I as expression of myocardial damage after major vascular surgery

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Introduction and methods: In the perioperative period different levels of Troponin I (TnI) increase allow the identification of different severity degrees of myocardial damage [1]. Aim of the present study was to verify the correlation of TnI increase with clinical, ECG and Echo TT data and with the stratification of risk in patients submitted to major vascular surgery. A prospective observational study was performed on 51 patients submitted to major vascular surgery and then admitted to ICU. Preoperative measurements of TnI, CK-MB isoform, ECG and Echo TT were obtained. Then blood samples for TnI and CK-MB were obtained every 6 hours for 72 hours after surgery and then once daily. Twelve-leads ECG was registered daily. A new echocardiogram was obtained 48–72 hours after surgery. According to our laboratory and to NACB [2], two cut-off values for TnI were used as follows: normal values = < 0.11 ng/ml; > 0.11 to < 1.5 ng/ml; > 1.5 ng/ml. Patients were then subdivided into three groups in relation to TnI levels: Group T0 = normal values (< 0.11 ng/ml); Group T1 = > 0.11 to < 1.5 ng/ml; Group T2 = > 1.5 ng/ml. In every group TnI values were related to CK-MB, ECG and echo TT results. Patients were reassessed 3 months after surgery by means of telephone survey, ECG, echo TT and clinical evaluation.

Results and discussion: In the T0 group TnI and CK-MB levels were normal, as ECG traces and echocardiography. In the T1 group TnI levels were higher than the first cutoff value, although CK-MB levels were normal as ECG and echocardiography. Finally, in four out of eight patients of the T2 group, with TnI > 6 ng/ml and CK-MB values > 3.6 ng/ml, an acute myocardial infarction was diagnosed. Two of these patients died. The 3 months follow-up did not detect any cardiac adverse events in survivors. Our results demonstrate a high incidence of TnI increase in the perioperative period after major vascular surgery. In the vast majority of cases serum TnI increase is limited. In our opinion a mild increase of TnI individuates a group of patients at low risk of cardiac adverse events. In the acute phase these patients with minimal myocardial cellular damage do not need any invasive diagnostic or therapeutic procedure nor any aggressive pharmacological treatment. Nevertheless, it is mandatory to re-evaluate this issue in a greater number of patients in order to establish a new and more reliable cutoff value of TnI in the perioperative setting of major vascular surgery.

References:

1. *Circulation* 2000, **102**:1221-1226.
2. *Clin Chem* 1999, **45(7)**:1104-1121.

P161 Effect of IV amiodarone on CPR haemodynamics and outcome: experimental study in dogs

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Amiodarone has been shown to be superior to placebo in improving admission to hospital for victims of out-of-hospital ventricular fibrillation. There is no data about haemodynamics induced by amiodarone alone or associated with epinephrine. This study compared outcome and haemodynamics of amiodarone alone, epinephrine alone, and the association of these two drugs in a model of resistant ventricular fibrillation in dogs (30 dogs were randomized; 10 to the epinephrine group, 10 to the amiodarone group and 10 to the association group). There were no differences among the groups in baseline variables. Compared to the association, epinephrine produced a better rate of ROSC, resuscitation, and 1-hour survival. There were no differences in outcome between

amiodarone and epinephrine or amiodarone and association. Aortic systolic and diastolic, and coronary perfusion pressures were lower in the amiodarone than in the other two groups. Associated to epinephrine, amiodarone produced pressures similar to epinephrine alone. Amiodarone may be used during cardiac arrest, if associated with a vasoconstrictor like epinephrine.

P162 Vasopressin in refractory out-of-hospital ventricular fibrillation: preliminary results

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Introduction: Survival after CPR with epinephrine therapy is disappointing. Increasing evidence from laboratory and clinical studies suggests that vasopressin may be a promising alternative vasopressor during cardiac arrest and resuscitation.

Methods and patients: We performed our study in the prehospital setting in Prehospital Unit Maribor after approval of The Ethical review board of The Ministry of Health. Patients were eligible if they had a cardiac arrest and required epinephrine according to ERC ACLS protocols for refractory VF. We gave patients one intravenous dose of vasopressin (40 U) after 3 × 1 mg epineprine. If there was no return of pulse after vasopressin, patients as before received epinephrine 1 mg every 3 min during CPR. We excluded patients who were younger than 18 years, had a documented terminal illness, had a traumatic cardiac arrest, were in severe hypothermia (< 30°C), had PEA or asystole as initial rhythm or received drugs via endotracheal tube.

Results: See Table 1. During the trial (from November 2000 to October 2001) we successfully followed up 20 patients and compared them with 20 patients with equal characteristics from retrospective study. Our preliminary study shows a significantly better results in patients treated with vasopressin for ROSC and 24 hour survival, additional doses of epinephrine were less needed ($P < 0.05$). Respectively more patients treated with vasopressin were discharged from hospital ($P = 0.18$).

Table 1

Baseline and treatment characteristic and survival outcomes

	Epinephrine only	Vasopressine	*P* value
Sex (M/F)	9/11	9/11	1*
Age	60.8 ± 11.2	59.6 ± 10.9	0.90†
Time collapse to CPR	7.2	8.1	0.81†
Additional epinephrine (number of patients)	20	10	< 0.05†
Any ROSC (Y/N)	9/11 (45%)	16/4 (80%)	< 0.05*
Hospitalization (Y/N)	8/12 (40%)	13/7 (65%)	0.26*
24 hour survival (Y/N)	5/15 (25%)	12/8 (60%)	< 0.05*
Discharge of hospital (Y/N)	3/17	7/13	0.18*

* Chi square test; † Student *t*-test.

Conclusion: These results suggest possible indication for vasopressin in refractory out-of-hospital VF, after initial application of epinephrine. Based upon our preliminary study larger and prolonger studies of vasopressin in treatment of out-of-hospital VF are needed.

P163 Continuous insufflation of oxygen (CIO) during cardiopulmonary resuscitation (CPR): preliminary results of a randomised controlled trial

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Introduction: The use of CIO through a special 'Boussignac' endotracheal tube during CPR for out-of-hospital cardiac arrest has been shown to be as efficient as standard manual ventilation and chest compression in terms of immediate resuscitation [1]. A multicentre trial was therefore undertaken to compare the outcome associated with CIO-CPR versus standard CPR. We report the preliminary results concerning the respective efficacy of the two techniques on oxygenation.

Methods: An independent Ethics Committee has approved the protocol. All patients were randomised to receive either CIO-CPR with no intermittent ventilation or standard CPR. Pulse oximetry (SpO_2) was recorded every 5 min until recovery or death. The number of patients with a reliable SpO_2 signal and the mean values of SpO_2 were compared between the two groups (Chi-square and Student's *t*-test).

Results: Between August 2000 and April 2001, 430 patients with a mean age of 64 ± 14 years have been included in the study, with 208 patients in the standard-CPR group and 222 in the ICO-CPR. The Table shows the percentage of patients with measurable SpO_2 values, significantly larger in the ICO-CPR group (*$P < 0.05$).

The measured values were always significantly higher in the ICO-CPR group (T 10: 78 ± 29 vs 68 ± 27%, T 15 78 ± 22 vs 71 ± 26%).

Conclusion: In out-of-hospital cardiac arrest, the CIO-CPR technique offers an attractive alternative to standard CPR since it does not need any intermittent ventilation and allows a better oxygenation. The study is still ongoing with a lack of difference in outcome.

Reference:

1. Saïssy J-M, Boussignac G, Cheptel E, Rouvin B, Fontaine D, Bargues L, Levecque J-P, Michel A, Brochard L: **Efficacy of continuous insufflation of oxygen combined with active cardiac compression-decompression during out-of-hospital cardiorespiratory arrest.** *Anesthesiology* 2000, **92**:1523-1530.

Table

SpO_2 signal	T 5	T 10	T 15	T 20	T 25	T 30
Standard-CPR(%)	38	42	41	37	34	29
CIO-CPR (%)	50*	51*	50*	49*	41*	39*

P164 Efficacy of in and out of hospital CPR

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Introduction: The aim of the study was to examine the efficacy of in-hospital (wards, ICU), and out of hospital (Emergency Medical System, EMS) cardiopulmonary resuscitation (CPR) application.

Materials and methods: We enrolled 193 patients (134 males, 69.4%) mean age (59.1 ± 1.4) who developed cardiac arrest either out of hospital (24 pts, 12.4%) or in-hospital (wards: 45 pts, 23.3%, ICU: 116, 60.1%). We examined underlying disease, current diagnosis and place of arrest, application or not of CPR, and outcome.

Results: Patients characteristics are shown in the Table.

CPR (basic and advanced cardiac life support) was performed in 137/193 patients (71%) by a CPR team. Cardiac function was restored in 106/137 (77.4%) of the patients within 5 min. Six, 12 and 24 hour survival was 29/106 (27.4%), 14 (13.2%) and 10/106 (9.4%) respectively.

Conclusions: CPR was performed in an accepted percentage (71%) of patients and was followed by higher percentage of automatic cardiac function (77.4%) compared to international data. However, 24 hour survival was lower than that expected.

Aknowledgement: Supported by the University of Athens.

Table

Underlying disease	Current diagnosis	Place of arrest
Cancer: 60 (31.1%)	Sepsis: 55 (21.8%)	Wards: 45 (21.8%)
Cardiac: 15 (7.8%)	MI-Arrhythmia: 32 (12.4%)	Operating Theater: 1 (0.5%)
Surgical: 10 (5.2%)	Hemorrhage: 36 (13.9%)	Emergency Room: 7 (3.1%)
Pulmonary: 29 (15%)	Metastasis: 19 (7.3)	ICU: 116 (56.5%)
CNS: 27 (14%)	Respiratory failure: 43 (17.1)	Home: 2 (1%)
Burns: 8 (4.1%)	DIC: 3 (0.5%)	Public place: 20 (9.8%)
Head injury: 21 (10.9%)	ARN: 5 (2.1)	Work place: 2 (1%)
Orthopedic: 23 (11.9%)		

P165 Brazilian heartsaver program: 'Time is Life' campaign

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The cardiac arrest by ventricular fibrillation (VF) is the main cause of sudden death. Its acknowledgment, followed by cardiopulmonary resuscitation (CPR) initiation and early defibrillation, before the arriving of advanced cardiac life support (ACLS) experts, are directly related with the survival chances. For this reason, the bystanders participation in performing the CPR is as important as the medical assistance in this event.

In Londrina, a city with a population of 610,000 and 1200 physicians, a campaign was held aiming to educate people about the importance of basic life support (BLS) instructions and the employ of automatic external defibrillators (AED).

Entitled 'Time is Life', the campaign was held in a site of great public concentration. It took 3 days and was widely covered by the media. 86,700 people attended the event site. It was a pioneer campaign, which called the attention and interest of the people to this subject. We could measure the impact of this campaign, through 1900 signatures of people who got straight knowledge in the event site and also for countless phone calls (about 1300) from people who looked for more information about the BLS course in the training center of the Londrina Medicine College. However, one data specially called our attention: 31 people had already attended the BLS course in 1999, before the campaign, and 168 in the year of 2000, after the campaign. Five physicians, in downtown area, attended the ACLS in 1999, before the campaign and 308 attended this course in 2000, after the campaign was held. An statistic analysis using the X2 method, found this difference significant.

We figured out that campaign like this should be held systematically, in order to educate people, to motivate authorities to develop continuous education programs in BLS and that an educated and informed population may positively interfere in sensitizing the medical community to improve the qualifying in CPR performance.

P166 Ultrastructural alterations in myocardial, pulmonary and cerebral tissues after resuscitation by closed chest cardiopulmonary bypass (CPB)

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Objective: To observe ultrastructural changes in myocardial, pulmonary and hippocampal tissues after resuscitation by closed chest CPB with mild and deep hypothermia following 15 min cardiac arrest in dogs.

Methods: After 15 min cardiac arrest by KCl-induced 10 dogs were resuscitated with the use of mild hypothermia (33–34°C) chest closed CPB in group 1 ($n = 5$) and with deep hypothermia (26–27°C) in group 2 ($n = 5$). The mean arteral pressures were maintained higher than 80 mmHg during CPB. The hippocampal, myocardial and pulmonary tissues were studied by light and electromicroscopy after 3 hours of CPB in group 1 and in group 2, in group 3 ($n = 3$) which was controlled after 15 min cardiac arrest.

Results: There are no significantly pathological injury in group 3. The numbers of oligodendrocytes at the light microscopy level were 4.6 ± 0.9 in group 1, less than 13.6 ± 5.2 in group 2 ($P < 0.01$) and 8.3 ± 4.7 in group 3. The average diameters of nuclei of oligodendrocytes at electromicroscopy were 4.563 ± 1.035 μm in group 3, more than 3.944 ± 0.90 μm in group 2 ($P < 0.05$) and less than 5.086 ± 0.80 μm in group 1 ($P < 0.05$), in group 1 more than in group 2 ($P < 0.01$).

In group 1, the broken cell membranes, the swollen nuclei and mitochondria in oligodendrocytes were found by electromicroscopy, whereas the cell membranes and nuclei were intact in group 2. In group 2, intra-aoveolar pulmonary surfactants showed by electromicroscopy were increased, whereas in group 1 were decreased. The swollen endoplasmic reticulum in type II pulmonary epithelial cells were found, and pulmonary vascular endothelium were showed weak intercellular connections in group 1, but in group 2 were closed. In group 2, the smaller and structurally altered mitochondrial, the thinned and fragmentation of myogenic fibrils, decrease of content in glycogen granules in the swollen myocardial cell were found, but in group 1 were no significantly pathological future.

Conclusions: The pathological changes were found during reperfusion after 15 min cardiac arrest in dogs,. The ultrastructure changes of reperfusion injury in pulmonary and hippocampal tissues was more severe by mild hypothermia CPB than by deep hypothermia CPB, but in myocardial tissues were no significantly injury. This suggests that resuscitation by mild hypothermia CPB with head deep hypothermia or by deep hypothermia CPB with myocardial protection may be more effective after prolong cardiac arrest.

P167 Epidemic poisoning with methanol in Estonia: experience of intensive care

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In September 2001, 147 patients were admitted to Pärnu county hospital in Estonia with suspicion of acute methanol poisoning due to consumption of illegal alcohol. From these patients, 35 (22 male and 13 female, age from 19 to 74, mean 41 years) were transferred into Tartu University Clinics for further intensive care, particularly for hemodialysis. Most of the transferred patients appeared in coma, 29 were in shock. First-line therapy (before and during transport) consisted of artificial ventilation, fluid resuscitation, vasopressors, if needed, and i.v. infusion of 10% ethylalcohol as an antidote. Arterial pH prior to transport was in range from 6.49 to 7.29, and base excess from −12 to −30. In average 690 mmoles (from 200 to 1700 mmoles) of sodium bicarbonate was administered before dialysis for management of acidemia. In our department, 30 patients were treated with single hemodialysis for 6 hours, while three patients underwent continuous venovenous hemodialysis for 12 to 16 hours. The blood level of methanol was in range from 0.24 to 5.9 (mean 1.67) mg/dl before dialysis. After discontinuation of the dialysis, the methanol level remained between 0.05 and 1.6 (mean 0.59) mg/dl, and infusion of 10% ethyl alcohol was continued until methanol level below 0.3 mg/dl was detected. Neurological impairment was evident in seven patients after dialysis. In CT-scans, intracerebral haemorrhages, white-matter lesions, and severe brain oedema were the common findings. Four patients, who complained visual disturbances in immediate post-dialysis period, were treated with hyperbaric oxygenation, and in three of them the symptoms were effectively reversed. Overall, from 35 patients six died (mortality 17%), two remained with persistent neurological disability (encelopathy, coma), while 27 patients (77%) were discharged from hospital in normal health status.

In conclusion, our experience demonstrates the importance of intravenous ethanol administration, hemodialysis, and hyperbaric oxygenation in the management of acute methanol poisoning.

P168 Acute in-hospital hyponatremia in children: an observational study

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Introduction: To develop hyponatremia (plasma sodium concentration (P_{Na}) < 136 mM), there must be a source of electrolyte free water (EFW) and actions of antidiuretic hormone (ADH) to prevent its excretion. A low P_{Na} is the most common electrolyte disorder in hospitalized children and it makes them more prone to neurological damage.

Objectives: To establish the incidence of and to identify risk factors for the development of hospital-acquired hyponatremia in a tertiary care hospital.

Methods: We included all children ($n = 432$) who had two or more P_{Na}-measurements in the Emergency Department in a 3-month period and in hospital over the first 48 hours.

Results: The incidence of hyponatremia was 22.5% of whom 14.4% were hyponatremic on presentation and 9.3% developed hyponatremia in hospital (five patients fell in both groups). ADH was likely elevated due to disease (7.9%; e.g. bronchiolitis), symptoms (47%; e.g. nausea) and treatment (45.1%; e.g. surgery). Eighty-three percent of the EFW responsible for the falls in P_{Na} was administered as either hypotonic intravenous (66%) or oral fluids (34%) and was excessive in 53% of the cases. Those who did not seem to receive excessive EFW had an occult source of water, hyperglycemia (16%), mannitol (8%) and/or excreted hypertonic urine (62%).

Conclusions: The most important factor for hospital-acquired hyponatremia is the administration of hypotonic fluids. Hospital-

acquired hyponatremia is iatrogenic and therefore preventable. It unnecessarily puts children at risk of neurological damage. The practice of IV-fluid therapy should be re-evaluated.

Reference:
1. Halberthal M, Halperin ML, Bohn D: **Acute hyponatraemia in children admitted to hospital: retrospective analysis of factors contributing to its development and resolution.** *BMJ* 2001, **322**:780-782.

P169 Predictive factors of mortality in polytrauma patients with life threatening pelvic hemorrhage after transarterial embolization (TAE)

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Objective: To determine the predictive factors of mortality in patients with severe pelvic trauma after transarterial embolization (TAE).

Methods and materials: We developed a protocol for the management of patients with severe pelvic trauma with stressing the roles of TAE, and performed a study according to it between January 1996 and December 2000. When patients with unstable pelvic fracture and without hemoperitoneum were in shock on admission, angiography was immediately performed after admission. In case of hemodynamically stable patients, angiography was performed only when contrast-enhanced CT showed hematoma in the pelvic cavity. For patients with stable pelvic fracture and without hemoperitoneum, angiography was performed when they were in shock and had CT evidence of hematoma in the pelvic cavity. When patients in shock with stable or unstable pelvic fracture had hemoperitoneum, we first chose either of angiography or laparotomy according to our previously reported protocol. All the patients who had angiographic evidence of extravasation of contrast medium underwent TAE. In addition, all the patients with unstable pelvic fracture immediately underwent external fixation after TAE.

Result: TAE was successfully performed to all the 61 patients with the angiographic evidence of extravasation of contrast medium. Forty-eight patients survived and 13 died. To analyze the predictive factors of mortality on admission, the damages that the patients sustained were divided into two types; anatomical and physiological. Tile's classification, the positions of arterial injury, ISS, and head injury (AIS $\geq$ 4) were used as anatomical damage parameters. For the physiological damage parameter, APACHE II score was used. Multivariate analysis was performed for these five factors inclusive of anatomical and physiological parameters. The arterial injury in the posterior position and APACHE II score had a significantly high odds ratio, 16.3 and 26.2, respectively. The items that were statistically significant among the APACHE II parameters were age, mean arterial blood pressure (MAP), core temperature and pH. Volume of positive water balance (ml/kg/hour) during the period from admission to TAE, total units of blood transfusion, time from onset to TAE, and numbers of surgery for complicated injuries (AIS $\geq$ 4) were examined using multivariate analysis for the predictive factors of mortality after admission. Among these four factors, only the positive water balance had significantly high odds ratio (8.3).

Conclusion: MAP, core temperature, pH, and volume of positive water balance were hemodynamic factors. Therefore, the predictive factors of mortality could be said to be determined by the location of arterial injury which should be the posterior position, age, and degree of deterioration of hemodynamics.

P170 Changing the practice of blood transfusion in intensive care

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Optimal red blood cell (RBC) transfusion in critically ill patients remains controversial and, amongst other complications, transfusion induced impaired immune response has been postulated. We modified our transfusion practice in ICU after Herbert *et al*.'s Canadian multi-centre trial, compared a liberal (10–12 g/dl) to restrictive (7–9 g/dl) RBC transfusion strategy [1]. They concluded that restrictive RBS usage was at least equivalent, and possibly superior, to a more liberal transfusion strategy.

Aim: Before and after change in transfusion practice, we documented ICU RBC usage, admission severity of illness (APACHE II), and ICU and hospital mortality.

Method: Retrospective study of RBCs transfused in two 6 month periods (135 patients in 1997 and 171 patients in 1998).

Results: Demographics were similar in the two groups. Average admission Hb in 1997 was 11.3 g/dl and in 1998 10.8 g/dl. Discharge Hb in 1997 was 10.9 (g/dl) and 10.0 (g/dl) in 1998. Average APACHE II was 20.5 in 1997 and 20.4 in 1998. ICU mortality was 28.8% in 1997 compared to 29.8% in 1998. Hospital mortality in 1997 was 34.8% compared to 37.4% in 1998. The average length of ICU stay in 1997 was 6.5 days compared with 5.6 in 1998. Standardised mortality ratio was 1.0 in 1997 and 1.02 in 1998. 586 RBC units were transfused in 1997 compared to 483 in 1998. This equates to 4.3 units per patient in 1997 and 2.8 units per patient in 1998 (35% reduction in RBC usage). 30.1% of patients received no blood in 1997, compared to 51.7% in 1998. In untransfused surgical patients in 1997 average APACHE II was 8.6 and in untransfused medical patients it was 18.5, compared to 12.2 and 20.3 respectively in 1998. In 1997 the medical patients received 230 RBC units, compared to 200 in 1998. 68.4% of medical patients were transfused in 1997 versus 60.5% in 1998. Average APACHE II for transfused medical patients in 1997 was 26.5 versus 29.1 in 1998 and for untransfused patients 18.5 in 1997 versus 20.3 in 1998. The surgical patients received 356 RBC units in 1997 compared to 283 in 1998. 20% of vascular patients remained untransfused in 1997 versus 39.3% in 1998. Average APACHE II of vascular patients was 13.3 in 1997 (average total surgical APACHE II 18.1) versus 15.0 in 1998 (average total surgical APACHE II 17.6). The average admission and discharge haemoglobins of vascular patients were 12.3 g/dl and 10.1 g/dl in 1997 versus 10.1 and 9.9 g/dl in 1998.

Conclusion: Restrictive blood transfusion strategy appears to be safe practice, even in patients with relatively high APACHE II scores. There was a reduction of 106 units of RBCs in 1998 compared to 1997. This translates into a considerable financial saving for the hospital (approximately £17,000 p.a.) and a better balanced use of vital blood products, in a time of national shortage.

Reference:

1. Herbert P, Wells G, Martin C, Tweedale M, *et al.*: **Variation in red cell transfusion practice in the intensive care unit: a multi-centre study.** *Crit Care* 1999, **3**:57-63.

P171 Hypoalbuminemia in the acutely ill — risks and rationale for treatment: a meta-analysis

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Hypoalbuminemia is associated with poor outcome; however, the causal role of low serum albumin concentration and appropriateness of albumin therapy are controversial. We conducted a meta-analysis focusing on two types of evidence: (1) cohort studies with multivariate analysis capable of more accurately assessing whether serum albumin is a direct contributor to poor outcome rather than merely a marker for other pathological processes; and (2) controlled trials of albumin therapy for hypoalbuminemia reporting data on morbidity, which may afford a comparatively sensitive endpoint. The meta-analysis included 66 cohort studies with 171,654 total patients evaluating hypoalbuminemia as an outcome predictor by multivariate analysis and seven prospective controlled trials with 449 total patients on correcting hypoalbuminemia. The pooled results of the included cohort studies revealed hypoalbuminemia to be a potent, dose-dependent, independent predictor of poor outcome. For each 10 g/l decline in serum albumin concentration the odds of mortality increased by 124% (OR, 2.24; CI, 1.83–2.74), morbidity by 78% (OR, 1.78; CI, 1.45–2.18), prolongations in intensive care unit and hospital stay respectively by 22% (OR, 1.22; CI, 1.06–1.41) and 64% (OR, 1.64; CI, 1.26–2.14), and increased resource utilization by 18% (OR, 1.18; CI, 1.03–1.35). These effects were independent of both nutritional status and inflammation. In controlled trials, albumin therapy reduced complications in hypoalbuminemic patients (OR, 0.79; CI, 0.36–1.72), although the overall effect was not statistically significant. However, there was a strong and significant ($P = 0.019$) inverse relationship between morbidity and attained serum albumin level during therapy, which suggested that complication rate may be diminished by exogenous albumin sufficient to elevate serum albumin level above 30 g/l. The value of albumin therapy for hypoalbuminemia needs to be investigated further in well-designed trials. At present, the evidence suggesting a causal link between hypoalbuminemia and poor outcome and a dose-dependent effect of exogenous albumin in reducing complications provides a logical basis for albumin therapy, and there appears to be no compelling argument for withholding albumin therapy if deemed clinically appropriate.

P172 HES 130 kD, but not crystalloid volume support reduces leukocyte–endothelial cell interaction during endotoxemia

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Background: Increased leukocyte/endothelial cell interaction and deterioration of capillary perfusion represent key mechanisms of septic organ dysfunction. Despite ongoing debate, however, the type of volume support to be used during septic disorders remains controversial. Using intravital microscopy we, therefore, studied microcirculatory effects of different clinically relevant volume therapy regimens, i.e. the synthetic colloid hydroxyethyl starch (HES, 160 kD) and a crystalloid regimen with isotonic saline solution (NaCl) in a new model of normotensive endotoxemia.

Methods: In Syrian hamsters, normotensive endotoxemia was induced by i.v. application of *E. coli* lipopolysaccharide (LPS, 2 mg/kg). The microcirculation was analysed in striated muscle of skinfold preparations. HES (Voluven®, 16 ml/kg, $n = 7$) or isotonic saline (NaCl, 66 ml/kg, $n = 6$) were infused 3 hours after LPS exposure over a 1-hour period (post-treatment mode). Animals, receiving LPS without volume therapy served as controls ($n = 8$, control). Leukocyte–endothelial cell interaction and functional capillary density (FCD, indicator of capillary perfusion quality) as well as macromolecular leakage were repeatedly analysed by intravital fluorescence microscopy in the awake animals during a 24 hour-period after LPS exposure.

Results: HES significantly attenuated LPS-induced arteriolar and venular leukocyte adherence ($P < 0.05$), whereas NaCl volume resuscitation had no effect when compared with non-treated controls. In parallel, the LPS-induced decrease in FCD and the increase in macromolecular leakage were significantly attenuated by HES, but not by NaCl.

Conclusions: Thus, our study indicates for the first time a protective effect on the microcirculation by HES volume resuscitation during endotoxemia, even when used in a clinically relevant post-treatment mode.

P173 Large-dose hydroxyethyl starch (HES) 130/0.4 in elective coronary artery bypass surgery

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Objective: To test the hypothesis that, in elective coronary artery bypass surgery, HES 130/0.4 at a dose of up to 50 ml/kg does not increase blood loss and transfusion requirements over the levels with HES 200/0.5, 33 ml/kg, plus gelatin.

Patients and methods: One hundred and twenty adult patients were randomized to receive up to 50 ml/kg of 6% HES 130/0.4 (Voluven®; Fresenius Kabi, Bad Homburg, Germany) or up to 33 ml/kg of 6% HES 200/0.5 (Haes-steril® 6%; Fresenius Kabi)

plus gelatin for volume replacement during elective coronary artery bypass surgery and until 24 hours thereafter. The first 33 ml/kg of HES 130/0.4 or HES 200/0.5 were administered in a double-blind fashion. Colloids (HES, gelatin) were given at the discretion of the attending physicians. Erythrocyte transfusions were administered per protocol. Outcome variables were (1) chest tube output during the first 24 hours after surgery, and (2) erythrocyte transfusion requirements until postoperative day 7. Data were compared using the Mann–Whitney test. A two-sided $P < 0.05$ was considered significant.

Results: One hundred and sixteen patients (58 patients from each group) completed the study according to protocol. Four patients (two from each group) required re-exploration for bleeding, which was confined to specific sites with no observation of generalized bleeding. These four patients were excluded from the analysis. The median (interquartile range) dose of HES administered was 49 (5.5) ml/kg and 33 (0) ml/kg in the HES 130/0.4 and HES 200/0.5 groups, respectively ($P < 0.0001$). The two groups (HES 130/0.4 vs HES 200/0.5) did not differ in postoperative (0–24 hours) chest tube output (635 [365] ml vs 705 [408] ml, $P = 0.48$), the hematocrit of the drainage fluid (0.17 [0.09] vs 0.18 [0.11], $P = 0.53$), and erythrocyte transfusion requirements until postoperative day 7 (1 [2] units vs 1 [2] units, $P = 0.62$).

Conclusion: In elective coronary artery bypass surgery, HES 130/0.4, 49 ml/kg, did not increase chest tube output and erythrocyte transfusion requirements over the levels with HES 200/0.5, 33 ml/kg, plus gelatin.

P174 Effects of three different resuscitation regimens on jejunal tissue oxygen supply after hemorrhagic shock

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Introduction: In this study we evaluated effects of blood (B; $n = 7$), gelatine (G; $n = 8$) and Ringer's lactate (R; $n = 8$) resuscitation on jejunal microvascular blood flow (PU), tissue microvascular hemoglobin oxygen saturation (HbO_2t) and jejunal mucosal tissue oxygen tension (PO_2muc) after severe haemorrhage (50% of estimated blood volume) in pigs.

Methods: Animals were anaesthetised, paralysed, and normoventilated. A small segment of the jejunal mucosa was exposed by midline laparotomy and antimesenteric incision. PO_2muc was measured using Clark-type surface oxygen electrodes. HbO_2t and PU were determined by tissue reflectance spectrophotometry and laser doppler velocimetry. Systemic hemodynamics, mesenteric-venous acid base and blood gas variables as well as systemic acid base and blood gas variables were recorded. Measurements were performed after a resting period, after a 50 min period of haemorrhage (H) and after resuscitation with B, G and R to achieve baseline pulmonary capillary wedge pressures at 70, 90, 110 and 130 min, respectively. ANOVA was performed to analyse differences in mean values between and within groups. Multiple comparisons were done by two tailed Dunnett's *t*-test followed by Bonferoni correction. $P \leq 0.05$ was considered significant. Data are presented as means ± SD.

Results: H resulted in significant hypotension and decreased systemic blood flow which was reversed after resuscitation in all groups. At baseline we observed no differences in PO_2muc (B: 29 ± 5.9 mmHg), HbO_2t (B: 48.5 ± 6.7%) and microvascular blood flow (B: 253 ± 66 PU) between groups. H equally and significantly decreased PU, PO_2muc and HbO_2t in B, G, R animals. However, after resuscitation R animals had significantly lower HbO_2t (time point 130 min; R: 25 ± 9%) when compared with B and G animals (time point 130 min; B: 39 ± 9%; G: 33 ± 10%). PO_2muc decreased similar in B and R animals after resuscitation (time point 130 min; B: 15 ± 6 mmHg; R 14 ± 7 mmHg). However, in G animals a trend towards higher PO_2muc values (time point 130 min; G: 20 ± 9 mmHg) was observed during resuscitation. There were no differences concerning microvascular blood flow during resuscitation.

Conclusion: Resuscitation after severe haemorrhage using whole blood, Ringer's lactate or gelatine results in distinct changes of jejunal tissue oxygen supply. Whole blood resuscitation favourably preserved HbO_2t without affecting PO_2muc while use of gelatine only, demonstrated a trend towards higher PO_2muc values when compared with R and B animals. Therefore type of resuscitation fluid seems to have some impact on tissue oxygen supply within the gastrointestinal tract.

Supported by a Lorenz Böhler Fonds 2000

P175 The prognostic value of gastric tonometry in severe polytrauma patients

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Objectives: First, to evaluate the prognostic value of gastric intramucosal pH (pHi) and pCO_2 gap during intensive care unit (ICU) and hospital stay. Second, to compare the prognostic value of gastric tonometry parameters with APACHE II, SOFA score and blood lactate levels.

Design: Prospective cohort of trauma patients in the first 24 hours after admission to ICU.

Setting: General ICU in a university hospital.

Patients: Forty consecutive severe polytrauma patients admitted to a General ICU.

Methods: A gastric tonometer (Trip NGS Catheter, Tonometrics, Finland) was introduced into the patients' stomach. Continuous air tonometry (Tonocap, Datex Engestrom, Finland) was used to measure gastric pCO_2. Gastric pHi, pCO_2 gap, arterial blood gases and lactate levels were measured at admission and 6, 12, 24 hours after admission. Organ dysfunction was evaluated using SOFA score at admission and 3, 7, 10, 14, 21 and 28 days after

admission. The patients were followed until death or discharge from the ICU.

Results: The mean age was 35 (14–79) years. Thirty-six were male (90%). Mortality rate was 35% (14/40). There were differences between survivors (S) and non-survivors (NS) on admission for APACHE II (13 ± 5 vs 21 ± 7, $P = 0.001$) and pHi (7.33 ± 0.11 vs 7.21 ± 0.20, $P = 0.02$). After 24 hours, pHi (7.33 ± 0.13 vs 7.15 ± 0.32, $P = 0.01$), pCO2 gap (12 ± 16 vs 28 ± 25 mmHg, $P = 0.03$), blood lactate levels (1.4 ± 0.9 vs 3.2 ± 3.4, $P = 0.01$) and HCO_3 (24.4 ± 2.3 vs 19.3 ± 5.5, $P = 0.001$) were different between S and NS. First day SOFA score (5.4 ± 4.0 vs 12.1 ± 6.4, $P = 0.001$) was different for S and NS. Kaplan–Meir surviving curves showed significant differences for S and NS whenever gastric intramucosal acidosis (pHi > 7.32 or pCO_2 gap ≤ 15 mmHg) was present at admission or 24 hours later. Gastric acidosis was associated both at admission and after 24 hours with a greater ICU stay (10 vs 16 days, $P = NS$ and 4 vs 19, $P = 0.02$), hospital stay (22 vs 40 days, $P = 0.05$ and 17 vs 28, $P = NS$) and SOFA score (4.3 vs 8.7, $P = 0.01$ and 4.9 vs 10.4, $P = 0.002$).

Conclusions: In severe trauma patients, gastric pHi and pCO_2 gap are reliable predictors of outcome. Inadequate regional oxygenation as detected by gastric intramucosal acidosis, but not by systemic measures as blood lactate, is an important contributor to morbidity and mortality in this group of patients.

P176 The effects of a single dose of furosemide on urine flow, fluid balance, and the course of plasma creatinine during cardiac surgery

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Introduction: Urine flow rate during cardiac surgery is frequently augmented with diuretics. Recent evidence has shown that a *continuous* infusion of low dose furosemide – starting before cardiopulmonary bypass (CPB) – has detrimental effects on renal function [1]. It is not known, if this does also apply to a *single dose* of a diuretic.

Methods: We performed a study to determine the effects of a single dose of furosemide – given immediately before or during CPB – on urine flow (UV), fluid balance and the course of plasma creatinine as a crude measure of renal function in patients subjected to coronary artery bypass grafting (CABG) procedures with CPB. Anesthesia charts from 1/01 to 3/01 were analysed retrospectively in alphabetical order until 24 patients had been selected that fulfilled the criteria: (a) isolated CABG procedure; (b) normal left ventricular function, and (c) no need for inotropes during surgery.

Results: Urine flow (UV), infused fluids and plasma creatinine values P_{CREA} (mean ± SEM) are given in Table 1. Three patients – all in the diuretics group – received transfusion of packed red cells. Subgroup analysis excluding these patients revealed that relative P_{CREA} was significantly higher ($P < 0.05$) after CPB in the diuretics group in comparison with control.

Conclusions: These retrospective data suggest that a single dose of furosemide during cardiac surgery does have no beneficial effects on the course of P_{CREA} and UV but conversely may lead to a greater need of fluids and to a trend to more blood transfusions and a deterioration of renal function.

Reference:
1. Lassnigg A, *et al.*: *J Am Soc Nephrol* 2000, **11**:97-104.

Table 1

	UV (ml/min)	Fluids (ml)	P_{CREA} (µmol/l)	P_{CREA} (% baseline)
No diuretics ($n = 12$; control)				
Before CPB	1.5 ± 0.5	1458 ± 498	86 ± 12	100
During CPB	7.1 ± 3.6			
After CPB	5.7 ± 2.9	1333 ± 443	81 ± 13	95 ± 47
Furosemide ($n = 12$), mean dose: 12 ± 9 mg				
Before CPB	1.8 ± 1.1	1333 ± 325	74 ± 10*	100
During CPB	9.0 ± 5.2			
After CPB	6.5 ± 2.5	1708 ± 541*	76 ± 15	106 ± 17

* $P < 0.05$ vs control.

P177 Continuous versus bolus furosemide therapy in critically ill patients with fluid overload

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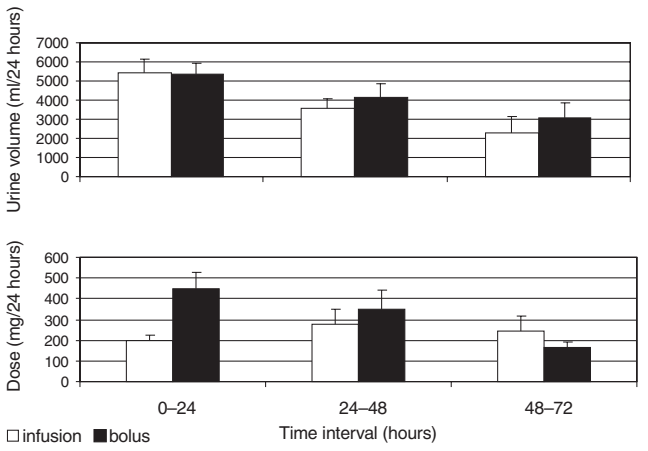
Loop diuretics are commonly used in critically ill patients with fluid overload and/or renal failure. Our objective was to compare the effects of furosemide administered by intermittent intravenous (i.v.) boluses versus continuous i.v. infusion on urine output and furosemide requirement. In an open randomised controlled fashion, 59 fluid overloaded adult patients in two University hospital mixed intensive care units were randomised to a treatment algorithm using either continuous ($n = 32$ patients) or bolus ($n = 27$ patients) furosemide to achieve a minimum hourly urine output. At baseline there was no significant difference in age, gender, hourly urine

output, creatinine clearance, APACHE II score and number of ventilated patients between the two groups. Algorithm-driven diuresis was equally efficacious using bolus or infusion furosemide but the total dosage of furosemide required was significantly less using continuous infusion therapy (Fig.). There were no significant differences in hospital mortality and the need for renal replacement therapy.

We conclude that continuous infusion of furosemide may be easier to manage and expose patients to a lower dose, potentially avoiding or reducing adverse events.

Figure



P178 Plasma-lyte® as dialysate for CRRT: institution of a new therapy and initial evaluation

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Introduction: At the R Adams Cowley Shock Trauma Center, dialysate for CRRT has traditionally been 0.9% saline with 0.5 amp sodium bicarbonate/l. Replacement fluids were 0.9% saline or 0.45% saline with additives adjusted as indicated by laboratory results. Plasma-lyte® was suggested as a new dialysate due to its electrolyte composition.

Methods: Prior to institution of Plasma-lyte® as dialysate, a review of existing dialysis and replacement fluids and electrolyte additives was undertaken. Disposables were recorded and a cost review was done. Dialysate was then changed to P-lyte® with close monitoring of laboratory parameters to identify metabolic or electrolyte abnormalities. Relative costs were compared. ICU nurses were polled with regard to ease of use.

Results: The average daily cost of all IV fluids for dialysate, replacement fluids with additives and disposables was US$71.00. (Does not include circuitry/filters.) The cost of P-lyte® is $1.72/l, compared to $0.70 of 0.9% saline and $0.75 for 0.45% saline. The pH of P-lyte® is 7.4 and the pH of 0.9% and 0.45% saline is 5.0. The composition of the various fluids is listed in the Table (in mEq/l).

Table

	Na^+	K^+	Cl^-	Mg^+	Acetate	Gluconate
P-lyte®	145	5.0	98	3.0	27	23
0.9% saline	154	–	154	–	–	–
0.45% saline	77	–	77	–	–	–

There were no major metabolic abnormalities identified due to the use of P-lyte® as dialysate. One patient developed and maintained a serum $K^+ > 5.0$ and the P-lyte® was discontinued. The nursing staff consistently rated the use of P-lyte® as superior to the saline solutions due to: (1) convenience of use, (2) improvement of serum electrolyte composition (leading to discontinuation of mixing multiple bags of replacement fluids), and (3) less risk of error. The costs were felt to be comparable, because of a decrease in the need for numerous electrolyte additives to the replacement fluids (and the disposables associated with this).

Conclusion: Plasma-lyte® appears to be a safe, cost effective and physiologic dialysate solution that can be used with ease. Diffusive losses of magnesium should be minimized with P-lyte®. Hyperglycemia is minimized due to a lower glucose content than that found in Dianeal®. The chloride load presented by isotonic dialysates should be reduced with the use of Plyte®. P-lyte® is now the first-choice dialysate and replacement fluid at the Shock Trauma Center for CRRT.

P179 Simplified method of regional citrate anticoagulation for continuous extra renal epuration

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Background: Regional anticoagulation with trisodium citrate is an effective form of anticoagulation for continuous renal replacement therapy (CRRT) for patients with high risk of bleeding complications and/or with contraindications to heparin. However, this technique is not used currently because of the metabolic complications, requiring specialized dialysis solution. We therefore evaluated the efficacy and safety of a simplified protocol for citrate regional anticoagulation in 22 critically ill patients treated by continuous venovenous hemodiafiltration (CVVHD).

Methods: A.C.D-A541 (Lab. BRAUN) solution containing 112.9 mmol/l of trisodium citrate (3.22%) was initially delivered at 250 ml/hour (mean, 251 ± 27 ml/hour) via the prefilter port of a COBE PRISMA with an AN-69 dialyzer, with the rate adjusted to

maintain a post-filter ionized calcium (iCa^{++}) between 0.3 and 0.4 mmol/l. Plasmatic iCa^{++} was maintained > 1.1 mmol/l by the infusion of calcium chloride (Calcium element concentration was 45.7 mmol/l) at the mean rate of 1.82 ± 0.36 mmol/hour. The blood flow rate was 100 ml/min. Replacement solution (Hemosol® Solution containing, Na^+ = 144 mmol/l; HCO_3^- = 35 mmol/l; CA^{++}= 1.75 mmol/l) was delivered at 1000 ml/hour. Dialysate was a modified Hemosol® Solution (containing, Na^+ = 126 mmol/l; HCO_3^- = 17 mmol/l; CA^{++} = 1.75 mmol/l) and was also delivered at 1000 ml/hour. Each seance was scheduled for 48 hours. We assessed the serum pH, serum bicarbonate, serum and post-filter iCa^{++} levels every 6 hours.

Results: Mean dialyzer survival was 39 ± 11 hours (median, 41.5 hours). Clotting of the dialyzer was observed in four cases (13 hours; 16 hours; 18 hours and 40 hours). CVVHD was stopped voluntarily in nine patients, without technical problems (median survival was 39 hours). The mean IGS-II score was 69 ± 12. There were neither bleeding events nor coagulation parameters modifications. Serum sodium, serum pH and serum bicarbonate were similar before and after CVVHD (respectively, 133 ± 8 vs 133 ± 7 mmol/l, $P > 0.05$; 7.39 ± 0.15 vs 7.38 ± 0.13, $P > 0.05$; 25.3 ± 5.5 vs 25.1 ± 6.1, $P > 0.05$).

Conclusion: Simplified 3.22% trisodium citrate regional anticoagulation for CRRT is efficacy and is not associated with bleeding complications or citrate toxicity.

P180 Fatal events on chronic hemodialysis (HD) in Croatia

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Introduction: In the year 2000, 2719 chronic renal failure patients in Croatia underwent chronic HD, the reported mortality was 10.3% which was not different from other countries. From 8 to 13 October 2001, 23 sudden and unexpected deaths during HD or within several hours thereafter were recorded.

Patients and methods: All dead 23 patients were dialyzed on cellulose diacetate membrane P15 (15 patients) and P18 (8 patients) in six dialysis centers. One patient suffered from metastatic uterine cancer with ascites, but was still ambulatory and in satisfactory condition. She died at home, within 2 hours of the termination of her HD. Another patient had a history of a coronary incident 8 days prior to death which occurred 37 hours after dialysis. In these two patients we must appreciate comorbidities but the clinical picture still pointed to a sudden death related to the HD. In all other 21 patients , the death was unexpected and associated with the above mentioned dialyzers. All other materials were different. All P15 dialyzers had the control number 2001F07 P, and all P18 dialyzers had the control number 2001B17R.

Discussion: Sudden death on HD is infrequent, and mostly cardiovascular events are reported as causes. Death occurred within 2 hours of the onset of HD or in the first hours after completion of dialysis. The clinical presentation was dominated by sudden worsening of the general condition accompanied by suffocation, chest pain, sweating, and in some cases generalized convulsions. Despite resuscitation in the hospital all 16 patients died. The other seven pts died at their homes. Autopsy findings pointed to foaming of blood. Effluent samples from incriminated dialyzers showed different gas chromatography findings (perfluorocarbon?) compared to other control cellulose diacetate dialyzers.

Conclusion: Sudden deaths during HD or in the first hours after dialysis are in causal relationship with dialyzers of cellulose diacetate manufactured by Baxter, distributed by Pliva, under designations P15 and P18. After withdrawal of the incriminated dialyzers no new lethal events were recorded.

References:

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P181 Outcome of patients with acute renal failure treated with intermittent or continuous renal replacement therapy depending on the initial diagnosis: a retrospective analysis

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Introduction: The mortality of patients with acute renal failure (ARF) remains high (50–60%). Predictive variables of outcome include, age, altered previous health status, severity of illness, multiorgan failure, oliguria, cause of ARF [1]. We retrospectively analyzed all patients without pre-existing renal insufficiency, admitted to the surgical ICU between 1993 and 2000, who developed ARF, that was treated with renal replacement therapy (RRT).

Methods: Three hundred and six (2.9%) of a total of 13,191 admitted patients were included in the study. Age, sex, APACHE II score, renal function parameters, initial diagnosis (hemorrhagic shock, trauma, post-liver transplantation, post-cardiac surgery, sepsis/MODS, other) were recorded as independent variables. Renal replacement therapy (intermittent, continuous, both), days in the ICU, emergency admission, and treatment with vasoactive drugs were recorded as dependent variables. Primary outcome variables were death in the ICU, poor renal recovery (poor outcome) or favorable renal recovery. Statistical analysis was performed by multiple logistic regression.

Results: A total of 51% of patients with ARF died after the initiation of RRT (mortality of patients without ARF 7%). Patients with sepsis/MODS who developed ARF had a significantly higher mortality (68%) compared to all ARF patients (OR 0.18 [0.06–0.49]). A significantly better outcome, was noted for patients after liver transplantation (mortality 28%; OR 6.50 [1.50–33.58]). Besides the initial diagnosis, APACHE II score and length of ICU stay were significantly correlated with mortality of these patients. The progression of creatinine clearance during RRT was predictive for mortality during ICU stay and was 4.5 times lower at the end of

therapy compared to surviving patients with initially comparable clearance values. However, poor (death, no renal recovery requiring dialysis post-ICU) or favorable (full renal recovery) outcome was independent of the type of RRT. The predictors were validated by a receiver operating characteristics (ROC) curve (AUC: 0.74).

Discussion: The overall incidence of patients with ARF, treated with RRT, and mortality of those patients was comparable to published data. Mortality was highest in patients with sepsis/MODS and post-cardiac surgery patients. Of those patients who survived, renal recovery was best after liver transplantation and hemorrhagic shock and worst in patients with sepsis/MODS and trauma. The progression of creatinine clearance predicted the outcome. Renal recovery was independent of the type of renal replacement therapy, as treatment was not randomized.

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P182 Renal function impairment (RFI) in the ICU: a 1-year prospective study

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We studied prospectively the characteristics and the outcome of patients with RFI in the ICU. RFI was defined as a serum creatinine concentration (sCr) remaining ≥ 1.6 mg/dl, for at least two consecutive days during hospitalization in the ICU (sCr normal value ≤ 1.5 mg/dl). From 1 October 2000 until 30 September 2001, among 362 adult patients (247 M, 115 F, aged 52.4 ± 19 years) who were admitted and remained into the ICU for at least 2 days (mean 13.2 ± 17.3 range 2–143), 60 patients, 16.5%, (42 M, 18 F, aged 58.5 ± 18.1 years) fulfilled the criteria for RFI. They were divided into two groups, A and B according to the timing of RFI development. Group A included 27 patients (19 M, 8 F, aged 60.5 ± 15.4 years) who developed RFI after their admission into the ICU. APACHE II score, BUN and sCr at admission were 18.5 ± 5.8, 23.3 ± 17.9 mg/dl and 1.2 ± 0.2 mg/dl respectively. The mean time to fulfill the criteria of RFI in these patients was 8.4 ± 6.2 days. Group B included 33 patients (23 M, 10 F, aged 56.8 ± 20.1 years, P = NS comparing to group A), who were admitted into the ICU with a sCr ≥ 1.6 mg/dl, which remained there at least for 2 days. APACHE II score, BUN and sCr at admission were 25.1 ± 7.4, 66.4 ± 43.7 mg/dl and 3.6 ± 2.9 mg/dl respectively ($P < 0.001$ for each parameter, comparing to group A). The mean time of ICU hospitalization was 21.5 ± 26.2 days in patients of group A and 25 ± 30.9 days in patients of group B (P = NS). Oliguria during ICU hospitalization (defined as 24 hour urine output < 450 ml/day) was observed in seven patients (25.9%) of group A and in 15 patients (45.4%) of group B (P = NS). Seven patients of group A and 13 patients of group B were treated finally with CVVH (P = NS). Among the 60 patients with the RFI 44 died (23/27 in group A and 21/33 in group B, $P = 0.055$). Among the rest 302 patients, without RFI, 76 patients died ($P < 0.0001$ comparing to the patients with RFI).

We conclude that in ICU patients a sCr which remains ≥ 1.6 mg/dl, for at least two consecutive days, constitute a bad prognostic factor.

P183 Factors affecting mortality from acute renal failure in the ICU

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Acute renal failure (ARF) in the Intensive Care Unit (ICU) is perceived as associated with a high mortality. We retrospectively analysed the RIPUG database of 26,689 patients admitted to 21 ICUs in the UK between June 1989 and September 1996. The incidence of ARF was 9%. Patients who were admitted with ARF (n = 1393) had a lower mortality than those who developed ARF

Table

	Maximum OFs at any time			OFs within 48 hours of death/discharge		
Type of OF	*n*	ICU mortality (%)	*P*	*n*	ICU mortality (%)	P
Any 1 OF				737	16.3	
ARF	608	9.4		517	11.6	< 0.05
CVS	N/A	N/A		20	45.0	< 0.001
RESP	N/A	N/A		123	34.2	< 0.001
2 OFs	713	35.6		555	55.0	
CVS + RESP	23	43.5	NS	30	73.3	< 0.05
CVS + ARF	183	47.5	< 0.01	320	87.8	< 0.001
RESP + ARF	297	36.0	NS	371	85.2	< 0.001
GI + ARF	89	13.5	< 0.001	94	70.2	< 0.01
GI + RESP	28	35.7	NS	30	60.0	NS
NEURO + ARF	36	41.7	NS	31	45.2	NS
3 OFs	685	66.0		482	83.4	
CVS + RESP + ARF	345	78.8	< 0.001	243	91.0	< 0.01
CVS + RESP + GI	10	80.0	NS	11	100	NS
CVS + NEURO + ARF	40	77.5	NS	36	86.1	NS
RESP + NEURO + ARF	38	65.8	NS	38	81.6	NS

CVS = cardiovascular failure; RESP = respiratory failure; GI = gastrointestinal failure; HAEM = haematological failure; NEURO = neurological failure; N/A = not applicable. (Only Groups with 10 patients included.)

($n = 1001$) during their stay in the ICU (40.8% versus 50.7%, $P < 0.001$). We determined the maximum number and *specific combinations* of organ failures (OF) at any time and the number and *specific combinations* within 48 hours of death or discharge and the associated outcomes (Table). The mortality rates of all patients with any single, two or three OFs served as references for comparison with the mortality rates of specific types or combinations. Forty-four percent of patients who died in the ICU had a serum creatinine of < 200 μmol/l.

Patients with ARF alone had a significantly lower mortality than patients with any other single OF. This superior outcome was abolished when ARF occurred in combination with other failed organ systems. The majority of patients die *with* ARF rather than *from* ARF.

P184 Need for renal replacement therapy in ICU is a marker of morbidity

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Patients in the intensive care unit (ICU) with acute renal failure (ARF) who need renal replacement therapy (RRT) have a high mortality. There is a widely held view that RRT *per se* is the reason. The aim of our study was to verify this hypothesis. We retrospectively analysed the RIPUG database of 26,689 patients admitted to 21 ICUs in the UK between June 1989 and September 1996. 2394 patients (9%) had ARF of whom 650 (27.2%) were treated with RRT. We compared the ICU mortality rates of patients who needed RRT with outcome of patients in ARF without RRT and the impact of the number of associated failed organ systems (Table).

ICU mortality of patients with ARF was higher in patients who needed RRT. Four hundred and twenty-seven (66%) of patients with ARF who needed RRT suffered from at least two additional failed organ systems, compared to 590 (36.7%) amongst patients with ARF who did not need RRT. There was no significant difference in mortality between patients with or without RRT if the same number of associated organ failures were accounted for. We looked at the temporal relationship between onset of systemic inflammatory response syndrome (SIRS) and start of RRT. Of all 353 patients who suffered from ARF for more than 3 days and required RRT, 335 patients fulfilled the criteria for SIRS either before or at time of initiation of RRT. ICU-mortality in this group was 54.3% compared to 44.4% amongst the 18 patients who developed SIRS after starting RRT (hospital mortality 63.3% versus 44.4%). This difference was statistically not significant. In patients with ARF *the need* for RRT should be viewed as a marker of severity of illness and not as a cause of death.

Table

	Patients in ARF with RRT		Patients in ARF without RRT		
Number of OFS	*n*	ICU mortality (%)	*n*	ICU mortality (%)	*P*
Total	650	57.5	1742	40.3	< 0.001
ARF alone	60	10	552	9.2	NS
ARF + 1 other	163	38.7	551	34.7	NS
ARF + 2 other	266	64.3	419	67.1	NS
ARF + 3 other	121	79.3	150	80	NS
ARF + 4 other	37	94.6	63	81	NS
ARF + ≥ 5 other	3	100	7	100	NS

OFS = failed organ systems.

P185 Use of Molecular Adsorbent Recycling System (MARS) treatment in severe liver failure: initial clinical experience

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Introduction: Despite significant advances in intensive care management, patients with severe liver failure (SLF) still have a high mortality rate and the orthotopic liver transplantation (OLT) remains the only effective treatment. Stange *et al*. [1] have introduced a new, cell-free, extracorporeal, liver assistance method for the selective removal of albumin-bound substances using a specific membrane and an albumin-enriched dialysate, namely Molecular Adsorbent Recycling System (MARS).

Methods: Eleven patients (mean age 46, range 23–71 years; 4 M, 7 F) affected by SLF, admitted to our ICU, were treated with MARS. Seven patients were candidates to OLT, while the other four patients were excluded from the list because of the sepsis. Patients were divided in three groups. Group I was composed of patients ($n = 7$) with acute exacerbation of chronic liver disease; Group II of patients ($n = 3$) with acute liver failure and Group III ($n = 1$) of one patient with delayed nonfunction after OLT. Thirty-one MARS sessions, lasting 6 hours each, in addiction to standard therapy, were performed. Laboratory parameters, Fischer's ratio and hepatic encephalopathy (HE) were evaluated before and after each MARS treatment in our three groups.

Results: No hemodynamic variations, technical problems or significant adverse reaction occurred during MARS sessions. In the three groups a statistically significant decrease in total and conjugated bilirubin, ammonia and bile acids levels was observed after MARS ($P < 0.01$). Bun and creatinine levels markedly decrease ($P < 0.01$ in Groups I and III; $P < 0.05$ in Group II). In the three groups HE was successfully reduced at least one point. The Fischer's ratio improved in all groups. Four patients having liver transplantation after MARS showed favourable outcome. One was discharged with improved condition, while six patients died.

Conclusions: MARS seems to be an effective depurative system and could be proposed as a bridge to OLT. Nevertheless, further studies will be necessary to know the optimal timing and favourable indication of MARS in SLF.

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P186 Renal blood flow in cirrhotic patients and hepatorenal syndrome (HRS)

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Aim: To assess the effect of liver cirrhosis and ascites on the renal blood flow.

Methods*:* A prospective study that includes 40 consecutive patients with liver cirrhosis divided into two groups according to presence of renal dysfunction (group B) or its absence (group A). Another 10 normal volunteers were considered as control (group C). All patients were subjected to clinical, laboratory, ultrasonographic, Duplex study on renal artery and isotopic study for the estimation of total effective renal plasma flow (ERPF). The renal fraction of cardiac output (CO) was also estimated (ERPF/CO). By renal Duplex, the renal vascular resistances were estimated using resistivity index (RI) and pulsitility index (PI).

Results: Mean total ERPF was significantly lower in-group B (HRS) compared to group A (cirrhotics) (330 ± 61 ml/min vs 708 ± 144 ml/min, $P = 0.00$). The mean (ERPF/CO) was significantly lower in-group B (HRS) than group A (cirrhotics). (4.02 ± 0.53% vs 9.5 ± 1.2%, $P = 0.00$). Both groups A&B had lower mean total ERPF & ERPF/CO than group C, (862 ± 130ml/min and 16.5 ± 0.8%, $P = 0.00$).

Both RI and PI were higher in group B and A than group C (0.73 ± 0.06, 1.3 ± 0.2 in group B, 0.66 ± 0.7, 1.2 ± 0.3 in group A vs 0.59 ± 0.05, 1.00 ± 0.3 in group C, $P = 0.00$). PI was similar in group A&B, while RI was significantly higher in group B than A, $P = 0.03$.

Conclusion: Patients with HRS showed marked diminution in total ERPF & ERPF/CO when compared with normal volunteers, while cirrhotics only showed mild diminution in total ERPF & ERPF/CO compared with volunteers. However, renal blood flow when measured by duplex showed similar elevation in the renal vascular resistance in both HRS & cirrhotics.

P187 The effect of induced hypernatraemia on intracranial pressure in patients with acute liver failure: a randomised controlled clinical trial

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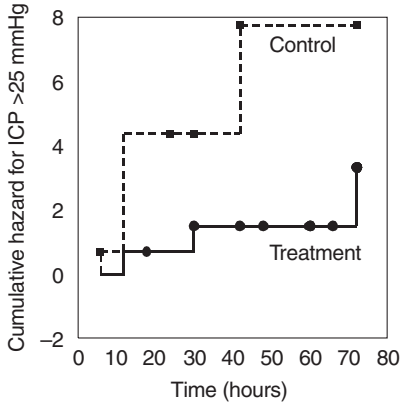
Introduction: Acute liver failure (ALF) is a rare condition characterised by the development of encephalopathy. This is complicated by the development of cerebral oedema and intracranial hypertension (IH) in up to 80% of cases that reach grade IV encephalopathy and is a common cause of death. Preliminary work in patients with traumatic brain injury suggests that inducing and maintaining hypernatraemia can limit the severity of IH. We examined the effect of induced hypernatraemia in patients with ALF on the incidence of clinically significant IH in a prospective randomised clinical trial.

Patients and methods: Thirty patients with acute or hyperacute liver failure and grade III or IV encephalopathy were randomised. Group 1 (15 patients) received normal standard of care (SOC). Group 2 (15 patients) received SOC and hypertonic (30%) saline (HS) by infusion. The aim was to maintain serum sodium between 145 and 155 mmol/l in the HS group. The primary end point was IH. Intracranial pressure (ICP) was monitored in all patients with a subdural catheter (Camino Systems). ICP, measured continuously, was noted at 6 hourly intervals. An ICP of > 25 mmHg was considered to be clinically significant. Patient's data was examined for up to 72 hours following inclusion. Case censoring occurred following death or liver transplantation.

Results: The risk of developing clinically significant IH was greater in the control group ($P = 0.04$, Breslow test) over the study period (see Fig.).

Figure



Hazard function.

Conclusion: Inducing and maintaining hypernatraemia can reduce the incidence and severity of IH in patients presenting with ALF.

P188 Plasma separation and bilirubin adsorption for excessive hyperbilirubinemia before and after liver transplantation

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Severe hyperbilirubinemia is known to exert multiple toxic effects, but there are very little tools against the bilirubin intoxication. Plasma separation and bilirubin adsorption by an anion-exchange adsorbent column (BR-350) were performed in 13 patients with severe jaundice and multiple organ failure developed either before or after orthotopic liver transplantation. Forty-four sessions were performed and in 30% of them the plasma procedure was combined with hemodialysis treatment.

Three to four liters of plasma were separated by membrane plasma separation, then perfused to a rate of 20–30 ml/min through an anion exchange adsorbent and returned to the venous blood line of the plasma separator.

The bilirubin removal rate for total bilirubin was 24.8 ± 12.9% for conjugated bilirubin and 25.2 ± 14% for the non-conjugated form. The final values of plasma bilirubin were directly related to the initial ones ($r = 0.824$, $P < 0001$). The mean adsorption rates on the BR-350 column were 72.6% in the first 30 min and 39% after perfusion of 500 and 1000 ml of plasma respectively. A rebound in the bilirubin levels was present from the very first minutes after the end of the procedure; 24 hours later the rebound recorded in 18 treatment was 34.9 ± 38.7% compared to the end of the treatment.

In patients undergoing four or more repeated sessions of plasma separation and bilirubin adsorption, the level of seric bilirubin decreased from 57 ± 12 to 17 ± 10 mg/dl.

In conclusion, extracorporeal anion exchange plasma perfusion/bilirubin adsorption is a safe and effective treatment and it should be considered as a supportive therapy for excessive hyperbilirubimenic side effects in cholestatic disorders.

P189 Non-invasive measurement of carboxyhemoglobin (COHb) by new pulse oximeter in human volunteers

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Introduction: Carbon monoxide is the most commonly encountered and pervasive poison in our environment. However, conventional pulse oximeters cannot detect the presence of carboxyhemoglobin (COHb) and overestimate arterial oxygenation in patients with severe carbon monoxide poisoning. We developed a new pulse oximeter utilizing three wavelengths which can discriminate three species, oxyhemoglobin (O_2Hb), deoxyhemoglobin (RHb) and COHb. We previously demonstrated that increases in COHb concentration measured by the new pulse oximeter (SpCO) highly correlated with increases in COHb concentration measured by a CO-oximeter (SaCO) in pigs. The present study determined whether COHb was detected by the pulse oximeter with three wavelengths in human.

Methods: The study was approved by the hospital Ethics Committee. Eight human healthy volunteers were tested in this study. They were ventilated with 100% oxygen. Probes of the new three wavelength pulse oximeter were attached to the finger. Then 50 ml of carbon monoxide gas was inhaled by human volunteers. SpCO was non-invasively and continuously measured by the new pulse oximeters. SaCO was also measured by a CO-oximeter after 3 min of inhalation. The same amount of carbon monoxide gas was repeatedly inhaled until SaCO reached 15–20%. Then they were ventilated with 100% oxygen until SaCO reached 5%. SpCO was compared with SaCO.

Results: COHb was non-invasively and continuously detected by the new pulse oximeter. There is a strong correlation between SpCO and SaCO ($r = 0.92$, $P < 0.001$).

Conclusion: The results of this study demonstrated that the new pulse oximeter might be useful for non-invasive diagnosis of carbon monoxide poisoning.

P190 *Helicobacter pylori* antigen scanning in stools in the patients and in the staff of the intensive care unit

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Background and goal: The pathogenesis of acute gastric ulceration of the ICU patients is still unclear and whether *Helicobacter pylori* (HP) plays a role in pathogenesis is not known [1,2]. In this study, we aimed to detect the presence of HP colonization in stools and the importance of the HP positivity of the ICU staff in spread of infection.

Materials and methods: The study included 52 patients, treated in the ICU and 40 healthcare staff from ICU of Department of Anaesthesia and 40 from the ICU of the other departments. Presence of HP antigen was assessed by using *Helicobacter pylori* Stool Antigen (HpSA) test (Primer Platinum HpSA; Meridian Diagnostic, Cincinnati, USA) in the first 24–48 hours and at the end of a week after admission for the patients and only once from the medical staff. The antigen titers were compared between the ICU staff and others based on the multiple factors.

Results and discussion: The hospitalization in ICU was a significant factor in HP antigen positivity. The incidence of HP positivity in ICU staff was higher than the others ($P < 0.05$). The antigen titers were also higher in ICU staff than the other staff and this difference was statistically significant ($P < 0.05$). The antigen titers were also well correlated with their duration of working in ICU ($P < 0.05$). Presence of a high incidence of HP infections in ICU patients lead us to the thought that HP might be suggested as one of the causative agents in nosocomial infections. High antigen titers in ICU staff suggested that transmission by oral–oral or

fecal–oral routes might be possible because they often exposed to secretions of patients such as feces, urine and saliva [1,3].

Conclusion: In the critically ill patients, acute ulcer prophylaxis was caused by HP infection. This study also showed the importance of knowledge of a new nosocomial causative agent for ICU staff and its probable spreading ways of oral–oral or fecal–oral.

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2. Hawker FH: *Crit Care Med* 1999, **27**:1385-1386.
3. Vaira D, Malfertheiner P, Megraud F, *et al.*: *Lancet* 1999, **354**:30-33.

P191 A comparison of two immediate-early genes, *c-fos* and *c-jun* in rat brain after occlusion of superior mesenteric artery (SMAO)

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Changes in level of consciousness and/or emotion are frequently experienced in the lethal gut necrosis. However, little is yet known about what a mechanism is underlying beneath the alteration of neuronal function. The aim of the present study was to investigate how the brain was influenced by massive gut necrosis. In an attempt to examine functionally activated neuron, we applied immunohistochemistry (IHC) for c-Fos and c-Jun, cellular transcriptional factors encoded by immediate early genes *c-fos* and *c-jun*, respectively, and widely used as metabolic markers for neuronal activity.

Materials and methods: Adult male Wistar rats ($n = 30$) were used. Under general anesthesia, 25 rats underwent celiotomies. Twenty of them received SMA clipping and the others were used as control. Control and treated rats at 2, 4, 8 hours were perfused and fixed. The brain were sectioned in 20 μm thick every 200 μm and stained by avidine–biotin-complex method using anti-c-Fos and c-Jun antibodies.

Results and discussion: *c-Fos IHC*: Very low or absent c-Fos immunoreactivity (IR) in control rat brain. In treated rat, c-Fos IR was increased in time course. The predominant c-Fos IR were demonstrated in the specific nuclei including the hypothalamus (PVN; paraventricular nuc.), amygdala (CeA; central amygdaloid nuc.), locus ceruleus and nucleus tractus solitarii. These areas were congruent with c-Jun IR.

c-Jun IHC: Basal c-Jun IR was evident in most brain site and higher than c-Fos IR. There were several notable differences from c-Fos IR: (1) in the treated rat, intense c-Fos IR was observed in the habenula, circumventricular organ (area postrema, subfornical organ) but c-Jun IR was very low; (2) c-Jun IR was very high in the hippocampus, cerebellum and cingulum, but c-Fos IR was very subtle. The congruent sites of both IR could be interpreted that the hypothalamus, brain stem and limbic system are activated in response to extensive gut necrosis, and participating in neuroendocrine, autonomic or behavioral responses.

P192 Cardiac output determination during experimental hemorrhage and resuscitation using a transesophageal Doppler monitor

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Introduction: Transesophageal Doppler (TED) has been considered a noninvasive and accurate alternative to pulmonary artery catheter for volume replacement and cardiac output measurement in patients undergoing major surgeries.

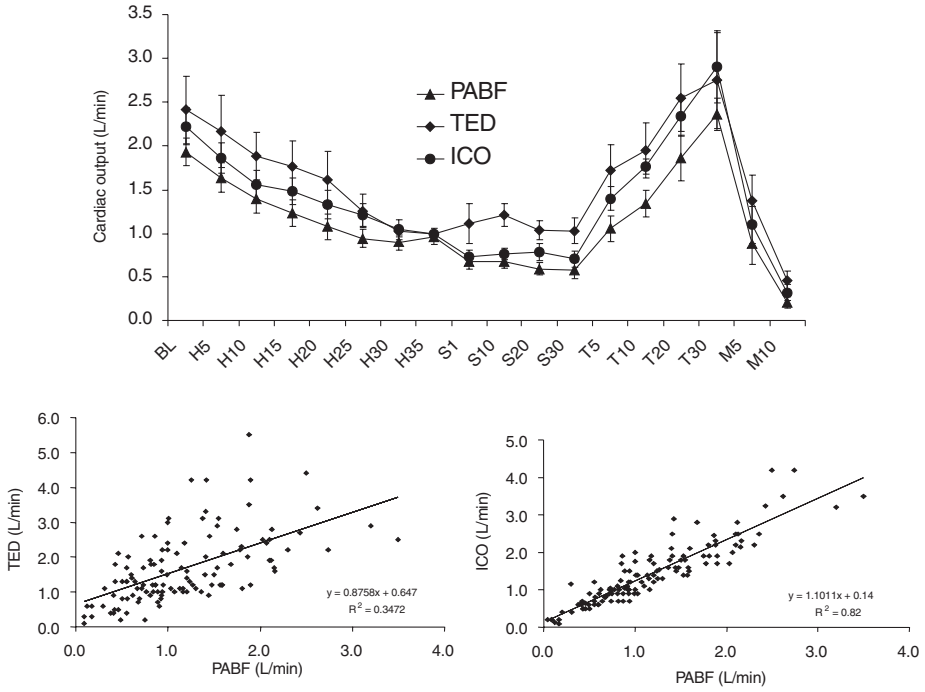
Objective: To test the hypothesis that TED can accurately predict cardiac output during hemorrhage, shock and resuscitation, by comparing it to total pulmonary artery blood flow (PABF), the gold standard for cardiac output estimation and to standard intermittent bolus cardiac output (ICO).

Methods: In eight anesthetized dogs (18 ± 1.0 kg), PABF was measured with an ultrasonic flowprobe while ICO and mixed venous O_2 saturation (SvO_2) were measured through a Swan–Ganz catheter. A TED probe (CardioQ™), designed for adult use (minimum 30 kg, 16 years), was placed in midesophageous to evaluate stroke volume. A graded hemorrhage (20 ml/min) was produced (H5–H35) to a mean arterial pressure (MAP) of 40 mmHg and maintained by additional blood removal for 30 min (S1–S30). Total shed blood volume was retransfused (541 ± 54.2 ml) over 30 min (T5–T30), after which a massive hemorrhage, 100 ml/min rate, was produced over 10 min (M5–M10).

Results (see Fig. overleaf): In general, TED overestimated PABF ($r^2 = 0.3472$), but changes in TED paralleled PABF throughout the experimental protocol, principally during massive hemorrhage ($r^2 = 0.9001$).

Conclusion: We conclude TED measures precisely cardiac output during massive hemorrhage. Probes designed for lower weights and smaller aortas may improve its accuracy in medium size animal models under less dramatic alterations induced by hemorrhage, shock and resuscitation.

Figure



P193 Is the blood velocity beat-to-beat variation in the descending aorta similar to the arterial pulse pressure variation?

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Introduction: The beat-to-beat analysis of the arterial pulse pressure (PP) [1] and of the maximal aortic velocity measured by the transesophageal echocardiographic Doppler technique (TEE) [2] have been demonstrated as good predictors of volume responsiveness in patients with circulatory failure. However, the PP analysis requires an invasive procedure for arterial catheter placement and TEE does not allow long-term continuous analysis. Therefore, we have tested the hypothesis that the beat-to-beat variation of the peak of velocity of blood in the descending aorta (PV Ao), measured by a transesophageal echo-doppler device (a less invasive monitoring technique using a small probe) was of the same degree as the beat-to-beat PP variation measured by an arterial catheter.

Patients and methods: In 12 patients receiving mechanical ventilation, the arterial pressure curve (arterial catheter) and the descending aorta velocity signal (transesophageal echo-doppler; HemoSonic100 – Arrow Intl.) have been recorded simultaneously on a computer allowing beat-to-beat analysis of the PP and PV Ao values.

Results: Three hundred and sixty measurements were obtained (30 per patient). Six patients had atrial fibrillation, three had a sinus rhythm with numerous supraventricular extra systoles and three had a regular sinus rhythm. There was an excellent correlation between beat-to-beat PP and PV Ao variation in every patient ($r = 0.85$, 0.88, 0.89, 0.90, 0.92 [three times], 0.94, 0.95 [two times], 0.96 and 0.98).

Conclusion: The beat-to-beat variation of blood velocity in the descending aorta obtained by the minimally invasive transesophageal echo-doppler method is quite similar to the beat-to-beat variation of the pulse pressure. This may open a large field of clinical investigation in the perspective of detecting cardiac preload dependence and fluid responsiveness in patients under mechanical ventilation.

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P194 Is it feasible to monitor total hepatic blood flow by use of transesophageal echography? A validation in patients

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Objective: In critically ill patients total hepato-splanchnic blood flow is usually determined using a primed continuous infusion of indocyanine green (ICG) with hepatic venous sampling [1]. The hepatic venous catheterisation, however, is an invasive procedure and we could recently demonstrate in an animal model that hepato-splanchnic blood flow could be reliably determined with trans-

esophageal echocardiography (TEE) [2]. In this study we investigated whether transesophageal echocardiography is a noninvasive method for bedside assessment of hepatic venous blood flow in clinical practice.

Patients and Methods: Thirteen anesthetized and ventilated critically ill patients in whom hepato-splanchnic blood flow was augmented by a dobutamine infusion were studied.

Hepatic venous blood flow values were derived with TEE using the following calculations: Diameter (*d*) and velocity time integral (VTI) of all three hepatic veins were determined by TEE, heart rate (HR) was derived from ECG and flow subsequently calculated as $Q = \pi\,(d/2)^2$ 0.57 VTI HR [2]. These values were compared with hepato-splanchnic blood flow (Qspl) measurements using a primed (12 mg) continuous (0.5 mg/min) infusion of indocyanine green with hepatic venous sampling as described before in detail [1]. Parameters were determined at baseline as well as after modulating splanchnic blood flow by the infusion of dobutamine.

Results: A significant increase in splanchnic blood flow could be determined with TEE (438 [387–555] vs 559 [495–709] ml/min/m^2) as well as using the ICG-method (889 [370–2285] vs 1098 [684–3479] ml/min/m^2). The Spearman correlation coefficient between both methods, however, was 0.77 at baseline and 0.63 after dobutamine-infusion.

Conclusion: The values of splanchnic blood flow determined by the two different methods had a great variance. TEE, hence, does not seem to offer a noninvasive approach for monitoring changes in hepato-splanchnic blood flow in critically ill patients.

References:

1. *Cardiovasc Res* 1995, **30**:106-112.
2. *Intensive Care Med* 2001, **27**:580-585.

P195 Assessment of the agreement between cardiac output measured by thermal filament continuous thermodilution (CCO) and noninvasive partial CO_2 rebreathing (NICO) with particular reference to $ETCO_2$ levels

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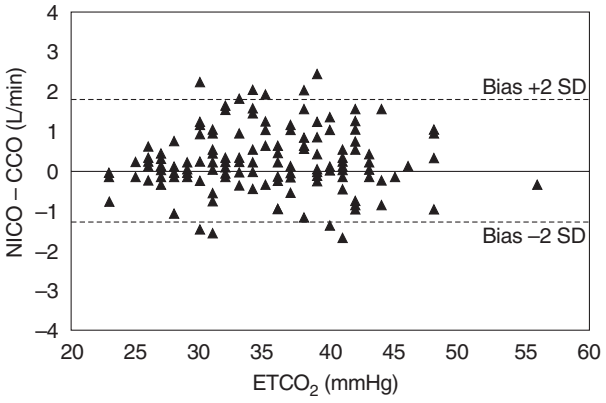
Introduction: Cardiac output (CO) is an important hemodynamic parameter and its continuous measurement has the potential to enable early recognition of hemodynamic trends and provide earlier therapeutic response. NICO is a new noninvasive cardiopulmonary monitor that provides an alternative to invasive CCO for measurement of CO. NICO uses a differential form of the Fick equation (change in CO_2 excretion and end-tidal CO_2, in response to a brief period of partial rebreathing) to provide noninvasive estimates of CO [1]. The accuracy and reliability of NICO as a function of the end-tidal CO_2 ($ETCO_2$) levels of the patient has not been studied. The purpose of this study was to determine if $ETCO_2$ levels affect the degree of agreement between NICO and CCO.

Methods: Matched sets of CO measurements from NICO (Novametrix Medical Systems, Wallingford, CT, USA) and CCO (Vigilance, Baxter-Edwards, Irvine, CA, USA) were collected in 25 patients undergoing elective cardiac surgery. The NICO sensor (consists of on-airway flow sensor, mainstream CO_2 sensor, adjustable dead space tubing, and a pneumatic valve) was attached between the endotracheal tube and the breathing circuit of the patient. The two measures, NICO and CCO were assessed for agreement by using methods proposed by Bland and Altman at different levels of $ETCO_2$.

Results: One hundred and fifty-four data points were obtained indicating variations in the difference of cardiac output compared with the variations of $ETCO_2$ of the patient. The range for CCO measures was 2.0–8.4 l/min and for NICO measures 2.5–8.3 l/min. The mean bias in CO between the two techniques for the entire protocol was 0.24 l/min and the precision (1 SD) was 0.77 l/min. The difference in CO was independent of the $ETCO_2$ levels of the patient (Fig.).

Figure



Difference in Cardiac Output (NICO-CCO) and $ETCO_2$.

Conclusion: The agreement between the NICO and CCO is clinically acceptable and is unaffected by $ETCO_2$.

Reference:

1. Haryadi DG, *et al.*: **Partial CO_2 rebreathing indirect Fick technique for non-invasive measurement of cardiac output.** *J Clin Monit* 2000, **16**:361-374.

P196 Comparison of cardiac output (CO) measurement before and after cardiopulmonary bypass: bolus thermodilution (TDco) and noninvasive partial CO_2 rebreathing (NICO)

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Introduction: NICO is a noninvasive cardiopulmonary monitor that provides an alternative to invasive TDco for measurement of CO. NICO uses a differential form of the Fick equation (change in CO_2 excretion and end-tidal CO_2, in response to a brief period of partial rebreathing) to provide noninvasive estimates of the CO [1]. The objective of this study was to compare the degree of agreement in

measurements of CO using NICO and TDco, at predetermined intervals in patients undergoing coronary artery bypass graft surgery (CABG).

Methods: Matched sets of CO measurements from a standard PA Catheter and NICO (Novametrix Medical Systems Inc, Wallingford, CT, USA, software version 4.2) were collected in 10 patients (age 35–62 years, weight 32–68 kg) undergoing elective CABG. Measurements were made at predetermined intervals during the surgery (during pre-cardiopulmonary bypass and post-cardiopulmonary bypass; chest wall open and closed). The NICO circuit was attached between the endotracheal tube and the breathing circuit of the patient. An average of three consecutive bolus (10 ml) TDco measurements made during end-expiration was compared with corresponding NICO measurements. Bland–Altman analysis was performed to compare the degree of agreement between the two methods.

Results: Bias, precision (1 standard deviation), and limits of agreement between the NICO and TDco during pre-CPB vs post CPB are shown in the Table.

Conclusion: The overall agreement between NICO and TDco was −0.03 (bias) and ± 0.80 (precision) l/min. There was no statistical difference in the CO measured by the two techniques neither during pre-CPB nor during post-CPB ($P < 0.01$) with the chest open or closed. The degree of agreement between NICO and TDco is within the recommended value [2] for NICO to be a clinically acceptable method for CO measurement during CABG.

Table

Study phase	Bias (l/min)	Precision (l/min), 1 SD deviation	Limits of agreement (bias ± 2 × SD)
Pre-bypass (chest closed)	+0.25	0.59	−0.93 to 1.43
Pre-bypass (chest open)	+0.10	0.81	−1.53 to 1.73
Post-bypass (chest open)	−0.31	0.92	−2.15 to 1.54
Post-bypass (chest closed)	−0.23	0.68	−1.58 to 1.13

References:
1. *J Clin Monit* 2000, **16**:361-374.
2. *J Clin Monit* 1999, **15**:85-91.

P197 Monitoring of intrathoracic blood volume in early septic patients: its correlation with survival

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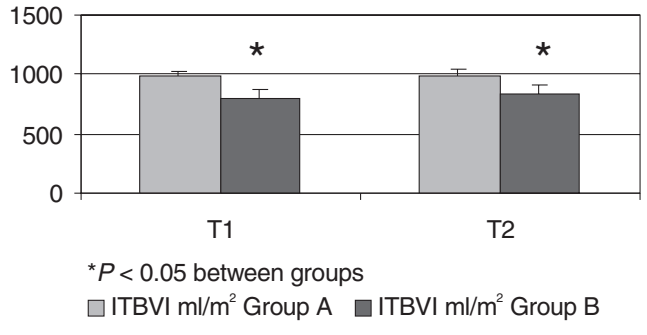
Introduction: Early goal directed therapy improves survival in sepsis, trough optimisation of contractility, oxygen balance and correction of fluids deficit [1]. Aim of the study is to investigate whether optimisation of ITBV (intrathoracic blood volume) an index of preload, could be a therapeutic end point in early sepsis, as previously demonstrated in burns patients [2].

Methods: Sixty septic patients (Bone criteria) were monitored with a central vein catheter and an artery femoral catheter connected to a fiberoptic system (Cold Z-02; Pulsion Medizintechnic) Patients were submitted to a fluid management protocol to obtain MAP ≥ 75 mm/Hg, maintaining ITBVI 800–1000 ml/m^2 and EVLWI < 7.5 ml/kg. At T0 (basal) and after 24 (T1), 48 (T2) 72 (T3) and 96 hours (T4) main volumetric, hemodynamic data were studied. ANOVA test was used to compare changes over time. A Fisher test was used to compare categorical data.

Results: Thirty-two patients survived (Group A) and 28 died at 28 days (Group B). ITBVI was higher in Group A than Group B at T1 and T2 (Fig. 1). And ITBVI > 800 ml/m^2 at T1 and T2 was predictive of survival.

Comment: (1) ITBVI improves earlier in survivors then non survivors during a reanimation period. (2) This improvement has a predictive value. (3) Optimisation of ITBVI during early sepsis should be evaluated in further trials.

Figure 1



Table

	ITBVI > 800 ml/m^2	95% CI
P	0.02	
Sensitivity	0.44	0.25–0.66
Specificity	0.84	0.67–0.94
RR	1.97	1.188–3.288
Positive predictive value	0.70	0.44–0.89
Negative predictive value	0.64	0.48–0.78

References:
1. *N Engl J Med* 2001, **345**:1368-1377.
2. *J Trauma* 2000, **48**:728-734.

P198 Preload index: pulmonary artery occlusion pressure and intrathoracic blood volume monitoring during lung transplantation

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Introduction: We analyzed two preload variables, pulmonary artery occlusion pressure (PAOP) and intrathoracic blood volume index (ITBVI), with respect to cardiac index (CIpa), obtained from pulmonary artery catheter (PAC) during lung transplantation. The reproducibility and precision of all transpulmonary single indicator dilution technique (CIart) and CIpa measurements were also evaluated.

Methods: Measurements were made in 48 patients monitored with PAC and with PiCCO System at six specific stages through the study. The relationship between the two different preload variables (PAOP and ITBVI) and the CIpa were analyzed by linear regression. Agreement between CI measurements obtained by PAC and PiCCO system was analyzed using the analysis suggested by Bland and Altman.

Results: Linear regression between ITBVI-CIpa was $r^2 = 0.40$ ($P < 0.0001$) while PAOP poor correlated to CIpa ($r^2 = 0.004$) (Figs 1 and 2). Mean bias between CIart and CIpa was 0.15 l min^{-1} m^{-2} (1.37).

Conclusion: ITBVI, rather than PAOP, is a reliable indicator of cardiac preload in patients undergoing lung transplantation.

References:
1. Bindels, AJGH, *et al.*: *Critical Care* 2000, **4(3)**:193-199.
2. Sakka, SG, *et al.*: *Intensive Care Med* 2000, **26(2)**:180-187.

Figure 1

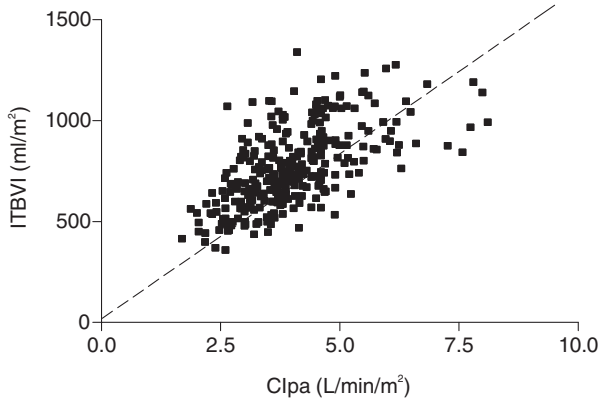
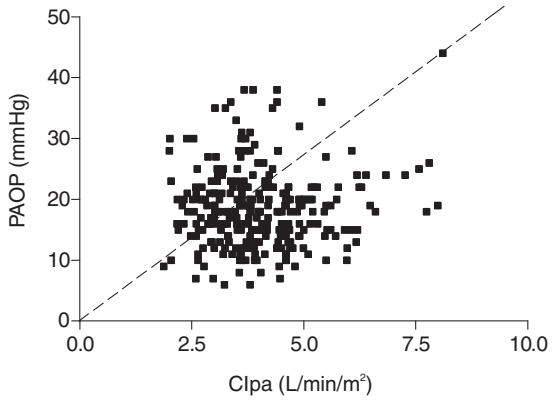


Figure 2



P199 Continuous and intermittent cardiac output measurement: pulmonary artery catheter vs aortic transpulmonary technique

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Introduction: We compared two methods of intermittent cardiac output measurements: pulmonary artery catheter (COpa) (Vigilance system SvO_2/CCO, Baxter Edwards Laboratories, Irvine, CA, USA), regarded as the current clinical standard, and an aortic transpulmonary thermodilution technique (COart) performed with the PiCCO System (Pulsion Medical System, Munich, Germany), and also compared the continuous thermodilution technique (CCO), the continuous pulse contour analysis cardiac output (PCCO) versus COpa in patients during lung transplantation,

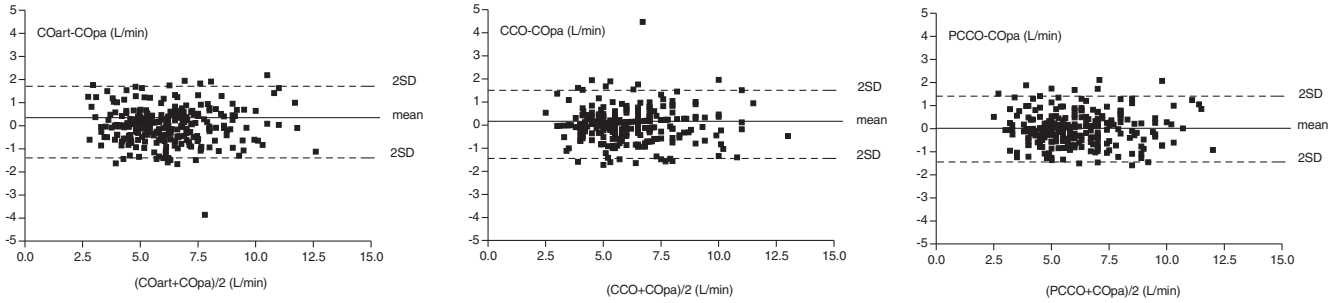
Methods: Measurements were made in 49 patients at six stages between the induction of anaesthesia and the end of surgery. Statistical analysis used the method described by Bland and Altman.

Results: We found close agreement between the techniques. Mean bias between COart and COpa was 0.21 l min^{-1} (2 SD of differences between methods = 1.6 l min^{-1}). Mean bias between CCO and COpa and PCCO and COpa was 0.16 l min^{-1} (2 SD = 1.40 l min^{-1}) and 0.09 l min^{-1} (2 SD = 1.39 l min^{-1}) respectively (see Fig. overleaf).

Conclusions: Measurements with the aortic transpulmonary thermodilution technique give continuous and intermittent values that agree with the pulmonary thermodilution method. Anyway, continuous CO data obtained with PAC reflect accurately the clinical standard thermodilution COpa.

References:
1. Sakka SG, *et al.*: *Intensive Care Med* 1999, **25**:843-846.
2. Rödig G, *et al.*: *Br J Anaesth* 1999, **82**:525-530.

Figure



P200 Prognostic value of indocyanine green-plasma disappearance rate in critically ill patients

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Background: Monitoring of regional organ blood flow and function is often crucial for guiding therapy in critically ill patients. In particular, indocyanine green-plasma disappearance rate (ICG-PDR) has been proposed for the assessment of liver function and its value has been demonstrated in evaluation of donor organs [1] and as prognostic marker in 39 critically ill patients [2].

Methods: We retrospectively analyzed 336 critically ill patients (120 female, 216 male, age 10–89 years, mean 53 ± 19 years) who were treated in our ICU between 1996 and 2000. All these patients were hemodynamically monitored by the transpulmonary double indicator (thermo-dye) dilution technique. Statistical analysis for ICG-PDR in survivors ($n = 168$) and non-survivors ($n = 168$) was based on the lowest value of ICG-PDR in each individual.

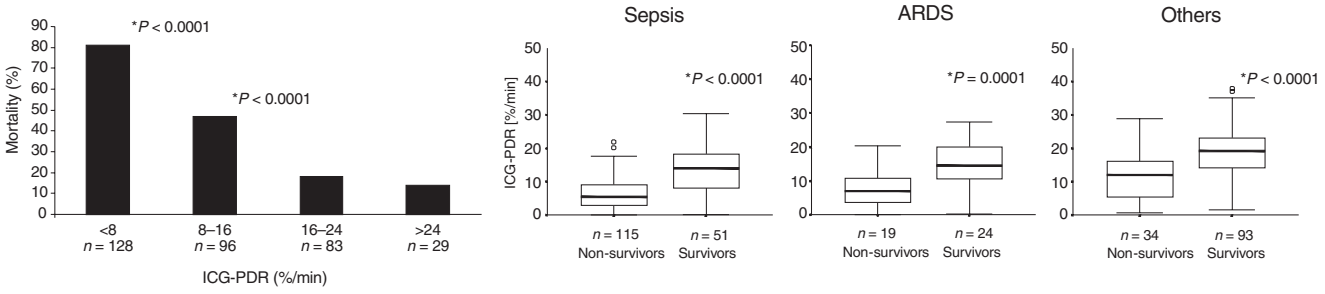
Results: ICG-PDR was significantly lower in non-survivors than in survivors (median 6.4 vs 16.5 [%/min]) ($P < 0.001$). Mortality was about 80% in patients with ICG-PDR below 8 (%/min) and survival about 80% in those with ICG-PDR above 16 (%/min). Within three different sub-groups of patients (sepsis, ARDS, and others) survivors had significantly higher ICG-PDR than non-survivors (Fig.).

Conclusion: ICG-PDR correlates well with survival of critically ill patients. For the future, measurement of ICG-PDR seems to be a promising clinical tool, particularly since accurate and non-invasive transcutaneous assessment at the bedside has become possible.

References:

1. Wesslau C: **Clinical investigations using indocyanine green clearance for evaluation of liver function in organ donors.** *Transplantology* 1994, **5**:1-3.
2. Kholoussy AM: **Prognostic significance of indocyanine green clearance in critically ill surgical patients.** *Crit Care Med* 1984, **12**:115-116.

Figure



P201 Arterial blood pressure monitoring during whole body hyperthermia

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Background: For monitoring of arterial blood pressure (ABP) during induced whole body hyperthermia (WBH) different methods have been recommended. This investigation was performed to evaluate the agreement of invasive measurements at various sites, and to compare invasive and non-invasive methods of ABP monitoring under conditions of a heat-induced extreme vasodilation.

Methods: In 19 patients, 48 treatments with WBH were performed. Measurements of ABP in radial and femoral artery, by oscillometry and sphygmomanometry, were taken at four temperature-levels during WBH (at 37°C, 40°C, 41.8°C and 39°C).

Results: For systolic ABP significant differences were seen between invasive and non-invasive methods with higher values for non-invasive measurements. For diastolic blood pressures sphygmomanometry gave higher and oscillimetry lower values when compared to both invasive measurements. Sphygmomanometry also showed higher values for mean ABP compared to all other techniques, while measurements in radial and femoral artery and by oscillometry differed only by about 5 mmHg.

Conclusion: The hemodynamic management during WBH should be guided by mean arterial pressure instead of the systolic and/or diastolic pressure. The sphygmomanometric technique is not recommended for use during hyperthermia.

P202 Monitoring of intrathoracic volumes in induced supranormal cardiac output

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Background: Induced whole body hyperthermia (WBH) up to 42°C leads to hypercirculation, large fluid shifting and a high demand of intravascular fluids. This study was performed to evaluate several parameters of systemic and intrathoracic hemodynamics during such a condition of hypercirculation with high cardiac output and low vascular resistance.

Methods: A combination of reflexion photometry and thermodilution (COLD Z-021-System, Pulsion, Germany) was used to obtain mean arterial pressure (MAP), cardiac output (CO), global end-diastolic volume index (GEDVI), intrathoracic blood volume index (ITBVI), total blood volume index (TBVI), right ventricular end-diastolic volume index (RVEDVI), right heart end-diastolic volume index (RHEDVI), left heart end-diastolic volume index (LHEDVI), pulmonary blood volume index (PBVI) and extravascular lung water index (EVLWI) at 37°C, 41.8°C and 39°C in 26 patients with metatased cancers during 51 WBH treatments. WBH was induced by infrared radiation (Iratherm 2000). Hemodynamics at 41.8°C and 39°C were compared with the initial values using Wilcoxon rank sum test for linked random samples.

Results: Compared with the initial values at 37°C significant increases of CO, GEDVI, ITBVI, TBVI, RVEDVI, RHEDVI and PBVI and a significant decrease of MAP could be found at 41.8°C. For LHEDVI and EVLWI no significant changes were observed. Some of these parameters were still significantly changed during the cooling-down phase at 39°C, but, with exception of EVLWI, all parameters showed a clear tendency to pre-treatment levels. Only EVLWI showed a slight tendency to further increase during the cooling-down phase.

Conclusions: Induced hyperthermia results in significant changes of cardiac output, intracardial and intrapulmonary volumes. Therefore monitoring of these parameters seems to be useful in risk patients and in other conditions of hypercirculation.

P203 Is the degree of multiple organ dysfunction related to severity of capillary leakage?

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Introduction: Multiple organ dysfunction syndrome (MODS) is believed to result from microcirculatory failure in surgical intensive care patients. We hypothesised that degree of MODS is mirrored by severity of capillary leakage assessed by venous congestion plethysmography.

Methods: Twenty-two patients with MODS [1] (moderate MODS group: less and equal 8 points, $n = 13$; severe MODS group: greater and equal 9 points, $n = 9$) were studied. All patients were monitored including a pulmonary artery catheter and a gastric tonometer during the study. Fluid filtration capacity and isovolumetric venous pressure were assessed using a electromechanical sensor with automated calibration for strain-gauge plethysmography (Filtrass 2001, Domed GmbH, Germany). In addition, arterial lactate concentrations, arterial-, mixed venous blood gas analysis and systemic hemodynamics were measured and systemic oxygen transport variables calculated. For statistical analysis paired Student's *t*-test and in cases of non-normal distribution the Wilcoxon signed-ranked test was performed. *P*-values < 0.05 were considered significant. Data are given as means ± SD.

Results: There were no differences in age, systemic oxygen delivery, consumption and oxygen extraction ratio between groups. Mortality in patients with moderate MODS was 15.4%, in patients with severe MODS 55.6% ($P = 0.049$). Patients with high MODS demonstrated significantly higher arterial lactate concentrations (4.5 ± 3 mmol/l) when compared with moderate MODS (1.7 ± 0.9 mmol/l; $P = 0.04$). There was a trend towards higher capillary filtration coefficients in patients with severe MODS (5.33 ± 2.04 ml/min/100 ml/mmHg $\times 10^{-3}$) when compared to moderate MODS (4.02 ± 1.48 ml/min/100 ml/mmHg $\times 10^{-3}$; $P = 0.062$).

Conclusion: Patients with severe MODS have a tendency towards higher capillary filtration coefficients suggesting increased capillary leakage. Neither systemic oxygen transport parameters nor tonometrically derived variables demonstrated any differences between MODS-groups despite significant differences in patients mortality.

Reference:

1. Goris RJA, Te Boekhorst TPA, Nuytinck JKS, Gimbrere JSF: **Multiple-organ failure.** *Arch Surg* 1985, **120**:1109-1115.

Acknowledgement: Study supported by a Lorenz Böhler Fonds 2000.

P204 Microvascular bed volume evaluated by near infrared spectroscopy in healthy and critically ill subjects

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Introduction: The microvascular tone regulation can be very useful to be assessed to titrate therapy in critical conditions. In the present study, we use near infrared (NIR) spectroscopy in the frequency domain on critically ill patients and healthy subjects, to obtain the measurement of microcirculatory compliance and the regulation of vascular tone.

Methods: Two groups of subjects have been studied: the first group was composed by 17 healthy subjects (H) at rest, in the second group five critically ill patients were treated with noradrenalin infusion (N). In the N group the measurements have been performed at different noradrenalin doses: the first dose (d1) was established by the head physician, then the dose was doubled (d2) and finally reduced at the half of the first dose (d3).

The probe of the spectrometer used in this study (ISS incorporated, Urbana, IL, USA), have been applied on the forearm skin, in a zone corresponding to brachioradial muscle. A serial of a pneumatic cuff compressions have been performed at the arm. Measurements of the total hemoglobin [Hbt] in tissue and blood volume, derived from [Hbt] have been obtained. The linear coefficient correlating blood volume to cuff compressions was considered as a measurement of venous and capillary compliance.

Results: The [Hbt] and Hb in the blood of the two groups are shown in Table 1, the Hb content in the blood was lower in N than in H group. There was no difference about [Hbt] between the groups. In the H group in no subject [Hbt] change, at cuff pressure of 10 mmHg, was evidenced while only five subjects out of 17 showed a [Hbt] increase at 20 mmHg. In the N group, three subjects out of five (60%) showed a [Hbt] increase at 20 mmHg pressure. The capillary and venular bed compliance is shown in Table 1.

Conclusions: From our results is shown clearly that in critically ill subjects the microvascular bed volume rose, in fact even if the Hb in blood was low the [Hbt] in tissue did not change.

References:

1. De Blasi RA, Ferrari M, Natali A, *et al*.: **A non invasive measurament of forearm blood flow and oxygen consumption by near–infrared spectroscopy.** *J Appl Physiolol* 1994, **76(3)**:1388-1393.
2. Fantini S, Franceschini MA, Maier JS, *et al*.: **Frequency domain multichannel optical detector for non-invasive tissue spectroscopy and oxymetry.** *Opt Eng* 1995, **34**:32-42.
3. Shrier I, Magder S: **Pressure–flow relationship in a vitro model of compartment syndrome.** *J Appl Physiolol* 1995, **79**:214-221.

Table 1

Group	H	N		
Hb (g 100 ml^{-1})	14.21 ± 1.1	8.64 ± 1.79		
		d1	d2	d3
[Hbt] μM l^{-1}	58.28 ± 16.63	51.3 ± 19.01	53.16 ± 20.67	52.62 ± 19.19
Compliance (μl·mmHg^{-1}·100 g^{-1}T)	20 ± 10	5.4 ± 4.5	3.9 ± 2.6	5.0 ± 3.2

Hb, blood hemoglobin; [Hbt], tissue hemoglobin.

P205 Utility of mixed venous vs central venous oximetry following cardiac surgery in infants

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Objective: Mixed venous oxygen saturation (PAsat) has been used as a surrogate marker for trends in cardiac output and oxygen utilisation:supply ratio following cardiac surgery in infants. We wished to ascertain whether superior vena cava oxygen saturation (CVsat) would provide similar trend-related information.

Method: Twenty infants were studied following cardiac surgery, median age 2 weeks (range: 2 days–18 weeks). Operations included complete correction of the following: transposition of the great arteries ($n = 10$), ventricular septal defect ($n = 7$), atrioventricular septal defect ($n = 2$), and total anomalous pulmonary venous drainage ($n = 1$). All patients had absence of postoperative anatomical shunt on colour Doppler echocardiography. Single-lumen pulmonary artery lines were placed intraoperatively, and position of the preoperatively placed percutaneous central venous lines was checked by chest X-ray. Oxygen saturation was measured by co-oximetry. Cardiac index was estimated using a typical oxygen consumption of 9 ml/min/kg, and adjusted by 10% for every degree of temperature change from 37°C. Analysis was by two-way, repeated measures ANOVA.

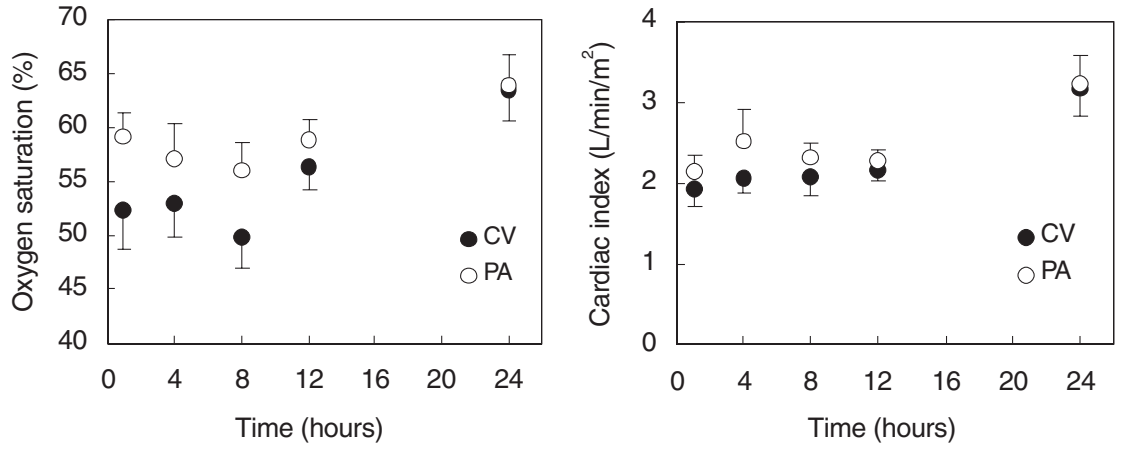
Results: PAsats were generally higher than CVsats (group effect $P = 0.02$), with a mean difference of 6.7% 1-hour post operatively (Fig.); however this had dropped to 2.6% at 12 hours, and 0.4% at 24 hours. This did not produce a significant difference in estimated cardiac index (group effect $P = 0.16$, interaction $P = 0.94$).

On sequential readings, PAsats and CVsats trended in the same direction on 75% occasions; however the greatest discrepancy was between the 4 and 8-hour readings, when concordance was only found 55% of the time.

Conclusion: PAsats and CVsats provide similar quantitative and qualitative haemodynamic information in the absence of anatomical shunts following cardiac surgery. Consistent differences between the two readings in the first 12 hours may be due either due to

regional perfusion and/or oxygen consumption differences between the upper and lower body, or may reflect a transient, small anatomical leak across sites of shunt correction which is missed by echocardiography.

Figure



P206 Intraoperative correction of low cardiac output to normal values improves outcome in patients with elective abdominal surgery

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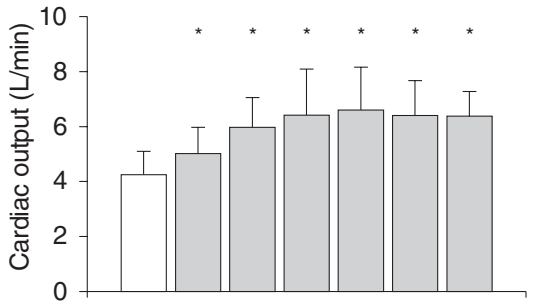
Introduction: Clinically unrecognised hypovolemia [1], low stroke volume and/or cardiac output [1,2] during the intraoperative period represent risk factors for unfavourable postoperative outcome. Several prospective randomized clinical studies have shown a decreased postoperative morbidity and mortality linked to perioperative cardiac output or DO_2 stimulation to so-called supranormal values (CI > 4.5 l/min/m^2 or DO_2I > 600 ml/min/m^2) [3]. The objective of our study was to find out whether intraoperative maintenance of at least normal values of cardiac output (i.e. 5–7 l/min) would influence postoperative outcome in a group of elective abdominal surgery patients. The reason to choose normal range of cardiac output as a therapeutic goal was the observation, that average values of intraoperatively measured cardiac output are frequently found in a range lower than normal values in a group of patients with unfavourable postoperative outcome [2].

Methods: Forty-nine consecutive adult patients, undergoing extensive elective abdominal surgery with expected duration of more than 90 min, were included in this prospective observational study (37 male and 12 female; average age: 61.6 ± 11 years; 84% – abdominal surgery for tumour, 14% – bowel resection for inflammatory disease, 2% – abdominal aortic surgery; average length of surgery: 172 ± 64 min). They were divided into two groups: the first group of consecutive 24 patients managed with oesophageal doppler and the second consecutive group of 25 patients managed according to usual intraoperative monitoring. In the first group of patients (doppler group [D]; n = 24, male: 67%, female: 33%; average age: 61.4 ± 13 years; 79% – abdominal surgery for tumour) intraoperative hemodynamic management was based on the continual CO monitoring using oesophageal doppler (HEMOSONIC™ 100, Arrow International, Inc.). Doppler probe was inserted on an average 15 min after induction of general anesthesia. Whenever during surgery there was a drop in cardiac output below 5 l/min, usual diagnostic and therapeutic intervention were carried out to reach its normal range 5–7 l/min. Cardiac output values, for data processing, obtained from oesophageal dopplerometry, were collected in 30 min interval (Fig. 1). Intraoperative hemodynamic management in the second group of patients (non-doppler group [ND]; n = 25, male: 84%, female: 16%; average age: 61.8 ± 9 years; 84% – abdominal surgery for tumour) was based on the monitoring of commonly used parameters: ECG, non-invasive blood pressure or invasive pressures (arterial blood pressure, central venous pressure), $ETCO_2$, SpO_2. Operating theatre staff, both anesthesiologic and surgical personnel, were blinded to patients' study inclusion. The postoperative management of both patient's groups was carried out in the Department of Surgery. Likewise the operating theatre staff, staff of the surgical department was also blinded to patients' study inclusion. In both D and ND group of patients we analysed and compared these data: ASA score, duration of surgery, blood units administered and fluid management intraoperatively, hemodynamic or respiratory instability occurrence during surgery, need for postoperative artificial ventilation longer than 24 hours, length of ICU stay, occurrence of postoperative complications (cardiovascular, respiratory, renal, gastrointestinal, coagulation, CNS and wound complication) total length of hospital stay and mortality. For statistic data processing following tests were used: Wilcox, Mann–Whitney and χ^2-test. Statistical significance was determined as $P < 0.05$. Values are shown as mean ± SE.

Results: Significantly lower frequency of postoperative complications (number of patients with complications: D: 5/24 vs ND: 14/25; total frequency of complications: D: 8/186 vs ND: 31/175; average frequency of complications per patient: D: 0.33 ± 0.63 vs ND: 1.24 ± l.69; the greatest difference in occurrence of complications was found for gastrointestinal and wound complications), shorter ICU stay (D: 3.9 ± 1.8 days vs ND: 5.8 ± 3.2 days) and total hospital stay (D 14.8 ± 7.3 days vs ND: 19.4 ± 8.1 days) were found in the group

Figure 1



Average CO values during surgery in doppler group. □, Initial CO value (15 min after general anesthesis induction). *$P < 0.05$, compared with initial CO value

of patients with intraoperative cardiac output maintained in normal range (46% of cases needed beyond fluid administration also inotropic support with dobutamin and 25% of cases needed administration of isosorbid-dinitrate). In the rest of observed parameters there was found no significant difference (Table 1).

Conclusion: Intraoperative correction of low cardiac output to normal range is linked to improvement of postoperative outcome in elective abdominal surgery patients. Randomly collected data with high comparability between both groups of patients (namely age, ASA score, duration of surgery, intraoperative blood units administered and fluid management, frequency of intraoperative complications), allow us to state that clinically unrecognised low cardiac output or drop of cardiac output during intraoperative period participates, in a crucial way, in postoperative unfavourable development.

Table 1

Average values of parameters that did not reach statistical significance

	Group D	Group ND
ASA score	2. 4 ± 0.9	2.2 ± 0.7
Duration of surgery	171 ± 69 min	172 ± 60 min
Fluids intraoperatively	2896 ± 1409 ml	2958 ± 1223 ml
Blood units	10/24	9/25
FFP, colloids	740 ± 743 ml	742 ± 713 ml
Crystalloids	1972 ± 859 ml	2094 ± 668 ml
Hemodynamic instability during surgery	4/24 (17%)	6/25 (24%)*
Respiratory instability during surgery	1/24 (4%)	2/25 (8%)
Artificial ventilation for > 24 hours postoperatively	0/24	2/25 (8%)
Mortality	0/24	2/25 (8%)

* Fluid administration and in three patients also dopamine was used in management of hemodynamic instability. Note: dobutamine and/or isosorbid-dinitrate was not used in any patient from ND group.

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P207 The cost-effectiveness of preoperative optimisation of high risk surgical patients

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Aims: This study aimed to determine the cost-effectiveness of a London National Health Service Hospital Trust providing preoptimisation with intravenous fluids, oxygen, and inotropes to High Risk Surgical Patients with the aim of reducing postoperative complications.

Design: A cost-effectiveness study.

Method: The cost of usual care for a 5 month cohort ($n = 40$) of High Risk Surgical patients was calculated by using the standard Health Resource Group costs provided by the NHS Executive which gives average costs for Hospital Stay based on procedures and treatment. Intensive care bed days were added at a local rate (£1072) multiplied by number of days spent in ITU. Group average costs were calculated for those who suffered postoperative complications ($n = 13$, £7751) and those that did not ($n = 27$, £2983). The cost of preoptimisation was estimated by including preoperative and postoperative costs such as Intensive care and HDU bed usage, equipment, and the time of a Consultant Anaesthetist (total cost per patient = £1328). Predicted reductions of morbidity were taken from a published randomised controlled trials. Sensitivity analysis was performed on a range of costs and effects.

Results: Results showed that preoptimisation is cost-effective as it dominates in comparison to usual care. Sensitivity analysis also showed that the treatment remained cost-effective even if the intervention gives a reduced effect.

Conclusion: Preoptimisation would be cost-effective for the London NHS Trust as it would reduce cost of hospitalisation care by reducing the recovery period of High Risk Surgical Patients.

P208 Outcome of hemodynamic instability therapy guided by pulmonary artery catheter in immunocompromised ICU patients

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Objectives: The aim of this study is to evaluate the outcome of the therapy guided by pulmonary artery catheter (PAC) in immunocompromised ICU patients.

Setting: A kidney transplant specialized ICU in a 90-bed public hospital.

Methods: We prospectively followed (from May 2000 to November 2001) kidney transplant recipients admitted to ICU who developed hemodynamic instability which required vasoactive drugs administration and PAC insertion in order to optimize therapy. After catheter insertion, based on hemodynamic profile, the patients were classified in one of the following types of shock: distributive, cardiogenic, obstructive and hypovolemic. ICU resource utilization, catheter-related complications and 28-day mortality were recorded.

Results: In the period of study, our institution had 2021 kidney transplant recipients in ambulatory management, performed 690 kidney transplant surgeries and the ICU admitted 289 kidney transplant recipients (not in postoperative period). There were 13 consecutive patients (3 F/10 M) who fulfilled inclusion criteria. The mean age was 45.4 ± 10.3. Of these patients 12 (92%) were in the first year of transplantation and all patients were receiving immunosuppression therapy at ICU admission. The mean Apache II score was 22 ± 8. The PAC was inserted within 24 hours of the beginning of hemodynamic instability in all patients. There were nine (70%) patients classified as distributive shock (sepsis) and the mortality in this group was 78% ($n = 7$). There were two (15%) patients with cardiogenic shock (acute myocardial infarction) and the mortality was 50% ($n = 1$). There were two (15%) patients with hypovolemic shock (acute drug-induced pancreatitis, nephrotic syndrome) and the mortality was 50% ($n = 1$). The mean permanence of CAP was 4.5 ± 2.6 days. In one (7.5%) patient there were complications related to catheterization procedure (pneumohemothorax). The mean length of ICU stay was 12.9 ± 15.1 days and of mechanical ventilation was 10.5 ± 15.6 days. In nine (70%) patients there was need for renal replacement therapy.

Conclusion: Based on these preliminary results, distributive shock associated with sepsis is more frequent and carries a higher mortality than cardiogenic and hypovolemic shock in immunocompromised patients.

P209 Assessment of energy consumption by indirect calorimetric method and Harris–Benedict equation in patients with severe head injury

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Objective: In this prospective study, indirect calorimetry (IC) and Harris–Benedict equation were compared to find out the daily energy consumption of the patients who have severe head injury and ventilation support.

Methods: The inclusion criteria were; head injury with Glasgow Coma Scale score (GCS) ≤ 8, peripheral oxygen saturation over 95% with inspired oxygen concentration lower than 0.5. Thirty-six patients who met these criteria and were admitted to our intensive care unit (ICU) between March and October 2000 were included in the study. The Injury Severity Score (ISS), Revised Trauma Score (RTS), Acute Physiology and Chronic Health Evaluation II (APACHE) score, Glasgow Outcome score (GOS), and intensive care stay of the patients were determined. The indirect calorimetric measurements were performed by Vmax 6200 Metabolic Measurement Cart (Sensor Medics, Yorba Linda, CA, USA) in the first 48 hours following admission of the patients to the ICU. Fifty-five measurements were carried out in 36 patients and after each measurement which lasted 12 hours the mean values of resting energy expenditure (REE), O_2 consumption, and CO_2 production were noted. All of the patients were in steady-state during the measurements. Moreover, the daily nitrogen balance of all patients were determined.

Results: The basal energy expenditure calculated with Harris–Benedict equation was 1674.6 ± 317.5 kcal, and daily average resting energy expenditure (REE) measured with IC was 1881.2 ± 465.0 kcal. The energy consumption measured with IC was 12.4% higher than the value which was calculated with Harris–Benedict equation ($P < 0.05$). Average daily nitrogen loss was 21.6 ± 16 g.

Conclusion: The energy consumption calculated with Harris–Benedict equation had no correlation with trauma severity.

The REE measured with IC was higher in the patients who had GCS 6 or higher, RTS over 5, and ISS 25 or lower compared with the other.

There was no correlation between nitrogen loss of the patients and trauma severity.

P210 Oxygen consumption in critically ill children

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Measurement of oxygen consumption (VO_2) in the critically ill patient has become an important tool because of its prognostic value and therapeutic implications. If oxygen delivery does not match VO_2, tissue hypoxia ensues followed by organ failure. It is well known that critically ill patients have increased VO_2, however what has not been fully explored is whether different disease categories have varying degrees of VO_2. The purpose of this study was to determine if VO_2 differs between subgroups of critically ill children.

Methods: Ninety patients between the ages of 5 weeks and 16 years who were mechanically ventilated were included in this study. Patients were excluded if: air leak around the endotracheal tube was > 5%, FiO_2 was > 0.6, or catecholamine infusion was required. VO_2 was measured within the first 24 hours of admission to the pediatric intensive care unit. A Deltatrac metabolic monitor, which uses a paramagnetic oxygen analyzer, was used to measure VO_2. Measurements were obtained over 20 min and standardized to body surface area. Patients were categorized into medical, surgical, trauma, sepsis or cardiac surgery subgroups. Mean VO_2 in the medical subgroup was compared to the other subgroups.

Data was analyzed using one-way ANOVA and Bonferroni Multiple Comparisons test.

Results: There was a statistically significant difference in the mean VO_2 between patients in the medical subgroup and patients in sepsis subgroup ($P < 0.001$), surgery subgroup ($P < 0.01$), and cardiac surgery subgroup ($P < 0.001$). There was no significant difference in the mean VO_2 between patients in the medical subgroup and trauma subgroup.

Table

	Medical ($n = 23$)	Trauma ($n = 30$)	Sepsis ($n = 16$)	Surgical ($n = 8$)	Cardiac surgery ($n = 13$)
Mean VO_2 (ml/m^2) (SD)	135.26 (20)	145.23 (18)	163.94 (19)	165.25 (19)	180.08 (22)

Discussion: We have demonstrated that VO_2 varies based on the category of critical illness. This finding is significant given the importance of optimizing and matching oxygen delivery to a patients' VO_2.

P211 Nutritional status in hypercatabolic patients with acute renal failure

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Introduction: In spite of optimized artificial nutrition, the development of malnutrition is often rapid in critically ill patients with acute renal failure undergoing a continuous venovenous hemofiltration (CVVH) [1].

Methods: In this prospective-observational study we evaluated all patients with hypercatabolic status during a period of 15 days. A Hospal Prisma blood pump at a ultrafiltrate rate of 1.2 l/h and polyacrylonitrile AN69HF hemofilters were employed. Daily caloric support and nitrogen intake as well as urinary nitrogen loss were recorded. Specimens of ultrafiltrate (200 ml) were collected every 48 hours from a 5 l pool ultrafiltrate. Daily nitrogen losses were calculated by multiplying the nitrogen concentration measured in each specimen by the total amount of ultrafiltrate produced over a 24-hour period and by adding to this the standard estimate for insensible nitrogen losses (15 mg/kg/day). Nitrogen balance was estimated as the difference between intake and losses after taking changes in total urea body pool into account. The evaluation of nutritional status was assessed collecting lost body weight everyday and lymphocyte count, serum albumin, serum pre-albumin, transferrin, at least twice a week. Comparison of nutritional parameters between the beginning of the treatment and after 15 days was made using Student's *t*-test ($P < 0.05$).

Results: Twelve critically ill patients (four burnt and eight septic) were studied. Their mean SAPS II was 48.6 ± 15.5 and the mean of SOFA was 11.1 ± 3.1. They received a mean amount of 43.4 kcal/kg/day. The protein intake was of 1.8 g/kg/day, in spite of fact that more aggressive renal replacement therapy was used to achieve adequate control of uremia (mean plasma urea 15.4 ± 7.2 mM/l). The mean nitrogen losses in the ultrafiltrate were 25.4 ± 5.4 g/day and the nitrogen balance was −9.8 ± 0.3 g/day. During the period of study the lost body weight was 0.53 ± 0.1 kg/day. The nutritional parameters measured (beginning vs 15th day) are shown in the Table.

Table

Lymphocyte count (lymph/mm^3)	0.60 ± 0.29 vs 0.84 ± 0.3, $P < 0.05$
Albumin (g/dl)	26.7 ± 3.5 vs 26.3 ± 3.5, NS
Prealbumin (mg/l)	90 ± 33 vs 111 ± 29, NS
Transferrin (g/l)	0.96 ± 0.15 vs 0.77 ± 0.1, $P < 0.05$

Conclusion: Hypercaloric and hyperprotein diet, considering standard nutritional protocols, does not assure adequate nutritional status in hypercatabolic patients with acute renal failure undergoing renal replacement therapy. Increase in lymphocyte count could be correlated with improvement of septic condition.

Reference:

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P212 The incidence and immediate respiratory consequences of pulmonary aspiration of enteral feed

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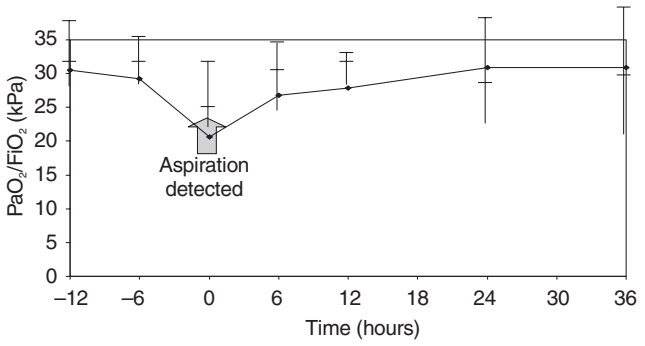
Introduction: The cause of a respiratory deterioration in a critically ill patient frequently remains unknown. Pulmonary aspiration of enteral feed during tracheal intubation may be recognised at the bedside by the appearance of feed in the tracheal aspirate but is commonly unrecognised. To reduce aspiration it is important to be able to detect it at the bedside and hence alter management to reduce risk factors. Techniques to detect feed aspiration using food colouring have poor sensitivity and are linked with mortality in septic patients [1]. The standard glucose oxidase strip method for detecting aspiration is also insensitive because the glucose levels in feeds are similar to those of normal tracheal aspirates. We have previously described a modified glucose oxidase test strip method with an improved sensitivity [2] whereby the glucose concentration of the feed is markedly increased.

Method: The glucose concentration of the feed was increased by adding 10 g of glucose to 500 ml of feed. This increased the carbohydrate load by only 14% from 68 g to 78 g, but markedly increased the glucose concentration by 1000% from 11 mmol/l to 120 mmol/l. Testing tracheal secretions with standard glucose oxidase strips allowed the detection of tracheal aspiration (when tracheal glucose exceeds blood glucose). Ten patients were studied and PaO_2/FiO_2 data were collected prospectively prior to and after each aspiration episode.

Results: Five of the 10 patients aspirated enteral feed on one or more occasion (incidence 50%). There were seven episodes of aspiration detected in 55 patient days studied (prevalence 13% per day ventilation). Following an aspiration there was a fall in

Figure 1



Deterioration in gas exchange associated with feed aspiration (mean/2 SEM).

PaO_2/FiO_2 from a mean of 29.2 to 20.7 kPa (Fig. 1; $P < 0.017$; Wilcoxon rank sum test).

Conclusion: Aspiration of feed in the critically ill is common and is associated with a fall in PaO_2/FiO_2.

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2. Young PJ: **A spoon full of sugar.** *Anaesth Intensive Care* 2001, **29**:539-543.

P213 The effect of preoperative immunonutrition on postoperative immune system and cytokine release in the cases undergoing major abdominal surgery

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Background and goal: We aimed to investigate the effects of use of preoperative and early postoperative standard and immunonutrient products on immune system and acute inflammatory response in the patients undergoing gastrointestinal malignancy surgery.

Materials and methods: Ninety patients of ASA II-III, were randomly divided into three groups. All patients were started to be given enteral nutrition in 1000 kcal/day in addition to standard oral nutrition on 5th preoperative day. Enteral nutrition was restarted with 30 kcal/kg/day via nasojejunal tube or jejunostomy at 12th hours of surgery. Group I patients ($n = 30$) received isocaloric, isonitrogenic standard oral nutrition (Osmolyte®, Abbott), Group II patients ($n = 30$) received oral immunonutrition (Impact®, Novartis), whereas Group III patients ($n = 30$) received enteral or oral nutrition (Supportan®, Fresenius Kabi). Studies of immune function and evaluation of nutritional parameters were made for all patients on 5th (T_1) and 1st (T_2) days preoperatively and 1st (T_3) and 5th days (T_4) postoperatively. For nutritional assessment; albumin, prealbumin, retinol binding protein (RBP) and transferrin levels were determined. For immunologic assessment; IL-2 and IL-6 levels, IgG, IgM, total lymphocytes, T-lymphocytes, B-lymphocytes were studied. Postoperative complications, ICU and hospital length of stay, duration of antibiotherapy were also compared between groups.

Results and discussion: In all groups nutritional parameters were significantly decreased on T_3 ($P < 0.05$). Prealbumin and RBP levels (i.e. early stage nutritional parameters) increased in group II on T_4 ($P < 0.05$). IL-6 and CRP measurements (i.e. predictors of acute systemic inflammatory response), increased significantly in all groups ($P < 0.05$) but this increase was lower in group II than the others. IL-2 levels (i.e. the cellular component of immune system) increased significantly on T_3 and T_4 in group II ($P < 0.05$). T-lymphocytes decreased in group I and III on T_3 and T_4. This decrease was not seen group II. The duration of antibiotherapy, ICU and hospital length of stay was significantly longer in group I than the others. The incidence of postoperative infection was less in group II.

Conclusion: Early enteral nutrition with arginin in hypercatabolic state after major operations results a decrease in severity of acute inflammatory reaction, augmentation in cellular immunologic support, and a decrease in ICU and hospital length of stays.

P214 Influence of muscle relaxants on the mass of intercostal and upper arm muscles in COPD patients during mechanical ventilation

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Purpose: The aim of the study is to assess the degree of intercostal and upper arm muscles atrophy in COPD patients requiring ventilatory support and muscular relaxants.

Methods: Twenty-four mechanically ventilated patients hospitalised in the ICU for 18.6 ± 3.6 days, were included in the study. Twelve patients with COPD exacerbation and 12 patients admitted in the ICU for various reasons (control group) received atracurium (0.3–0.6 mg/kg/h) for 2.8 ± 0.4 days. The groups did not differ significantly for age (62.5 ± 6.4 versus 65.6 ± 5.9 years, respectively). Both groups were under the same nutritional schedule. Muscular mass (MM) of intercostals and upper arm muscles were measured in cm by U/S at the 1st and the 5th ICU hospitalisation day. A 10 MHz linear transducer was used and the same intercostal space was scanned in all patients. Measurements were also done at the same position of the right upper-arm. All scans were

Table

	Intercostal muscle mass			Upper arm muscle mass		
Group	1st day MM	5th day MM	ΔMM	1st day MM	5th day MM	ΔMM
COPD	0.28 ± 0.01	0.20 ± 0.01	0.07 ± 0.02	2.13 ± 0.33	1.65 ± 0.27	0.47 ± 0.33
Control	0.42 ± 0.04	0.31 ± 0.03	0.10 ± 0.03	3.03 ± 0.21	2.33 ± 0.36	0.70 ± 0.21

performed by the same sonographer. The corresponding differences (ΔMM) were compared between the two groups of patients with the aid of the Student *t*-test ($P < 0.05$).

Results: Our results concerning measurements of muscle mass (in cm) are presented in the Table as mean values ± standard deviations.

Intercostal and upper arm MM was significantly greater in the control group than in the COPD group in the 1st as well as in the 5th hospitalization day. MM thickness was significantly reduced between the 1st and the 5th hospitalization day in both the COPD and the control groups. Nevertheless, the ΔMM difference between COPD and controls was significant for intercostals ($P < 0.03$) and not significant for upper arm muscles.

Conclusions: MM is significantly lower in COPD mechanically ventilated patients in comparison to other patients under ventilatory support. Muscle relaxants reduce significantly the MM in COPD patients requiring assisted ventilation. Nevertheless, the MM changes are not uniform in various muscles as indicated by the comparison of the COPD to the control group, concerning the intercostals and the upper arm muscles. It seems that a more precise and complete information for the reduction of MM should be estimated at different muscle groups.

P215 Bombesine in critically ill patients receiving enteral and total parenteral nutrition

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Purpose: Bombesine (BN) is a hormone with a critical role on the control of the secretory gastrointestinal (GI) function and the immunological sufficiency of the human body. The aim of this study is to evaluate the influence of nutritional schedule (enteral vs total parenteral) on BN levels, during the first 5 days of ICU hospitalization.

Methods: Twenty-one sedated and mechanically ventilated patients were randomly divided into two groups. Group A consisted of 11 patients, who received continuous nasogastric nutrition, and Group B consisted of 10 patients, who received continuous Total Parenteral Nutrition (TPN). Serum hormone levels were measured on the 2nd, 3rd and the 5th day of patients admission with radioimmunoassay method. BN levels were compared between the three measurements with the aid of ANOVA for each group, while the corresponding measurements between the two groups were compared with the aid of Wilcoxon test.

Results: Values of BN (ng/ml) as mean values ± standard deviations during subsequent measurements in the two groups of patients are presented in the Table.

Table

Days of hospitalization	EN	TPN
Day 1	11.8 ± 9.8	9.4 ± 10.5
Day 2	12.0 ± 8.2	9.9 ± 9.9
Day 3	15.8 ± 11.7	6.2 ± 7.8

No statistically significant changes between hormone levels are observed in each group for the three different measurements ($P > 0.05$). The corresponding differences between the two groups are also not significant ($P > 0.05$). Despite the non-significance of the differences it should be noted that BN is increased through measurements in the enteral nutrition (EN) group whereas a decrease is observed in the TPN group on the 5th day.

Conclusions: The administration of either enteral or parenteral nutritional formulas for a short period of hospitalization in the Intensive Care Unit does not affect the levels of BN. The extra-gastrointestinal presence of BN might explain the non-significant differences observed in our study between the EN and TPN groups. The results of the present study refer to a short-term application of the tested nutritional schedules. BN showed a clear tendency to increase, during EN. A longer follow up of the gastrointestinal hormones profile seems necessary.

P216 Intravenous total parenteral nutrition elevates oxidant production in critically ill patients

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Introduction: Critical illness is associated with increased oxidant stress. This is manifested by reduced antoxidant potential and an increase in measured oxidant species (ROS). ROS have the capacity to cause cellular injury and to activate NFKB in inflammatory cells.

TPN provides a source of lipid for systemic peroxidation particularly in the presence of reduced antoxidant potential. TPN generally contains inadequate nutrient-antoxidants and precursors to glutathione. Total parenteral nutrition (TPN) is also a source of lipid peroxides which are pro-inflammatory.

Materials and methods: This study was approved by the Committee for Research on Human Subjects of the University of the Witwatersrand. Patients were recruited sequentially if they required TPN. Blood was taken 1 hour pre initiation of TPN, at the time of and 1 hour and 2 hours post initiation of TPN. Urine was also collected at the same times. Vitamin C, glutathione, IL6 and F_2-isoprostanes were measured in the urine.

Results: There were no changes in the vitamin C levels and no definite trend was seen with IL6. The F_2-isoprostanes in the urine remained constant for the −1, 0 and 1 periods, then increased significantly by 4.24 units (95% CI, 0.03–8.21) at time +2. This was significant (Friedman ANOVA $P < 0.01$).

Conclusions: Administration of TPN is associated with an increase in lipid peroxide formation which may itself be proinflammatory and account for adverse outcomes of patients on TPN.

P217 Patients after acute pancreatitis benefit from long-term home enteral nutrition

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Background: Stimulation of exocrine pancreatic function by oral intake impairs resolving of necrotic peripancreatic masses after severe acute pancreatitis. A long-term parenteral or enteral nutrition may be beneficial in the therapy of postpancreatitic complications. Aim of the study was to verify efficacy and safety of long-term home enteral nutrition for therapy of pancreatic pseudocysts after severe acute pancreatitis.

Patients and methods: Eighty-nine patients with severe acute pancreatitis were evaluated in the prospective clinical study: females 38, males 51, mean age 53.2 years (18–80). After initial period of total parenteral nutrition (TPN) and early enteral nutrition (EEN) with mean duration 13.2 days (5–23), patients were matched into two groups with either enteral or oral nutrition, matching in Ranson's score, age, and size of peripancreatic pseudocysts. Fifty-nine patients (enteral group) were administered an enteral oligopeptide formula, 30 patients (oral group) were administered a pancreatic diet. Criteria of effectiveness of home enteral nutrition were disappearance or substantial regression of the peripancreatic necrotic masses. The results were compared between both groups and evaluated by the paired Student's *t*-test.

Results: A significant regression of pseudocysts was reached in 65 patients (73.0%) overall: in 48 (81.4%) patients in the group treated with enteral nutrition, and in 17 (50.9%) patients with oral intake. The difference was statistically significant ($P < 0.01$). Number of severe complications within the enteral group was 1 (1.7%). Mean period of enteral nutrition was 28.9 days, mean period of controlled oral diet was 27.4 days (n.s.).

Conclusions: The results indicate that the long-term home enteral nutrition was a potent method in the therapy of pancreatic pseudocysts and it was superior to oral diet. Its effectiveness is similar with total parenteral nutrition, which has been tested in our previous study [1].

Reference:

1. Tesinsky P, Rusavy Z, Staudinger T: **Enteral nutrition: an effective method of treatment of pancreatic pseudocysts [abstract 45].** *J Parenter Enteral Nutr* 1999, **23(1)**:S12.

P218 Investigation of the factors which influence insulin sensitivity in septic patients with glucose intolerance: analysis with glucose clamp method by means of artificial pancreas

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Purpose: Insulin Sensitivity (IS) is often impaired in septic patients and its evaluation is important in terms of the nutritional support for those patients. However, accurate measurement of IS is not easy, partly because Insulin Clearance (IC) is usually increased in septic patients as we reported at this congress last year. We investigated IS excluding the influence of IC and the factors which affect IS in septic patients with glucose intolerance.

Method: Twenty-one septic patients without diabetes mellitus were investigated. IS was measured by Glucose Clamp method (GC) by means of bedside-type artificial pancreas (STG-22: manufactured by NIKKISO corporation in Japan). GC was performed twice for each patient basically (first measurement was done in acute condition or within 3 days after admission, and second measurement was done 1 week after the first measurement). GC was performed with clamped blood glucose level of 80 mg/dl and Insulin Infusion Rate (IIR) of 1.12 and 3.36 mU/kg min. I1/I3 and M1/M3 indicates the blood insulin level (μU/ml) and glucose disposal rate: M value (mg/kg min), when IIR is 1.12/3.36 mU/kg min respectively. IC was calculated from the following formula: IC = (3.36 − 1.12) × 1000/(I3 − I1) (normal value of IC: 10–15 ml/kg min). M/I: M1/I1 (M1/I1 × 1000) and M3/I3 (M3/I3 × 1000) (ml l/kg min μU) were calculated as the parameter of IS. Relationships between M/I and the following factors were investigated: (1) blood stress hormone levels (SH) (adrenaline, noradrenaline, glucagon, cortisol, growth hormone), (2) serum fat levels (SF) (triglyceride, free fatty acid, total cholesterol), (3) blood endotoxin and β-D glucan levels, (4) degree of organ dysfunction/failure (MOF score: calculated from the MOF criteria of Japanese Association for Critical Care Medicine), and (5) blood IL-6 level.

Results: The results are as follows (shown in mean ± SD [*n*]). (1) (maximum, minimum, mean) of I1, I3, and IC were I1 (133, 23, 62 ± 31 [28]), I3 (705, 19, 209 ± 121 [36]), IC (26, 4, 16 ± 6 [27]) respectively. (2) Mean of M3/I3 of the patients with MOF score more than 7 was significantly lower than that of the patients with MOF score = 0 (29 ± 18 [10] vs 57 ± 20 [7], $P < 0.025$). The same tendency was found as for M1/I1 (44 ± 54 [12] vs 102 ± 76 [7], $P < 0.10$). (3) Platelet count was positively correlated with M3/I3 ($n = 35$, $r = 0.62$, $P < 0.002$) and M1/I1 ($n = 35$,

$r = 0.45$, $P < 0.006$). (4) As IL-6 increased, M/I decreased in one patient, but increased in another patient. (5) There was no definite relationship between M/I and SH, SF, endotoxin, and β-D glucan.

Interpretation and conclusions: M/I seemed to be one of the useful indicators of IS in septic patients, because IC was variable in those patients. Multiple organ dysfunction and coagulopathy with thrombocytopenia were the factors which decreased IS. Difference of the influence of blood IL-6 level to M/I among the patients might be related to the balance of the type of glucose transporters affected by the inflammatory cytokines (ex. activation of glucose transporter-1, suppression of glucose transporter-4, etc.).

P219 Glucagon processes on intestines in surgically stressed patients

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Introduction: Although insulin/glucagon molar ratio (I/G) in serum is one of the most important factor to regulate the energy metabolic status of critically ill patients, the kinetics of I/G, especially glucagon, is still not well known. In this study, we investigated the I/G and the kinetics of glucagon related peptides and discuss the glucagon processes in pancreas and intestine in surgically stressed patients. Furthermore, we investigated the energy metabolic status and discuss the correlation between these results and the glucagon processes.

Subjects and methods: Sixteen patients with acute abdomen or trauma who had undergone emergency surgeries served as the subjects. At the 2nd and 7th days after surgeries, the following items were estimated. Serum I/G and glucagon related peptides were assessed using N-terminal and C-terminal specific RIA. Molecular forms of the glucagon related peptides were also estimated using gel filtration chromatography method. Furthermore the energy metabolic status were assessed using indirect calorimetry.

Results: On the 2nd days, 75% of patients showed lower I/Gs compared to those of normal subjects and the very peculiar peptides similar to the glicentin in molecular weights which were not seen in normal subjects and supposed to be produced by peculiar glucagon processes in intestines, were observed. Furthermore, in these patients, carbohydrates were well utilized as energy sources, while, in the residual 25% of patients who did not show the peculiar glicentin like peptides in chromatographies, carbohydrates were not sufficiently utilized, and lipid metabolism were increased.

Conclusion: The I/G and the processes of glucagon, especially in the intestine in surgically stressed patients were much different from those of normal subjects and must influence the energy metabolic status.

P220 Corticoids and ACTH test in septic shock: a prospective study over 15 months

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Introduction: Inflammatory and vascular manifestations have a considerable physiological role during septic shock. The place of corticoids is discussed since 30 years.

Aim: To determine the interest of the use of corticoids in septic shock.

Patients and methods: During a period of 15 months (June 2000–August 2001), are enrolled all the patients presenting a septic shock requiring high and/or increasing doses of vaso-active agents because of the obstinacy of a low blood pressure in spite of a satisfactory colloid infusion. A test with ACTH is realized in all patients, then treatment with 300 mg daily Hydrocortisone (3 × 100) is administered.

Results: Twenty-one patients are enrolled. Their mean age is 46 ± 17 years. The mean severity score (IGSII) is 42 ± 14. The etiology is pneumonia in 62% of cases. Nosocomial infection is found 13 times (62%). The administration of corticoids is begun at the 10th hour on average. Evolution is favorable in 17 patients (81%), judged on the increase of blood pressure, the beginning of weaning or the stabilization of necessities in vaso-active agents. This occurs in 21 ± 16 H.

The result of the ACTH test allowed to distinguish three groups of patients.

Six patients have adequate adrenal response: high basal serum cortisol level which increase after ACTH's injection. Hydrocortisone is stopped. Evolution in this group is always favorable (100%).

Thirteen patients have a relative adrenal insufficiency: normal or high serum cortisol level but with a weak increase after the test. Hydrocortisone is maintained for 5 days. Evolution is favorable in nine patients (69%).

Two patients with very high serum cortisol level, had quickly fatal evolution.

Conclusion: The ACTH test must be realized at the patients in state of septic shock to discover those that can benefit from a contribution of corticoids.

P221 Reduced cortisol in acute liver failure is not due to pituitary failure or reduced binding proteins

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Reduced cortisol is common in patients with acute liver failure (ALF). The aetiology of this phenomenon is unclear, relating potentially to reduced levels of cortisol binding proteins, pituitary or adrenal dysfunction. We examined the relative importance of these factors.

Methods: Twenty patients with ALF, admitted to a 10 bedded specialist liver intensive care unit, were investigated. We sampled blood at 9:00 a.m. and measured total cortisol, ACTH and the two main binding proteins CBG and albumin as well as standard biochemistry. Cholesterol was measured as precursor of cortisol synthesis. From these data, the unbound cortisol was calculated. Normal ranges are: cortisol > 250 nmol/l, CBG 39.7 ± 6.3 μg/l for males and 42.2 ± 5.6 μg/l for females, ACTH 39 pg/ ml (range < 25–65), albumin 35–50 g/l. Absolute values are given as median and interquartile range. Comparisons were performed using the Mann–Whitney U test and correlations using the Spearman Rank Correlation coefficient.

Results: All patients had CBG below the normal range (BNR) and albumin was BNR in 19/20 patients. Fifty percent of patients had a total cortisol BNR all of whom also had a free cortisol BNR. All patients with normal cortisol had normal free cortisol. Cholesterol, albumin, and CBG were all significantly lower in patients with cortisol BNR (Table). The CBG was significantly correlated with total cortisol ($R = 0.519$, $P < 0.05$). ACTH is above normal range in 18/20 patients and was higher in those with cortisol above 250 nmol/l (Table).

Table

	Total cortisol BNR	Normal total cortisol	*P*
Cholesterol	1.05 (0.4–2)	1.9 (2–3)	< 0.005
Albumin	13.5 (9–17)	18.5 (17–23)	< 0.025
CBG	12.85 (10–15)	22.4 (17–30)	< 0.005
ACTH	41 (31–61)	60 (52–169)	0.025

Conclusion: In ALF, reduced total cortisol is accompanied by reduced free cortisol despite reduced CBG and albumin. The ACTH results suggest adrenal dysfunction rather than pituitary failure as the cause of the reduction in total cortisol seen in these critically ill patients. The low cholesterol in those with suboptimal cortisol levels may suggest lack of this precursor is of importance and requires further study.

P222 Review of the use of hydrocortisone in intensive care patients with sepsis

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Introduction: Corticosteroids may be beneficial in septic shock. Hydrocortisone (HC) has been the most widely studied steroid and is used on our ICU.

Aim: The aim of the study was to review the use of HC on the ICU, adherence to evidence-based guidelines, and the effect on inotrope (INO) and vasopressor (VP) requirements.

Method: Prescriptions were reviewed daily to identify patients (pts) on INO/VPs. Pts were excluded if corticosteroids were administered for other indications. Pt demographics, details of the HC prescription, INO/VP doses, and markers of sepsis were recorded.

Results: Twenty-five pts fulfilled the trial criteria for shock in the time period of this audit and 17 were prescribed steroids. However three were in cardiogenic rather than septic shock. Norepinephrine (NE) was used in 23, dobutamine (DB) in four and epinephrine (EPI) in three pts whilst five pts received more than one INO/VP. The median time to introduction of HC was 76 hours and 12 (17) did not adhere to ICU guidelines. The dose (expressed as mean dose per day, MDD) of NE fell from 0.30 μg/kg/min to 0.15 μg/kg/min over the following 48 hours ($P < 0.02$). The MDD for DB and EPI also decreased following HC administration. At the same time points, the MDD of NE in pts *not* receiving HC was lower, with a non-significant reduction in MDD over the same time frame. HC pts were on INO/VPs longer than the non-HC group (166 hours vs 112 hours) and had higher TISS scores (58.6 vs 49.8).

Conclusion: This audit confirms the beneficial effect of steroids on VP/INO requirements in septic shock. Non-adherence to the therapy guidelines in prescribing was common, probably due to anxieties surrounding the perceived detrimental effects of steroids in early sepsis and lack of prescription review.

Table

Mean daily inotrope and vasopressor doses

	Mean daily dose (μg/kg/min)							
	52–76 hours		77–100 hours		101–125 hours		Students *t*-test	
	HC	Non-HC	HC	Non-HC	HC	Non-HC	HC *P*	Non HC *P*
Norepinephrine	0.30	0.06	0.22	0.07	0.15	0.09	< 0.02	0.24
Epinephrine	0.70	–	0.48	–	0.37	–	< 0.03	–
Dobutamine	11.40	–	11.23	–	9.42	–	0.44	–

P223 Adrenal function in protracted critical illness: evaluation with the low-dose (1 μg) corticotropin stimulation test

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To investigate the adrenocortical function in protracted critical illness, 43 patients (29 men and 14 women), having a mean (± SD) age of 55 ± 21 years were studied. First, a morning blood sample was obtained to determine baseline plasma cortisol. Subsequently, 1 μg of corticotropin (ACTH, synacthen) was injected intravenously and a second blood sample was drawn 30 min following the injection to measure stimulated plasma cortisol. Patients having a stimulated cortisol level of at least 18 μg/dl were defined as responders. In 36 patients, morning interleukin-6 (IL-6) concentrations were also measured. Mean baseline and stimulated plasma cortisol were 16.8 ± 4.1 μ/dl and 21.2 ± 5.1 μg/dl respectively. The median increment in cortisol was 4.1 μg/dl. Median IL-6 was high (39.3 pg/ml, interquartile range 24.9–86.6 pg/ml). There was a negative correlation between IL-6 and stimulated plasma cortisol ($r = -0.40$, $P = 0.01$). Of the 43 patients, 31 patients (72%) were responders, and 12 patients (28%) were non-responders to the low-dose synacthen test. Non-responders had significantly higher IL-6 levels compared to responders (76.6 vs 37.3 pg/ml, $P = 0.01$). Overall, 18 patients died and 25 patients survived to hospital discharge. Non-survivors had significantly lower baseline (15.1 ± 2.9 vs 18.0 ± 4.5 μg/dl, $P = 0.02$) and stimulated (19.1 ± 3.3 vs 23.0 ± 5.6, $P = 0.01$) cortisol levels compared to survivors. In conclusion, patients with protracted critical illness may have an altered adrenal responsiveness to stimulation by ACTH. This finding is in part explained by an increase in the production of IL-6 and carries a poor prognosis.

P224 Time-dependence of dehydroepiandrosterone (DHEA), dehydroepiandrosterone-sulfate (DHEAS), and cortisol in survivors and non-survivors of severe sepsis

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Objective: The adrenal-derived androgens dehydroepiandrosterone (DHEA) and dehydroepiandrosterone-sulfate (DHEAS) have important immunoactivating properties. They show a considerable decrease with increasing age. In contrast, cortisol is an endogenous immunosuppressing hormone. Both activation and suppression of immune responses are crucial events during sepsis.

Patients: Twenty-eight non-surgical patients with severe sepsis (ACCM/ SCCM criteria, 15 survivors (mean age 53 ± 17, APACHE III score 63.5 ± 7.5) and 13 non-survivors (61 ± 15 years, APACHE III score 64.3 ± 10.4) were included. Hormones were compared at fulfillment of sepsis criteria and time of recovery/death intra-individually as well as between survivors and non-survivors.

Results: During early sepsis, cortisol levels (nmol/l) were higher in survivors than non-survivors (761 ± 120 vs 356 ± 78, $P < 0.02$) and they decreased in survivors ($P < 0.009$) during late sepsis. During early sepsis, DHEAS levels (% of age-matched normal levels) were significantly higher in survivors than non-survivors (80 ± 21 vs 18 ± 5, $P < 0.009$). They decreased in survivors ($P = 0.0002$) but remained low in non-survivors during late sepsis. In contrast, during early sepsis, DHEA levels (% of age-matched normal levels) were significantly elevated in survivors compared to non-survivors (289 ± 46 vs 123 ± 31, $P < 0.007$). They decreased in survivors ($P = 0.002$) but increased in non-survivors ($P < 0.04$) during late sepsis. ACTH levels did not significantly change.

Conclusions: (1) The observed hormonal changes during course of sepsis seem to be linked to immunoactivation during early and immunosuppression during late sepsis, thus underlining the importance of time-dependence. (2) The changes have prognostic importance and integrate the component of age to prognosis. (3) The concept of relative adrenocortical insufficiency is extended to changes of adrenal androgens. (4) The results may help to define subgroups which benefit from hydrocortisone substitution.

P225 High incidence of decreased cortisol reserve in brain-dead potential organ-donors

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To investigate the adrenocortical function in brain-dead, potential organ donors, 36 patients (27 men, 9 women) with severe brain injury (BI), having a mean age of 42 ± 18 years were studied. Group A, consisted of 20 BI patients who did not develop brain-death (BD), and group B, was comprised of 16 BI patients who became brain-dead. Of these, seven patients were admitted in the hospital after clinical BD. In all patients (group A and group B), a morning blood sample was obtained upon admission in the ICU to determine baseline plasma cortisol levels. Subsequently, 1 μg of corticotropin (ACTH, synacthen) was administered intravenously and a second blood sample was drawn 30 min following the injection. In group B patients, the same procedure was repeated the morning following the confirmation of BD. Patients having a cortisol level of at least 18 μg/dl following the administration of ACTH were defined as responders. After the occurrence of BD, group B patients had significantly lower values for baseline (8.8 ± 6.3 vs 17.0 ± 6.6 μg/dl, $P < 0.001$) and stimulated (16.8 ± 6.5 vs. 23.9 ± 5.7 μg/dl, $P = 0.001$) plasma cortisol levels compared to group A patients. Hormonal data of the nine brain-dead patients studied upon admission in the ICU and after the occurrence of BD were the following: baseline plasma cortisol 23.8 ± 12.0 vs

7.1 ± 4.3 μg/dl, $P = 0.008$, and stimulated plasma cortisol 28.9 ± 10.5 vs 16.0 ± 4.4 μg/dl, $P = 0.01$. Thirteen group B patients (81%) and two group A patients (10%) were non-responders to synacthen ($P < 0.0001$). In group B patients, baseline and stimulated cortisol concentrations were significantly related ($r = 0.72$, $P = 0.002$), whereas there was no correlation between baseline cortisol and the increment in cortisol ($r = -0.33$, $P = 0.21$). In conclusion, adrenal cortisol secretion following dynamic stimulation is deficient in a substantial proportion of brain-dead patients. This finding calls for reconsideration of corticosteroid replacement therapy, at least in a subset, of brain-dead potential organ donors.

P226 Unlicensed drug use on ICU

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Introduction: The use of medicines outside the terms of the product licence is a common occurrence on the ICU. While the extent of unlicensed prescribing has been quantified in paediatric practice [1], no studies have so far addressed this in the adult ICU setting. There are various types of unlicensed drug use including an unlicensed drug or a licensed drug used in an unlicensed manner. Identifying unlicensed drug use is important because the prescriber is responsible for any adverse effects suffered by the patient.

Aims: To assess unlicensed drug use in the Intensive Care Unit of the Middlesex Hospital.

Method: Specific drug charts were selected at random over a 14 day period. Details of each administered drug was compared with the product licence of the drug. Aspects of use examined included indications, route, dose, dilution, diluent and compatibility. For generic drugs, the parent branded drug's product licence was used, where applicable, to define the licensed use.

Results: Eighteen out of the 20 patients (90%) received at least one unlicensed drug administration. Of the 176 drugs prescribed, 41% were 'unlicensed' due to: unlicensed indication 13%, unlicensed route 51%, unlicensed dose 11%, unlicensed dilution/diluent 21%, unlicensed drug 4%.

Conclusion: In this sample 41% of drug use was 'unlicensed' and 90% of patients received medication administered in an 'unlicensed' manner. All nasogastrically administered drugs, adrenaline and morphine infusions were considered 'unlicensed'. Although licensed drugs for licensed uses should be used where possible, ICU doctors are generally unaware of licence specifics despite being potentially legally responsible for any adverse effects that arise from this use.

Reference:

1. Turner S, *et al.*: **Use of 'off–label' and unlicensed drugs in paediatric ICU.** *Lancet* 1996, **347**:549-550.

P227 Look-alikes favor emergency drug administration errors: a national survey in Belgium

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Errors in drug administration have been identified as a possible cause of serious morbidity or even patient death. Emergency situations increase the chances for human error. The Belgian Society of Anesthesia and Resuscitation (BSAR), the Belgian Society of Emergency and Disaster Medicine (BESEDIM), and The Belgian Society of Intensive Medicine and Emergency Medicine (SIZ) performed a joint survey among 1404 Belgian specialists in these fields about errors in drug administration in their daily practice. Among the 441 responders 64.6% ever drew a drug for another, and 43.5% ever injected one for another (themselves); 96.4% yet experienced such an error, made by themselves or by somebody else; 91.4% said they ever found ampoules in the wrong drawer or box. Among the 89 drugs cited as involved in such errors, the most frequent where atropine (107 times, 24% of responders), adrenaline (94 times, 21%), ephedrine (75 times, 17%), NaCl vs KCl vs *aqua pro injectione* (17%), xylocaine (11%) and morphine (7%). The major cause of confusing was likeness. Almost everyone involved in a drug error (91.8%) evoked look-alike ampoules (for different drugs), 71.2% look-alike labels and/or packaging, and 56% poor legibility of labels or printing on ampoules. The need to dilute emergency drugs (like inotropes) on the field was cited as a cause of calculation error by 22.9%. Sound-alike names (e.g. epinephrine vs ephedrin, levorenin vs levophed) were also cited. For 23.1%, look-alike i.v. bags containing different solutions caused problem. Among responding MDs 63.5% wore glasses or lenses for one vision impairment, 3% for more than one, and 2% were color-blind.

We conclude that there is an obvious and major problem with legibility of drugs labels, particularly emergency drugs. There is a demand from practitioners to standardize the names, concentrations and designs of emergency drugs. We propose minimal standards or norms to be defined at the European level for emergency drugs, concerning their design, (e.g. pre-diluted drugs in pre-filled ready to use glass syringes), their concentrations, their names, their packaging and labeling, and concerning the legibility of what is printed on ampoules or syringes.

P228 Optimization of morphine ampoules for injection

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Confusion between two drugs or dosages is a major risk in the hospital. One major cause of confusion is similarity between ampoules. Beside this aspect, the cost/quality ratio has to be considered for economical reasons. Thus, efforts should be made by producers to provide ampoules with a perfect and easily recognizable identification at the lowest price. Wishing to increase safety

of our medication use system, we asked a team of 23 different users (doctors, pharmacists and nurses) to compare four different systems of identifying and labelling ampoules containing injectable morphine, a drug typically used in almost all wards, and especially in anaesthetics, emergency medicine and intensive care. Two of the examined ampoules were from the same producer, DENOLIN, who wished to test a new prototype (DN) beside his ampoule currently available (DO). The two other morphine ampoules available on the Belgian market were from two other producers, STEROP (ST) and STELLA (SE), respectively. The 10, 20, 30 and 40-mg dosages were examined when available. Twenty-one subjective criteria were evaluated using a five-point Likert scale (from 1 = unsatisfying to 5 = excellent): five criteria concerned global packaging, nine evaluated unit-dose packaging and seven scored the ampoule itself. No criteria concerned the content supposed equivalent for all producers. Each participant provided an individual evaluation for all criteria and all drugs. Data were analysed by ANOVA with Newman–Keuls *post-hoc* tests ($P < 0.05$). For the DN, DO, ST and SE products, global quality was rated 3.99, 3.61, 2.30 and 2.20, respectively. External packaging scored 3.55, 3.49, 2.82 and 2.61. Similarly, unit-dose packaging was 4.27, 4.00, 1.89 and 1.99 while ampoule was rated 3.94, 3.20, 2.48 and 2.19. Quality/cost ratios were 4.2, 3.1, 2.1 and 1.8, respectively. The DN prototype was thus the first-choice product, as confirmed by statistical tests. Suggestions were made to still improve its quality and safety.

P229 The incidence and mortality rate of ventilator-associated pneumonia in elderly patients

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Objective: Elderly critically ill patients are in high risk for pneumonia acquired in the intensive care unit. The aim of our study is to investigate the incidence and the mortality rate of Ventilator-Associated Pneumonia (VAP) in elderly patients.

Design: Prospective consecutive study in a six bed medical-surgical ICU of a general hospital.

Materials and methods: We examined 91 (54 men and 37 women) postoperative and/or multiple trauma patients. Patients older than 60 years old and mechanically ventilated for ≥ 48 hours were included in this study. We considered that a patient developed VAP when he had (i) a new infiltrate on chest X-ray, for ≥ 24 hours, (ii) fever > 38.3°C, and (iii) one or more microorganisms in concentrations ≥ 10^5 cfu/ml in the samples of bronchoalveolar lavage through fiberoptic bronchoscope.

Results: Twenty-five out of 91 (27%) patients developed VAP. Age was 73 ± 8, Apache II score 24 ± 8, duration of mechanical ventilation 31 ± 15 days and 72 ± 6 in patients with VAP and without VAP respectively ($P < 0.05$). Sixteen out of 25 VAP patients (64%) and 33/66 patients (50%) without VAP died ($P < 0.05$). Additionally bivariate analysis, using age > 60 years as independent variable, showed significant difference in: ARDS ($P < 0.01$), enteral nutrition ($P < 0.05$), flail chest ($P < 0.01$), tracheotomy ($P = 0.001$), and neuromuscular blocker drugs ($P < 0.01$) between patients with and without VAP.

Conclusions: Our findings suggest that one fourth of elderly patients developed VAP and that there is no difference in the mortality rate between patients with and without VAP.

P230 Profile and outcome in elderly patients requiring mechanical ventilation

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Purpose: To describe the profile and outcome in elderly requiring mechanical ventilation (MV) in ICU.

Methods: This cohort study included all consecutive patients with age ≥ 80 years admitted to the ICU between January 1998 and November 2001. All patients had age, gender, APACHE II at admission, MODS score on day 1, need of MV, length of stay (LOS) in ICU and hospital, occurrence of sepsis and septic shock, and ICU and hospital outcomes collected. Statistical analysis comparing patients who required mechanical ventilation or not were done by Mann–Whitney and chi-square, as indicated.

Results: There were 1769 admissions in the ICU during the study period, of whom 167 (9.4%) met age criteria for inclusion in the study. A group of 116 (70%) patients required MV. The mean age was 84.2 ± 4 years, ranging from 80 to 96 years. One hundred and five (63%) patients were females. The mean APACHE II score was 18 ± 7, mean total MODS score was 4.1 ± 3 on day 1. There were 80 (48%) patients with sepsis, of whom 49 (61%) had septic shock. The mean LOS in ICU and hospital was 10 ± 12 and 28 ± 28 days, respectively. Clinical causes were responsible for 117 (70%) admissions. The ICU and hospital mortality were 55% ($n = 92$) and 67% ($n = 111$). The Table compares the characteristics of the patients, regarding with the use of MV.

Table

Variable	MV group ($n = 116$)	No MV ($n = 51$)	P
Age (years)	84.4 ± 4.2	83.8 ± 3.7	0.46
Females	73 (69.5%)	32 (30.5%)	NS
Clinical admission	81 (69%)	36 (31%)	0.54
APACHE II	20 ± 7.2	14.8 ± 5	< 0.0001
MODS total	4.9 ± 3.1	2.4 ± 2.2	< 0.0001
Central nervous system	0.9 ± 1.4	0.65 ± 1.2	0.5
Cardiovascular	1.2 ± 1.3	0.5 ± 0.9	< 0.0001
Respiratory	1.5 ± 1.2	0.4 ± 0.7	< 0.0001
Renal	0.9 ± 1.1	0.45 ± 0.8	0.007
Hematologic	0.26 ± 0.65	0.2 ± 0.5	0.6
Hepatic	0.25 ± 0.6	0.2 ± 0.5	0.9
Sepsis	68 (85%)	12 (15%)	< 0.0001
Septic shock	47 (96%)	2 (4%)	< 0.0001
Length of stay – ICU (days)	12 ± 13	5.5 ± 5.2	0.002
Length of stay – hospital (days)	27.3 ± 26	30.5 ± 33	0.64
ICU mortality	91 (78%)	1 (1.8%)	< 0.0001
Hospital mortality	100 (86%)	11 (20%)	< 0.0001

Conclusion: The elderly requiring MV had a higher mortality, which could be explained by the severity of their illness expressed by higher scores APACHE II and MODS on admission and the occurrence of sepsis and septic shock. Our patients who needed MV in the elderly had a high incidence of septic shock, LOS in ICU and poor outcome.

P231 Comparison of three scoring systems for mortality risk assessment among retrieved children

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Objective: A variety of mortality risk assessment tools exist for paediatric intensive care unit (ICU) patients. Over the last decade there has been a move towards transportation of children to regional ICUs utilising specialised retrieval teams. The impact of this on the validity of commonly used scoring systems is unknown.

Method: Data were prospectively collected on all children retrieved by two teaching hospitals in the South-East of England over a 21-month period (December 1997–September 1999). Three scoring systems were compared: (1) PIM, a point of care score encompassing eight variables from time of first patient contact by the retrieval team up until 1 hour after physical ICU admission; (2) PRISM II, a physiological based system incorporating 14 variables over the first 24 hours of physical ICU admission; and (3) pre-ICU PRISM, which includes variables collected up to 24 hours before and after ICU admission.

Results: Data were available on 929 retrieved patients (hospital A 593, B 336). The median (interquartile) age was 15 months (3–54), with a crude mortality of 7.8% (72/929). Seventy-six percent were mechanically ventilated. Accurate data collection was verified by an intraclass correlation coefficient of >0.80 on all scoring systems for 50 randomly selected patients.

Disease categories differed between the two hospitals, with A having a higher proportion of respiratory and cardiac illness, and B a greater degree of sepsis ($P=0.002$). Distribution of patients across mortality risk bands ($<1\%$, 1–5%, 5–15%, 15–30%, $>30\%$) was similar between hospital A and B using PRISM II ($P=0.27$) and pre-ICU PRISM ($P=0.82$), but not with PIM ($P=0.006$).

Conclusion: All three scoring systems produce acceptable discrimination. PRISM II appears to be best calibrated. PIM however, is easiest to collect, and with recalibration may represent a more attractive alternative.

Table

	Pre-ICU PRISM	PIM	PRISM II
Median % risk (interquartile)	6.1 (2.9–17.5)	6.9 (4.1–12.6)	3.3 (1.4–10.8)
AUC (95% CI)	0.83 (0.78–0.89)	0.86 (0.81–0.91)	0.86 (0.81–0.92)
SMR (95% CI)	0.54 (0.41–0.67)	0.68 (0.52–0.84)	0.71 (0.53–0.89)
Hosmer–Lemeshow χ^2	59.4	20.6	14.2
Hosmer–Lemeshow *P*	<0.0001	0.008	0.08

AUC = area under receiver operating characteristic curve; SMR = standardised mortality ratio.

P232 Comparison of three scoring systems for mortality risk assessment among retrieved children with meningococcal sepsis

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Objective: Scoring systems assess mortality risk following intensive care unit (ICU) admission. They may also be used as risk stratification tools, both to assess severity of illness between ICUs, and as a screening tool to select patients who may benefit from novel therapies. The latter is particularly relevant to meningococcal sepsis (MNS), as mortality is highest in this condition in the first 24 hours. With the advent of paediatric retrieval teams, ICU care now essentially begins with the arrival of the team, prior to *physical* admission of the patient to the ICU. The effect of this practice on mortality risk assessment in MNS is unknown.

Method: Data were prospectively collected on all children with MNS retrieved by two teaching hospitals in the South-East of England over a 21-month period (December 1997–September 1999). Three scoring systems were compared: PIM, a point of care score encompassing eight variables from time of first patient contact by the retrieval team up until 1 hour after physical ICU admission; PRISM II, a physiological based system incorporating 14 variables over the first 24 hours of physical ICU admission; and pre-ICU PRISM, which includes variables collected up to 24 hours before and after ICU admission.

Results: One hundred and sixty-four children were evaluated (hospital A 62, B 102), with a crude mortality of 7.23%. Accurate data collection was verified by an intraclass correlation coefficient of >0.80 on all scoring systems for 15 randomly selected patients. Scoring performance is shown in the Table.

Distribution of patients across mortality risk bands ($<1\%$, 1–5%, 5–15%, 15–30%, $>30\%$) was similar between hospital A and B using PIM ($P=0.42$) and pre-ICU PRISM ($P=0.40$), but not with PRISM II ($P=0.006$).

Conclusion: PIM, pre-ICU PRISM and PRISM II provide similar discrimination for mortality in retrieved children with MNS, however PIM exhibits superior calibration. In addition, distribution of patients

Table

	Pre-ICU PRISM	PIM	PRISM II
Mean % risk (standard deviation)	18.5 (22.9)	15.2 (16.2)	12.4 (19.6)
Median % risk (interquartile)	8.8 (3.5–22.9)	11.4 (5.6–18.0)	4.8 (1.5–11.9)
AUC (95% CI)	0.93 (0.88–0.98)	0.90 (0.80–1.00)	0.97 (0.95–1.00)
Hosmer–Lemeshow χ^2	22.02	11.44	76.04
Hosmer–Lemeshow *P*	0.005	0.18	< 0.0001

AUC = area under receiver operating characteristic curve.

across mortality risk bands varies between hospitals according to the scoring technique used. Scores which take into account variables collected prior to ICU admission (PIM and pre-ICU PRISM) appear to be least affected by retrieval team practice, and are thus preferable for risk stratification.

P233 Norepinephrine requirement is not an independent variable to predict outcome in severe septic shock patients

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Introduction: Although no ideal vasopressor agent is currently available, norepinephrine has been used to stabilize arterial pressure in euvolemic patients with septic shock. Few studies have suggested an association between norepinephrine dose and poor outcome.

Objective: To verify if norepinephrine dose requirement in severe septic shock is an independent variable to predict outcome.

Methods: We built a database, including demographic, hemodynamic and oxygen-derived variables, from 43 consecutive septic shock patients treated with norepinephrine, after fluid replacement, according to our institutional protocols. APACHE II at admission and daily LODS and SOFA scores were obtained to assess multiple organ dysfunctions. We chose standard prognostic variables including age, gender, mean arterial pressure (MAP), arterial pH, base excess, lactate levels and, norepinephrine dose requirements during 5 days after admission. We developed models to predict in-ICU mortality using univariate and multivariate analysis with stepwise regression. Consecutive variables were expressed as means ± SD. The best cut-off value was chosen using Youden's Index; $P < 0.05$ was considered significant. All statistical analyses were conducted using statistical software (SAS, Cary, NC, USA).

Results: There were 29 males (67%) and 14 females (33%), with a mean age of 61 ± 2 years. Mean APACHE II score was 22.1 ± 1.1, with an overall mortality rate of 53.5%. ICU length of stay was 14.8 ± 1.2 days. Twelve variables were identified through univariate analysis, including age, SOFA (1st day), LODS (1st and 2nd days), arterial pH (1st and 2nd days), base excess (1st and 2nd days), norepinephrine dose (1st and 2nd days) and the highest norepinephrine dose in 5 days. Only two variables retained statistical significance following multivariate analysis with stepwise regression. They were LODS (2nd day) and arterial pH (2nd day). LODS (2nd day) ≥ 5 and arterial pH (second day) ≤ 7.33 were associated with a 29.6 and 19.9 times odds to death, respectively.

Conclusion: Although norepinephrine dose is associated with mortality by univariate analysis, it is not an independent variable in severe septic patients. The importance of the severity condition (LODS) is greater than the norepinephrine dose requirement.

P234 Low urine output in acute renal dysfunction (ARI/ARFS) diagnosis

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Introduction: Low urine output (UO) has been recently suggested to define acute renal dysfunction/failure (ARI/ARFS) in addition to urea/creatinine levels [1]. We tested how inclusion of UO would change the incidence of ARI/ARFS in long term ICU patients.

Patients and methods: Medical records of long term ICU patients (> 3 days) hospitalised in 2000 were analysed for UO during the first 8 days of ICU stay. When low UO (< 200 ml/6 hours or 800 ml/24 hours minimal) was found scoring for ARI/ARFS was performed. In case creatinine was not available urea was considered sufficient for ARI/ARFS diagnosis. Furosemide medication was also recorded.

Results: Out of 189 admissions in 2000, 90 patients (62 males, 28 females), in age of 59 years (median; range 16–85 years) were hospitalised > 3 days. Altogether 98 hospitalisations were analysed (eight re-admissions in seven patients). APACHE II on admission was 25.4 ± 7.7. Four patients died within the period analysed and one was discharged from the ICU. Thirty-nine ICU days when seven patients required renal replacement therapies were also excluded from the analysis. Altogether 735 ICU days were subject to analysis.

Based on decreased UO 66 ARI/ARFS days in 34 patients were recorded. Twenty five ARI/ARFS days were found in nine patients with normal urea/creatinine values (14 in a single patient). In three cases classification of ARI/ARFS including UO would lead to a more severe classification of renal dysfunction. Eight patients would have been missed if ARI/ARFS was based on urea/creatinine values only. In all but one patient where an episode with low UO was recorded no furosemide was given.

Conclusion: When diuretics are not given, inclusion of low urine output into an acute renal dysfunction definition significantly increases the number of ARI/ARFS patients.

Reference:
1. Belomo R, *et al.*: **Acute renal failure: time for consensus.** *Intensive Care Med* 2001, **27**:1685-1688.

P235 Long-term outcome and IL-6 levels in critically ill septic patients: results from the sepsis longitudinal epidemiological outcomes tracking study (SELECT I)

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Methods: The SELECT I study is a prospective, multi-center, observational study to assess the long-term clinical and economic outcomes in patients with sepsis from presumed infectious etiology during and beyond their acute care hospitalization, along with the clinical, economic, and prognostic relevance of baseline IL-6 levels, as measured by a dichotomous rapid test (SEPTEST™: ST-positive and ST-negative readings with a cut-off at about 1000 pg/ml [1]). All eligible patients with standard clinical criteria for severe sepsis were enrolled from ICUs in 52 centres in six European countries during the study period (May 1998–October 2000). The SEPTEST™ was administered within 24 hours after inclusion in the study. Patients received usual care and were observed in the ICUs until death or discharge. After discharge the vital status and the functional and general health status (EuroQol 5D) were collected at days 30, 60, 90 and 180 following study entry. The main focus of the analysis reported here is the comparison of the survival rates in the ST-positive and ST-negative groups (Kaplan–Maier curves).

Results: Data was derived from the initial 350 patients of a total of 433 enrolled patients. Of these, 113 (32.3%) were ST-positive, 237 (67.7%) were ST-negative. There was no evidence of an association between IL-6 status and either gender, age, co-morbid condition upon admission, major interventions during hospitalization, or participation in a clinical trial. Table 1 shows the survival by group (ST-negative, overall, ST-positive). The survival difference between ST-positive and ST-negative is highly significant ($P < 0.0001$, log rank test). The difference on day 30 was 17.3% (95% CI: 6.5%, 28.2%) and remains nearly stable during follow-up (day 60: 23.9%, day 90: 1.9%, day 180: 19.8%).

Table 1

Survival rates

Group/time point	Day 30	Day 60	Day 90	Day 180*
All patients	65.7%	55.1%	52%	49.7%
ST positive	54.0%	38.9%	37.2%	36.3%
ST negative	71.3%	62.9%	59.1%	56.1%
Risk difference	17.3%	23.9%	21.9%	19.8%

* $P < 0.0001$, log rank test.

Conclusions: Overall mortality observed in this study is in the range expected in critically ill patients with severe sepsis/septic shock. However, a remarkable statistically significant difference between patients with high (ST-positive) and low (ST-negative) baseline IL-6 titers are observed. The excess mortality in the ST-positive patients occurs mostly before day 30 (i.e. in the acute phase of the condition). After this time the hazard of death seems to remain similar in the two groups over the observation time of 180 days after study entry. The study confirms the high prognostic value of IL-6 for mortality in severe sepsis as reported by others [1].

Reference:
1. Reinhard, *et al.*: *Crit Care Med* 2001, **29(4)**:765-769.

Funded by a grant from Abbott Laboratories, Chicago, IL, USA.

P236 Brazilian Sepsis Epidemiological Study (BASES): preliminary results from first 439 patients

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Introduction: Severe sepsis is one of the major causes of mortality in intensive care units (ICUs) around the world. There are few epidemiological studies based on ACCP/SCCM consensus conference criteria. The incidence of severe sepsis is largely unknown in countries like Brazil.

Objective: To determine the incidence and outcome of sepsis in Brazilian ICUs.

Methods: This is an observational, prospective, multicenter cohort study from four adult, general ICUs from two Brazilian regions.

Table 1

Incidence and outcome in 354 patients with more than 24 hours of ICU length of stay, based on ACCP/SCCM conference definitions

	Non-SIRS	SIRS	Sepsis	Severe sepsis	Septic shock
Number of patients	33	321	123	121	65
Mortality rate (%)	8.6	20.3	33.3	33.9	53.8

From May to October 2001, all patients admitted to those ICUs were prospectively followed for 28 days or until discharge. Demographic data, admission diagnosis, associated chronic diseases, APACHE II score, daily SOFA score, clinical and laboratory SIRS, sepsis, and septic shock criteria, as well as early and late outcome were collected. Data management was performed by a TELEform Elite V6 – Cardiff Software. Data were expressed as mean ± standard error. The *t*-test was used to compare mortality rates in different diagnostic categories.

Results: Mean age was 63 ± 1 years and overall mortality rate was 20%. Mean ICU length of stay was 4.5 ± 1.7 days. The main admission diagnoses (by APACHE II diagnosis categories) were sepsis, cancer, neurologic disturbances, cardiovascular surgery and metabolic disorders.

Conclusion: In those patients with more than 24 hours of ICU length of stay, the incidence of sepsis was of 34.7%. ACCP/SCCM definitions were feasible and were associated with mortality rates. Expansion of these data to other Brazilian regions is crucial to estimate the actual incidence of sepsis in our ICUs.

Supported by a grant from Eli Lilly of Brazil.

P237 Application of SOFA score to neurological patients admitted to intensive care unit

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Objective: To assess the ability of the SOFA score (Sequential Organ Failure Assessment) to discriminate outcome in neurological patients admitted to intensive care unit (ICU).

Setting: A 24-bed general ICU in a 260-bed public hospital.

Methods: We prospectively followed (from May to September 2001) neurological patients admitted to our ICU measuring daily SOFA score throughout the first 7-day ICU stay and recording the 28-day mortality. We compared median scores between survivors and non-survivors (Mann–Whitney U-test) and calculated risk relative of death. Admission APACHE II score was calculated for each patient.

Results: We studied 45 patients (29 M/16 F). The mean age was 47.8 ± 13.2 years and mean APACHE II was 14.2 ± 5.1. The mean LOS was 12.8 ± 8.3 days. The 28-day ICU mortality was 31% ($n = 14$).The best cut-off value of SOFA score was 7. Clinical diagnosis at admission were: intracerebral haematoma ($n = 14$), extradural haematoma ($n = 9$), subarachnoid hemorrhage ($n = 7$), brain swelling ($n = 5$), subdural haematoma ($n = 4$), gun shot injury ($n = 3$), diffuse axonal lesion ($n = 2$), meningitis ($n = 1$).

Conclusions: SOFA score can be used to discriminate outcome in neurological patients admitted in ICU.

Table 1

Comparison between median SOFA score in survivors and non-survivors

	Survivors	Non-survivors	P
SOFA			
D0	5 (4–6)	6 (6–7)	0.03
D1	5 (3–6)	7 (6–8)	0.006
D2	6 (3–7)	7 (6.5–8)	0.03
D7	4 (3–5)	7.5 (7–9.5)	0.0001

Table 2

Risk relative of death on days 0, 1, 2 and 7

	D0	D1	D2	D7
SOFA *f* 7				
RR	2.3	2.6	6.0	14.3
CI	1.03–5.2	1.13–6.2	1.5–24.5	1.9–105

P238 'Treatment profile': a new concept that must be considered when comparing data obtained from physiological severity of illness scores

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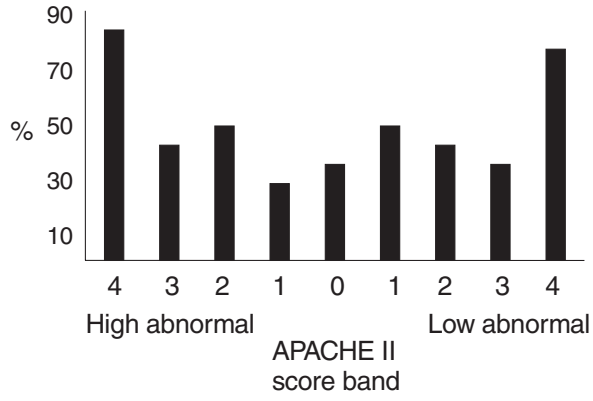
Most of the physiological derangements that contribute to critical care outcome prediction models are responsive to direct therapy to correct them. For example K^+ infusions for serum K^+ levels; and inotropes for blood pressure changes. The total physiological score attained by a patient is therefore a product of the patient's illness and also the degree of physiological control that is achieved by critical care therapy. Differences in therapeutic culture between critical care units (and indeed the same critical care units over time) may therefore have a major influence on the final/score outcome prediction. We have assessed the percentage of patients in each score band of high abnormal range (+4), normal (0) and low abnormal range (+4) for each physiological variable for APACHE II [1] having treatment specifically targeted to correct that variable to normal, in order to define a treatment profile for our ICU.

Method: The notes, treatment cards and clinical observations for 100 consecutive patients were reviewed to find the most deranged of 11 physiological variables using the APACHE II methodology (i.e. the most deranged variable within the first 24 hours of ICU admission), and the occurrence of treatment specifically targeted to correct any derangement. Analysis of Glasgow Coma Scale was not included.

Results: The results for individual parameters are shown in the Table and for combined results in the Figure. Most parameters

Figure



Summary data showing the mean percentage of patients in each score band being treated for the physiological derrangement.

have more treatment the further the value from the 'normal' range, but the converse is true for respiratory rate. Within the group of patients who fall into the zero score band for physiological derangement, 30% (see Fig.) are being actively treated to maintain that parameter within that band. Zero percent to 100% of patients (see Table) are being actively treated depending on the physiological parameter.

Conclusion: We have described the 'treatment profile' for our ICU with regard to management of physiological parameters used in the APACHE II score. We speculate that different ICUs will have different treatment profiles. Possibilities to explain this include variations in targets of treatment in different ICUs (e.g. Haematocrit) or in the expediency that deviations from a defined range are treated. We suggest that the way patients are treated on different ICUs is unlikely to be the same altering the physiological score obtained in different ICUs. These variations may or may not be reflected in changes in mortality. This precludes meaningful comparisons between ICUs using data obtained from physiological scoring systems without also comparisons of 'treatment profile'.

Reference:

1. Knaus, *et al.*: *Crit Care Med* 1985, **13**:818-829.

Table

The patients falling into each APACHE II scoring band being actively treated for each physiological parameter (% [*n*])

	+4	+3	+2	+1	0	+1	+2	+3	+4
Temp	–	38 (22)	na	8 (12)	10 (60)	10 (10)	66 (3)	–	–
MAP	–	–	–	na	12 (26)	na	42 (53)	na	82 (17)
Heart R	100 (1)	55 (11)	22 (41)	na	12 (42)	na	–	–	–
Resp R	0 (2)	0 (11)	na	3 (32)	60 (15)	29 (14)	50 (2)	na	0 (1)
pO_2	100 (24)	100 (9)	100 (16)	na	100 (30)	–	na	–	–
pH	–	–	na	88 (8)	25 (53)	na	23 (18)	32 (12)	67 (5)
Sodium	–	–	0 (2)	0 (4)	16 (79)	na	–	–	–
K^+	–	–	na	0 (2)	44 (64)	88 (17)	100 (5)	na	100 (1)
Creat	38 (8)	14 (7)	0 (4)	na	0 (45)	na	0 (25)	na	na
Hct	–	na	–	–	5 (36)	na	48 (73)	na	88 (8)
WBC	100 (1)	na	86 (14)	90 (10)	82 (68)	na	100 (1)	na	100 (1)

na = not applicable, – = no patients in that group in our data.

P239 Mortality probability model II (MPM_{0-72}) in 1667 patients with acute cardiovascular disorders

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Objectives: Aim of this prospective study was to evaluate the mortality probability model (MPM II) in terms of outcome prediction (hospital mortality [HM]) and calibration in patients with predominantly cardiovascular disorders admitted to a medical intensive care unit (MICU).

Methods: 1677 patients (pts) (age 64 ± 13 years, 68.9% male, SAPS II 27 ± 15.9, 418 pts acute myocardial infarction, 337 pts unstable angina, 217 pts rhythm disturbances, 141 pts heart failure, 103 pts cardiac arrest, 416 pts other admission diagnosis) were included between April 1999 and April 2001. SAPS II and MPM_{0-72} were determined according to the published guidelines. Discrimination power of SAPS II and MPM_{0-72} for survivors (S) and non-survivors (NS) (HM) was assessed by the area under the Receiver Operating Characteristic (AUROC) curve, calibration of the models with the Goodness of Fit H-Test (GOF-H) and standardized mortality ratio (SMR).

Results: Two hundred and sixty-one (15.6%) pts died. ICU mortality was 10.9%. AUROC for SAPS II was 0.83 (0.79–0.81), for MPM_0 0.80 (0.76–0.84), for MPM_{24} 0.83 (0.79–0.87), for MPM_{48} 0.82 (0.78–0.86) and for MPM_{72} 0.87 (0.82–0.89). MPM_{0-72} II significantly overestimated mortality (Table 1). Moreover stratifying pts in subgroups according to age, admission process and diag-

Table 1

χ^2 value GOF-H and SMR (95% confidence interval)

	χ^2 value (GOF-H)	SMR (95% CI)
SAPS II	6.84 ($P = 0.653$, df = 9)	1.048 (0.925–1.183)
MPM_0	38.63 ($P < 0.0001$, df = 9)	0.754 (0.665–0.852)
MPM_{24}	65.31 ($P < 0.0001$, df = 9)	0.691 (0.608–0.782)
MPM_{48}	31.86 ($P = 0.0002$, df = 9)	0.755 (0.644–0.879)
MPM_{72}	27.40 ($P = 0.0012$, df = 9)	0.736 (0.615–0.874)

nostic categories revealed a poor calibration with overestimation of mortality too.

Conclusion: Discrimination of MPM_{0-72} II was reliable. However, all models showed a most significant lack of calibration overestimating mortality mainly in the low risk strata and other pt related criteria. These results evidence the importance of a difference in the uniformity of fit and case mix of the present study population compared to the original population in which the model was developed.

P240 To verify four 5-year-old mathematical models to predict the outcome of ICU patients

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Background: In 1995 a retrospective study was made on all the patients admitted in our ICU from 2 April 1990 to 31 December 1995 with a length of stay of at least 24 hours. For each patient APACHE II score was calculated after 24 hours and, depending on the length of ICU stay, on the 5th, 10th and 15th day from the admission. The case mix of 1254 patients was subdivided in two series. The first series was used for developing the models and the second series to verify them.

Data of the patients from the first series were used to make four mathematical models (1st, 5th, 10th, 15th day from the admission) to predict the outcome from the calculated APACHE II score. Stepwise logistic regression (BMDP, Los Angeles) was used to make these four models. For each model calibration was tested with the Hosmer–Lemeshow Goodness-of-Fit test and discrimination was tested with the ROC-curve. These four models were validated for calibration and discrimination also in the second series.

The aim of this study is to verify these four models in patients admitted in the same ICU during the year 2000 and, in this way, to make a quality control of ICU care.

Material and methods: A prospective study was made on patients admitted in our ICU during the year 2000 with a length of stay of at least 24 hours. On the base of the four old mathematical models the risk of death was calculated for each of the four days (on the 1st, 5th, 10th, 15th day from the admission) and calibration and discrimination were tested.

Results: Three hundred and fifty-seven patients with more than 24 hours ICU stay were admitted in the study. The first model, at 24 hours from the admission, had a bad calibration at the Hosmer–Lemeshow test ($P = 0.000088$), while area under the ROC-curve was equal to 0.74 ± 0.32. The model at the 5th day had a bad calibration too ($P = 0.000588$), with an area under the curve equal to 0.83 ± 0.04. At the 10th day from the admission the model was well calibrated (Hosmer–Lemeshow test: $P = 0.112247$) with a ROC = 0.89 ±0.04. Finally at the 15th day the model was again bad calibrated ($P = 0.001422$), but with a very good discrimination (area = 0.91 ± 0.06).

Discussion: A further analysis suggest that to be increased was outcome of neurosurgical and trauma patients, while outcome of patients with other pathologies remained unchanged. To be increased is not the general quality of ICU care, but only the treatment of neurosurgical and trauma patients. Moreover for the neurosurgical patients, the introduction of neuroradiological treatment of cerebral aneurysm with Guglielmi's coil has contributed to increase the outcome of these patients.

Conclusion: These self-made models help the physician to understand ICU outcome changes during the years and if increased amount of money are justified from increased outcome.

P241 Markers of in surgical intensive care unit length of stay in patients submitted to heart surgery: the intensivist point of view

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Background: Postoperative management of heart surgery (HS) has been changing in the last decade. 'Fast-track strategy' has been proposed, but not for all patients. Markers of length of stay (LOS) in surgical intensive care unit (SICU) are still needed.

Objectives: To analyze data of preoperative, peroperative and postoperative period to identify factors that could be correlated to higher SICU-LOS among patients submitted to HS in our hospital.

Methods: Three hundred and fifty patients submitted to HS in our hospital, from June 2000 to November 2001 were retrospectively analyzed from prospective collected data in a Customized Database System. Applying Cox Regression with stepwise (Likelihood ratio) of 62 variables obtained preoperative, peroperative and postoperative period, we observed its correlation with higher SICU-LOS.

Results: Variables considered significant under multivariate analysis with respectively odds ratio (OR) and P value were: age (OR = 1.0, $P = 0.02$), type of surgery, Emergency (E) HS (OR = 0.7,

$P = 0.01$), Urgency (U) HS (OR = 0.6, $P = 0.01$), need of re-operation (OR = 2.8, $P = 0.0008$), occurrence of acute atrial fibrillation (OR = 1.7, $P = 0{,}0001$) and following the first postoperative day (FPD): LOS in mechanical ventilation (MV) (OR = 0.9, $P = 0.01$), use of pulmonary artery catheter (PAC) (OR = 2.2, $P = 0.00001$) and intra-aortic balloon (IAB) use (OR = 1.9, $P = 0.01$).

Conclusion: In our series using preoperative, peroperative and postoperative variables, we found three preoperative markers of longer SICU-LOS (Age, U-HS and E-HS), three FPD occurrence (PAC, IAB, LOS-MV) that could show the severity of hemodynamic disturbance, also two postoperative markers that were HS complications (AAF and need of re-operation). The strongest variables to predict higher SICU-LOS are found in the postoperative period in our hospital and are supported by highest OR. We need further step by step (pre, per and FPD) data analyses to format a predictive SICU-LOS model in HS.

P242 The extent and effect of sepsis in the first 24-hours of intensive care in one country

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Introduction: The PROWESS [1] study reported the development of an apparently successful, but expensive, treatment for severe sepsis. All but two of the 26 adult, general intensive care units (ICUs) in Scotland participated in a prospective audit of admissions during 1999 and 2000. We reviewed our data to assess the extent and effect of sepsis, evident in the first day of intensive care, in this 2-year period.

Results: Almost 40% of all patients were septic within the first 24 hours of ICU admission, and 44% of these had severe sepsis (18% of all admissions). This proportion was consistent in both 1999 and 2000. The ICU mortality was 30% in the sepsis group and 50% in the severe sepsis group, compared to an overall Scottish ICU mortality of 21.5%. A further 9% die before hospital discharge. Although this attrition rate is similar to that in the general ICU population, it means that patients with severe sepsis are twice as likely to die before hospital discharge as the general ICU population. Patients with severe sepsis have higher APACHE II scores (mean 25) compared to those with sepsis (21) or the ICU population in general (19) and stay in ICU longer (mean increase 1.8 days, median 1.1). The standardised mortality ratio (SMR) of 1.16 in the severe sepsis group is clearly of concern, but is unlikely to be due to poor quality of care since the SMRs for Scottish ICUs are known to be in line with expectation [2].

Conclusion: Severe sepsis has important consequences for individual patients, ICU resources and community health. There is the potential for new therapies to make a significant impact on all of these but close surveillance on a national rather than selective basis will be required to assess the cost and benefit.

References:

1. Bernard GR, Vincent J-L, Laterre P-F, *et al.: N Engl J Med* 2001, **344**:699-709.
2. Livingston BM, MacKirdy FN, Howie JC, Jones R, Norrie JD: *Crit Care Med* 2000, **28**:1820-1827.

Table 1

Summary of data collected during 1999 and 2000 in Scottish ICUs

		All admissions ($n = 16{,}000$)	Sepsis ($n = 6504$)	Severe sepsis ($n = 2892$)
LOS (days)	Median/mean	1.8/4.53	2.2/5.26	2.9/6.3
Age (years)	Mean	58.3	57.9	61.4
Mortality (%)	ICU/hospital	21.5/29.9	29.6/38.6	50.4/58.7
APACHE II	Probability (%)	33.0	38.5	50.1
	SMR (95% CI)	0.905 (0.884–0.927)	0.990 (0.970–1.01)	1.16 (1.12–1.19)

P243 Predictors of hospital costs in patients submitted to heart surgery: the intensivist point of view

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Background: Heart surgery (HS) has been considered one of the most cost consuming procedures in health care, therefore many strategies has been studied in order to reduce its final costs.

Objective: To evaluate factors collected during preoperative, peroperative and postoperative period in Surgical Intensive Care Unit (SICU) that could be correlated to higher hospital costs (HHC) of patients submitted to HS.

Methods: We retrospectively analyzed prospective collected data from a Customized Database System. Hospital cost data was available in 246 of 350 patients submitted to HS from June 2000 to November 2001. Applying linear regression and goodness-of-fit statistics to 62 variables obtained preoperative, peroperative and postoperative period in SICU we observed its correlation with HHC.

Results: Variables considered significant under multivariate analysis ($R = 0.950$, $R^2 = 0.903$, R^2 adjusted = 0.898) revealed higher hospital costs in the presence of pulmonary hypertension (PH) ($P = 0.04$), increased left atrial diameters (ILAD) ($P = 0.013$), use of anti-platelet agents in the previous 7 days (UAPA) ($P = 0.006$),

intra-aortic balloon (IAB) use for extra-corporeal circulation delivery, admission SICU bicarbonate level (BL) ($P = 0.0001$), SICU LOS ($P = 0.0001$), occurrence of acute atrial fibrillation (AAF) ($P = 0{,}039$), and the following first postoperative day (FPD) variables: higher serum levels of creatinine (HSLC) ($P < 0.003$), fluid imbalance (FI) ($P = 0{,}001$), Nor-adrenaline tritation > 0.1 μg/kg/min (Nor > 0.1) and length of stay (LOS) in mechanical ventilation (MV) ($P = 0.012$).

Conclusion: In our sample using preoperative, peroperative and postoperative variables, we had only three preoperative markers of HHC (PH, ILAD, UAPA) and eight peroperative or postoperative (IAB, admission SICU BL, HSLC FPD, FI in FPD, FPD Nor > 0.1, LOS in MV, SICU LOS and AAF). We interestingly showed that in hospital with our characteristics (high risk and urgency HS) it is difficult to predict HHC with only preoperative variables. We will need further step by step (pre, per and FPD) data analysis to format a predictive HHC for HS.

P244 Comparison of DRG system funding and actual costs for intensive care in Hungary

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Introduction: Since its introduction in 1993, there has been continuous underfunding of the Heath System in Hungary; it is especially true for expensive specialties, like Intensive Care. In many other countries that use DRG costing, there is individual funding available for ICUs, but it is not the case in Hungary. In this study, we compared actual ICU costs with reimbursed funds during a 1-month period.

Methods: We selected 1 month for which the amount of reimbursed fund was available (August 2001). Retrospectively, we collected the actual variable costs for every patient during that period, using nursing and medical records. These variable costs included drugs, disposables, nutrition, blood and diagnostics. Fixed costs (non-clinical support and personnel) were then calculated with the top-down method. We did not include estate costs in our study as it was proven to show little importance in cost analysis [1]. General patient data, reason for admission, SAPS-II score, length of ICU stay and length of mechanical ventilation were assessed as well. These potential cost indicators were then evaluated to the actual cost of ICU care and reimbursed DRG funds.

Results: There were 12 patients during August 2001, who had been admitted to and discharged from our ICU. The overall costs of these cases were 7.72 M Ft (SD = 0.60 M Ft) and there was only 7.26 M Ft (SD = 0.61 M Ft) refunded to the unit.

The length of stay correlated very well with actual cost ($r^2 = 0.98$) and less well with reimbursed DRG funds ($r^2 = 0.75$). The length of mechanical ventilation showed better correlation with DRG funding ($r^2 = 0.86$), then with actual costs ($r^2 = 0.66$). However, there was no correlation between SAPS-II and actual or reimbursed funds ($r^2 = -0.54, -0.08$).

Table

	HUF	EURO	
Drugs/fluids	981,687	3974	12.70%
Disposables	545,566	2209	7.06%
Nutrition/blood	266,212	1078	3.45%
Clinical support	191,537	775	2.48%
Non-clinical support	1,094,840	4433	14.17%
Personnel	4,648,614	18,820	60.15%
Total cost	7,728,456	31,289	100%

Conclusion: The actual cost of Intensive Care was significantly higher then the reimbursed DRG fund given to the unit. In our Health System, DRG refund is supposed to cover estate costs and capital equipment as well. There was a negative balance without including these cost blocks, which highlights the importance of individual funding for Intensive Care. DRG refund was less than actual cost for patients who were not ventilated. Our study confirmed that SAPS II could not be used as a cost indicator.

Reference:

1. DL Edbrooke, *et al.*: **Variations in expenditure between adult general intensive care units in the UK.** *Anaesthesia* 2001, **56**:208-216.

P245 Compliance with intensive care admission guidelines on triage

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Introduction: Appropriate utilization of expensive resources has become an important issue due to limited health budgets. Admission to the Intensive care unit (ICU) should be reserved for those patients with reversible medical conditions who have a 'reasonable prospect of substantial recovery' [1]. The Task Force of the American College of Critical Care Medicine, Society of Critical Care Medicine have introduced guidelines for prioritizing admission. These define those that will benefit most from ICU (Priority 1) to those that will not benefit at all (Priority 4). We aimed to test our compliance to the model and to critically analyze its usefulness as a triage tool.

Method: We performed a prospective audit of all adult referrals for admission to our 22 bed multidisciplinary University ICU between 13 November and 13 December 2001. Patients were categorized according to the guidelines by two investigators not involved in the triage decision. The proportion of patients admitted in each priority group was calculated.

Results: The audit consisted of 117 patients. The mean age was 58 and the mean Mortality Prediction Model at admission (MPM II_0) 0.37. The results obtained are shown in the Table overleaf.

Table

Priority category	Number of patients (% of total)	Number admitted (% of admission)
1	84 (72%)	79 (94%)
2	17 (15%)	11 (65%)
3	7 (6%)	3 (43%)
4	9 (7%)	0 (0%)

Conclusion: Our triage decisions complied well with the guidelines. This is evident from the high admission rate in the Priority 1 group and a reducing admission rate in the subsequent categories. Due to our limited health resources some category 1 patients were refused. In healthcare systems with limited resources a method of selecting between category 1 patients may be necessary.

Reference:

1. **Guidelines for intensive care unit admission, discharge, and triage. Task Force of the American College of Critical Care Medicine, Society of Critical Care Medicine.** *Crit Care Med* 1999, **27**:633-638.

P246 Clinical outcomes in a controlled trial of early identification and rapid systematic treatment of shock, modeled after the trauma system

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Hypothesis: Early identification and rapid systematic treatment of shock will improve outcomes.

Inclusion criteria: Sustained inadequate tissue perfusion not responsive to initial volume resuscitation.

Hypotension. SBP < 90, MAP ≤ 60, not corrected with one liter rapidly infused crystalloid and one or more of the following: or

Normotension. With three of the following: Temperature ≤ 36; Cool extremities or skin mottling; Altered mental status; RR ≥ 20; Oliguria; Lactic acidosis or BE ≤ –5.

Identified to be in shock by the caregiver (i.e. septic, cardiogenic, hypovolemic).

Exclusion criteria: Trauma, acute MI, patients already receiving mechanical ventilation/pressors, and patients who are not candidates for ACLS.

Methods: Patients at Redding Medical Center between 1998 and 1 June 2000 in shock (control group) were treated in the standard fashion. The outcomes of those patients were compared to the outcome of patients at Redding Medical Center in shock after 1 July 2000 (treatment group). Both groups had the same inclusion and exclusion criteria and assessed for severity of illness using APACHE III. During the month of June 2000 intensive education to all nursing personnel, Emergency Department physicians, intensivists, surgeons, interventional radiologists, and medical staff at large was undertaken for the purpose of improving earlier identification and treatment of shock. Beginning 1 July 2000 standardized treatment protocols utilizing best practice were implemented for the EMS, Emergency Department, critical care units and general nursing units and a 'shock bed' in ICU became available at all times. Activated by a shock alert a shock team comprised of intensivists, Emergency Department physicians, critical care nurse, nursing supervisor, respiratory therapy, radiology, clinical laboratory, electrocardiography, social and pastoral services rapidly responds to the patient's bedside and implements the treatment protocols. The primary care physician is notified.

Table

	APS	APACHE III	Actual mortality
Control	60.4	73.9	40.7%
Tx	61.8	75.1	29.1%

Control Group = 86; treatment group = 103; absolute reduction = 11.6%*; relative reduction = 28.5%*.*$P < 0.05$.

Discussion: No significant changes in types of therapy or in the physician mix in the treatment of shock were made from the time intervals of the historical control group compared to the treatment group. The severity of illness between the two groups is equivalent. Therefore, it is likely that the observed changes in the time intervals for treatment and the mortality outcome are due to the initiation of the Shock Program at Redding Medical Center.

Conclusion: Early identification of shock and rapid initiation of treatment reduces the time to the initiation of therapy and mortality.

Table

	Time intervals (hours:min)					
	Shock alert	ICU admit*	2 l Fluid***	Central line	PA line*	Abx**
Average for control	NA	4:25	5:21	3:29	4:23	6:04
n		75	76	33	53	54
Average for treatment	0:48	2:38	2:31	2:42	3:20	4:18
n	75	103	101	68	61	65

These intervals are from time zero which was the time that signs and symptoms of shock could have first been recognized determined by retrospective review. * $P < 0.1$, ** $P < 0.05$, *** $P < 0.001$.

P247 Reduction in post-ICU, in-hospital mortality following the introduction of an ICU nursing outreach service

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Mortality on hospital wards after discharge from intensive care has been reported to range from 6.1% to 16.3% [1]. At the John Radcliffe hospital a nursing outreach service was introduced to assist with the post-ICU management of patients discharged to the wards. Patients received regular outreach nurse review until no longer causing concern. ICU medical staff were alerted at an early point to patients at risk of deterioration.

Following introduction of the service, April–September 2001 post-ICU in-hospital mortality was 7.8% compared with 12.8% for April–September 1999 and April–September 2000 combined, $P = 0.068$. ICU activity and case mix were unchanged. Patients expected to die on discharge from ICU remain included in the data.

It has been suggested that mortality after discharge from intensive care may be reduced if patients at risk were to stay in intensive care a further 48 hours [2]. Whilst outreach does not replace extended ICU stay, it may have a contribution to mortality reduction following discharge from ICU.

Table 1

Patients discharged from ICU to hospital wards

	April–September 1999 and 2000	April–September 2001
n	421	223
Age, years (SD)	58 (19)	60 (18)
Sex M/F	292/129	149/74
Acute Physiology Score (SD)	23(6)	24(6)
Post-ICU mortality (%)	54 (12.8%)	18 (7.8%), $P = 0.068$
Post-ICU LOS, days (SD)	19 (40)	15 (17)

References:

1. Rowan K, *et al.*: **Outcome comparisons of intensive care units after adjustment for case mix by the American APACHE II method.** *BMJ* 1993, **307**:977-981.
2. Daly K, Beale R, Chang RWS: **Reduction in mortality after inappropriate early discharge from intensive care unit: logistic regression triage model.** *BMJ* 2001, **322**:1-6.

P248 Emergency airway service by anaesthetists: a selective referral approach

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Introduction: We describe our experience with the provision of an emergency airway service by specialist-grade anaesthestists to assist the primary physicians who are the first-line personnel in airway management and resuscitation in our 1249-bedded multidisciplinary, tertiary hospital. A dedicated paging system was set up to facilitate rapid activation of the designated anaesthetist.

Method: A prospective audit was conducted over 6 months to assess the demand and effectiveness of the service. A questionnaire was completed for each activation by the anaesthesiologist involved.

Results: There were 68 activations (average of 11.3/month), 64.7% of which occurred after 16:30 hours. The main locations were the Neurological Intensive Care Unit (24%), Medical Intensive Care Unit (11.8%) and Coronary Care Unit (11.8%). In 54.4% of the activations, endotracheal intubation was already attempted by the primary physicians, with 19.1% of the patients requiring more than two attempts. In 19.1% of cases, the involvement extended to participating in other aspects of resuscitation. Majority of the scenarios were clinically challenging, benefiting from a specialist anaesthetist input. Forty-three percent of the patients had anterior larynces. One patient required an emergency tracheostomy.

Discussion: Cardiac arrest teams are costly and there remains a lack of concrete evidence to show that they improve patient outcome. Recently, medical emergency teams are introduced to provide rapid response to critically ill patients. However, these teams face many practical problems, such as limited understanding of the implication of cardiac arrest and hence, the appropriateness of resuscitation. While retaining a 'primary physician team resuscitation' approach, the emergency airway service provided a scope of care equivalent to both cardiac and medical emergency teams as required, at a lower cost.

Conclusion: We conclude that this system of emergency airway management support by anaesthesiologists is effective and optimises manpower resources.

P249 Critical care in internal medicine department: EBM approach and new organizational model for Italian National Health Service

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During the last decade the number of over-60 patients with multiple organ dysfunction admitted in the Departments of Internal Medicine in Italy has considerably increased. Many of these patients are critically ill and needs to be treated by trained medical staff with experience in internal medicine and an olistic approach. Several studies carried out in ICUs show that prognosis of elderly patients affected by multiple organ dysfunction is related to the number and severity of comorbidity regardless of age. Furthermore many survived patients dismissed from ICUs cannot reach the previous level of performance and global quality of life. One randomized controlled trial on chronically critically ill patients compared performances of traditional intensive care units with low technology

'Special Care Unit' managed by specialist in internal medicine, supported by sub-intensive nursing. These units obtained comparable clinical outcomes (mortality, complications) and better value (economic cost, stay of hospitalization). On the basis of these data and the characteristics of Italian National Health Service, we created in our Department of Internal Medicine a 'protected area' for critically ill patients affected by internistic diseases with complex comorbidities needing continuous monitoring of vital parameters and therapies. Medical staff working in this area have been trained in emergency medicine and are supported by nurses ACLS (Advanced Cardiac Life Support) certified. This unity is constituted by four beds with monitoring of EKG, non-invasive blood pressure, pulse, oximetry, body temperature, connected with a central computerized unit. Moreover, in this room are available ABG, ph-metry, and CPR equipment. Currently in Italy, this kind of patients are admitted in ICUs, often with unappropriated use of resources or in Department of Internal Medicine with inadequate quality of care. We are planning a case–control study to compare the outcomes of patients admitted in our new 'protected area' with those of matched patients previously admitted in our Department of Internal Medicine. The results of this investigation could supply data to support the creation of other 'protected areas' in Departments of Internal Medicine in our country. Furthermore this new approach could promote the renaissance of the role of Internal Medicine in Italian National Hospital System and help to release resources for the ICUs and other specialties.

References:

1. Pettila V, Kaarlola A, Makelainen A: **Health-related quality of life of multiple organ dysfunction patients one year after intensive care.** *Intensive Care Med* 2000, **26(10)**:1473-1479.
2. Rudy EB, Daly BJ, Douglas S, Montenegro HD, Song R, Dyer MA: **Patients outcomes for chronically critically ill: special care unit versus intrensive care unit.** *Nurs Res* 1995, **44**:324-331.
3. Ip SP, Leung YF, Ip CY, Mak WP: **Outcomes of critically ill elderly patients: is high-dependency care for geriatric patients worthwhile?** *Crit Care Med* 1999, **27**:2351-2357.

P250 Health-related quality of life of multiple organ dysfunction patients: changes and comparison with normative population data

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Introduction: Few studies analyzing health-related quality of life (HRQOL) in patients with multiple organ dysfunction (MOD) have used pre-ICU and follow-up data. Generic HRQOL instruments allow comparisons with normative population data and have recently demonstrated good reliability and validity when applied to intensive care unit (ICU) survivors [1].

Patients and methods: During June 1998 and May 1999 HRQOL was assessed in 318 consecutive adults admitted for > 24 hours to our non-coronary medical ICU. Baseline HRQOL measures were collected by interview during the first 24 hours of ICU stay and 6 months after admission using the Short Form (SF)-36 Health Survey, a generic health status measure that evaluates eight health domains that reflect physical and mental health. MOD was assessed using daily SOFA scores. MOD was defined as a SOFA total maximum score (TMS) of ≥ 6 points. Baseline SF-36 data of ICU patients were compared with age and gender adjusted population norms obtained in the German Federal Health Survey 1998 (n = 6964). Changes in individual domains for each patient at follow-up were measured using normalized standard Z-scores (i.e. difference between baseline mean and follow-up mean divided by baseline standard deviation [SD]). A Z-score of 1.0 or more was used as a cut-off to identify patients with a relevant deterioration of HRQOL at follow-up.

Results: Mean age of the study cohort (n = 318) was 57 ± 17 (± SD) years, median 59; 58% were male. Mean ICU length of stay was 11 ± 19 days, median 4.5. Mean APACHE II score after 24 hours was 18 ± 10, mean TISS score was 33 ± 14. One hundred and seventy patients (53%) had MOD with a mean SOFA TMS of 11.8 ± 4. Cumulative mortality rates for non-MOD/MOD patients were 3%/45% in the ICU, 6%/57% in the hospital, and 12%/64% at 6 month follow-up. At follow-up HRQOL data could be obtained in 118 non-MOD and 53 MOD patients, 19 patients were lost to follow-up.

Compared with normative population data pre-ICU HRQOL was significantly (P < 0.0005) impaired in all ICU patients. MOD patients demonstrated more severe deteriorated pre-ICU physical health scores than non-MOD patients (P < 0.0005), whereas mental health domains did not differ between the two groups (P = 0.61). Survivors of MOD showed further deteriorated physical health scores at follow-up (P = 0.002) but unchanged mental health (P = 0.51). Non-MOD patients demonstrated unchanged or even improved scores in all eight SF-36 domains. The majority of the survivors (94%) were living at home. Ninety-one percent of those previously in employment had returned to their former work.

Conclusion: Using age and gender matched population norms MOD patients demonstrated more severe impaired pre-ICU physical health scores than non-MOD patients. At follow-up a deterioration in most areas of physical health was noted in MOD but not in non-MOD patients, whereas domains of mental health did not differ between the two groups. The SF-36 seems to have sufficient discriminative validity when used to measure HRQOL in survivors of MOD.

Reference:

1. Heyland DK, *et al.*: *Crit Care Med* 2000, **28**:3599-3605.

P251 Are clinical diagnoses prior to death reliable in critically ill patients?

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Background: European and American studies have recently highlighted discrepancies between clinical diagnoses and post mortem findings in patients who died on the intensive care unit (ICU). This study set out to determine if similar findings were present in patients that died on an ICU in the UK.

Methods: Patients that died between January 1998 and June 2001 were identified from a database of ICU admissions. From this list, patients that had undergone a post mortem were identified and their medical notes reviewed retrospectively to establish the clinical diagnoses prior to death. These were compared to the post

mortem cause of death and classified using the Goldman system. This system categorises discrepancies between clinical and post mortem diagnoses into three groups – major, minor and complete agreement. Major discrepancies were those where the principle, underlying cause of death was missed. Minor were missed diagnoses that may have contributed to death or important diagnoses that were unrelated to the cause of death. Complete agreement indicated concordance between clinical and post mortem diagnoses. Differences between the groups demographics were tested for using repeated measure ANOVA on ranks and chi-squared test.

Results: Nine hundred and thirty-nine patients died during the 3.5 year study period, of which 49 (5.2%) underwent a post mortem examination. Medical records were available and analysed for 38 of these patients. Major missed diagnoses were present in 18 cases (47%). In contrast, less than half of the cases ($n = 16$, 42%) showed complete agreement between clinical diagnoses and post mortem findings. There were no difference in age, admitting speciality, APACHE II score, predicted mortality or hospital length of stay between the three groups. Undiagnosed carcinoma, pulmonary embolism, left ventricular failure or infections represented the most frequently missed major diagnoses.

Conclusion: This small study has demonstrated that, in the critically ill, major underlying diagnoses were frequently missed prior to death. This may have led to unnecessary early death (if known for reversible causes) or unnecessary prolongation of life where terminal disease was present.

P252 Terminal weaning in critically ill patients

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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 analyze patients undergoing terminal weaning (TW) at ICU in tertiary care hospital during period 1999–2001.

Methods: A prospective, descriptive study of all patients experienced TW during a 3 years period was conducted. Diagnosis, length of ICU stay (LOS) in days before decision of TW was made, length of TW (LTW) in minutes, way of TW (SW = step-wise reduction or VW = ventilator withdrawal), providing information about TW to the family, adequacy of documentation and difference in LTW between selected patients subgroups were also evaluated. Data as mean ± SD (minimum–maximum) or median (25–75%), *t*-test or Mann–Whitney Rank Sum Test were used, $P < 0.05$ was considered statistically significant.

Results: Thirty-nine patients were studied, age 52 ± 22 years, LOS 8.7 ± 14 (0.2–84) days, LTW 196 ± 344 (3–1634) min. The TW procedure was step-wise reduction of ventilatory support (SW) in 18 patients and ventilator withdrawal (VW) in 21 patients. There was significant difference in LTW between patients with SW compared to patients with VW (20, 13–58 min resp. 82, 20–597, $P = 0.04$). There were 26 patients with primary brain damage (group BD) and 13 patients without primary brain damage (group NBD). Selected results are presented:

Table

	Group BD ($n = 26$)	Group NBD ($n = 13$)
LOS (days)	2.2 (1–4.5)	13 (9–19)*
Step-wise/ventilator withdrawal	8/18	10/3
Family information about TW given: yes/no	4/22	3/10
Written order of TW: yes/no	23/3	11/2
Respiratory activity before TW: yes/no	11/15	12/1
LTW (min)	24 (15–125)	30 (17–241)
LTW (min) (step-wise)	22.5 (13–690)	161 (30–597)
LTW (min) (ventilator withdrawal)	22.5 (15–49)	12 (7.5–66)

Data as median (25–75%), * $P < 0.05$.

Discussion: LOS before decision of TW was significantly longer in patients without brain damage. The LTW did not differ significantly between patients with or without brain damage, however LTW was shorter in patients undergoing ventilator withdrawal compared to step-wise reduction of ventilatory support.

Reference:

1. 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.

P253 Ethical attitudes of ICU physicians in Hong Kong

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Introduction: Medical practice in HK is based on Western principles. However, most local doctors and patients are Chinese with a strong Chinese cultural and religious background. This study explores the practice and ethical attitudes of ICU doctors in HK, using a structured questionnaire modified from recent European ethical questionnaires [1,2].

Results: Of 90 questionnaires distributed to 12 ICUs in HK, 65(72%) were returned.

In HK, 99% of physicians would sometimes withhold and 89% sometimes withdraw therapy from patients with no chance of recovery, compared to 93 and 77% in Europe. More respondents

Table

Demographics	Europe (%)	HK (%)	*P*
Age			
< 40	32	89	< 0.001
40–49	47	9	
50+	21	2	
Sex			
Male:female	6.7:1	1.6:1	< 0.001
Religious background			
Yes	78	46	< 0.001

in HK involved patients and/or families in decision making (83% compared to 49%, $P < 0.001$).

Conclusion: Although demographically different, the ethical behavior and attitudes of ICU doctors in HK and Europe are similar. HK doctors involve families more often in the discussion of end-of-life issues.

Table

ICU admission limited by bed availability (% of respondents)

Country	Generally (%)	Often (%)	Sometimes (%)	Almost never (%)	*P*
HK	6	25	51	18	0.5
Belgium [2]	7	34	44	14	

References:
1. *Intensive Care Med* 1990, **16**:256-264.
2. *Crit Care Med* 1999, **27**:1626-1633.

Table

ICU admission for patients with poor prognosis or poor quality of life (% respondents)

	No hope of survival for more than a few weeks		Poor QOL according to physician		Poor QOL according to patient	
Country	Admitted	Should be admitted	Admitted	Should be admitted	Admitted	Should be admitted
HK	69	45	86	66	81	51
Belgium [2]	63	34	91	75	83	53

Table

Application and discussion of DNR orders (% of respondents)

	Written DNR orders		Discuss with patient		Discuss with family	
Country	Apply	Should apply	Yes	Should	Yes	Should
HK	61	80	52	88	90	92
Belgium [2]	79	92	16	48	80	80

P254 Life sustaining treatment decisions in Portuguese intensive care units

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Objectives: To evaluate current views and practice of Portuguese intensive care physicians regarding end-of-life decisions, namely 'do not resuscitate' (DNR) orders and withhold/withdraw treatment decisions.

Design and methods: An individual questionnaire was sent to full-time intensive care physicians working in the intensive care units (ICUs) registered in the Portuguese Intensive Care Society. High dependency and specialised units (like burns and coronary care units) were excluded. A comparison was done between religious and non-religious, more and less experienced (>10 years or ≤ 10 years of practice in ICU), younger and older (< 45 or ≥ 45 years), female and male doctors, as well as between doctors working in small and larger (≤ 8 beds or > 8 beds) ICUs. Chi-square test was used to compare different groups.

Results: A total of 250 questionnaires were sent in October 2001 and 140 returned (56%) until the end of November. Physicians from 68% of the country ICUs participated in the study. The vast majority of physicians answered that DNR orders (100%) and with-

hold and withdraw treatment decisions (98.6%) are made in their units. Regarding these decisions approximately three-quarters of the physicians answered that they are made by the medical group alone and this answer is more prevalent in the group of religious and less experienced doctors ($P < 0.05$). Thirteen to sixteen per cent of the physicians, mainly the more experienced ($P < 0.05$) answered that the nurses are involved in the decision. Eleven to sixteen per cent, mainly the non-religious doctors ($P < 0.05$), involve the patient or relatives in the decision. When asked about who they think these decisions should involve: 45–50% think that the patient or relatives should participate – mainly the non-religious ($P < 0.05$); 27–36% think that nurses should be involved – mainly the more experienced doctors ($P < 0.05$); 43–48% of the doctors feel that these decisions should be made by the medical group alone – mainly the religious and less experienced. Regarding documentation of DNR orders only 2.1% answered that their unit uses a specific document and 49.3% said that it is just transmitted orally to the working group. The same applies for withhold and withdraw treatment decisions, with 43.5% and 38.4% of the physicians answering that they are just transmitted orally. Probability of survival to the current episode and the patient wishes were the most important factors pointed out by the physicians that influence refusal of ICU admission, DNR orders and withhold or withdraw treatment decisions. Only 37.9% of the physicians said that a DNR order precedes a withdraw treatment decision. Eighty-two per cent continue or start comfort measures like morphine infusion, after a withdraw treatment decision is made.

Conclusions: End-of-life decisions are a current practice in the inquired Portuguese ICUs. These decisions are taken by the medical group alone in most ICUs, although there is a will to involve the nurses and the patient or relatives in the process. The experience and religious beliefs of the respondents influence the way these decisions are taken (but not age, sex or the ICU size). The practice of writing down these decisions is not done on a regular basis and needs to be improved.