Oral Presentations
Patient-ventilator interactions – 466-471

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DOES NIV BY HELMET REDUCE THE INSPIRATORY EFFORT? A PHYSIOLOGIC STUDY IN HEALTHY VOLUNTEERS.

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INTRODUCTION. The helmet has been shown to be effective in ventilating patients with hypoxemic ARF (1). Its use has been limited by several issues related to its intrinsic characteristics. Few physiologic data in healthy subjects have been published. Aim of this study was to investigate the helmet efficacy in unloading respiratory muscles, reducing the inspiratory effort and the WOB by the PTPPes analysis.CO2 rebreathing by analyzing PiCO2 was evaluated.

METHODS. 8 volunteers were enrolled. After the positioning of an oesophageal balloon and a 20' spontaneous breathing trial, subjects were ventilated through the helmet with 4 different ventilator settings (10/5, 15/5, 20/5 and 15/10 of PS and PEEP).The helmet cushion was inflated only at 15/5 and the subject was ventilated with same ventilator setting. V',Pao,Pes,PiCO2 traces were recorded and the data were analyzed by specific softwares. ANOVA for repeated measures and Tukey test were performed. P<0.05 was significant.

RESULTS. During pressure support delivered through the helmet there was a significant reduction in swingPes (p=0.04), PTP per min (p<0.0001), PTPPes/L (p=0.0002) and RR (p<0.0001) and a significant increase in Vt (p<0.0001) and Vmin (p=0.005) compare to the spontaneous breathing. By increasing the pressure support delivered we also observed a significant decrease in the CO2 inspiratory pressure.

CONCLUSION. The results of this study show as NIMV delivered by helmet with all the tested levels of PS and PEEP is efficient in unloading the respiratory muscles and reducing the PTP. In healthy subjects with normal respiratory drive we rarely noticed subject-ventilator asynchrony. Analysis of CO2 rebreathing showed a significant reduction of PiCO2 by increasing PS level.

REFERENCE(S). 1. Antonelli M et al. New treatment of acute hypoxemic respiratory failure: Non-invasive mechanical ventilation delivered by helmet-A pilot trial study. Crit Care Med 2002, 30: 602-608;
2. Nava S et al. Physiological effects of flow and pressure triggering during non-invasive mechanical ventilation in patients with chronic obstructive pulmonary disease. Thorax 1997, 52: 249-254.

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COMPARISON OF OXYGEN COST OF BREATHING BETWEEN PSV AND APRV

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INTRODUCTION. Breathing workload in mechanically ventilated patients is a very important concern during weaning. Oxygen cost of breathing is an indirect measure of work of breathing and is useful in predicting whether patients would tolerate a decrease in level of ventilatory support (1). In this study we aimed to measure oxygen consumption with either pressure-support ventilation (PSV) or airway pressure release ventilation (APRV) in a prospective, randomized and crossover fashion.

METHODS. Twenty clinically stable and spontaneously breathing patients after long-term mechanical ventilation included. Patients were randomized to start on either PSV or APRV mode and measurements were obtained after an adaptation period of 30 min to have PaCO2 between 35-45 mmHg and PaO2 above 60 mmHg. Indirect calorimetry was performed during each ventilatory mode for a period of 30 min. O2 consumption (VO2), energy expenditure (EE), CO2 production (VCO2), and respiratory quotient were measured.

RESULTS. All of the metabolic parameters did not differ significantly between the two ventilatory modes, regardless of the patients' randomization. There were no statistically significant differences with regard to respiratory rate, minute volume, and blood gas analysis. All patients tolerated both ventilatory modes without any signs of discomfort.

Minute ventilation, respiratory rates and metabolic monitor data (mean±SD)

	PS (baseline)	PS (30 min)	APRV (baseline)	APRV (30 min)
Min vent (L/min)	7.7±2.0	7.4±1.5	7.8±1.4	7.9±1.6
RR (breaths/min)	19.1±4.2	19.2±5.4	18.2±5.0	19.7±6.0
VCO2 (ml/min)	223.8±53.2	227.9±52.8	226.5±54.8	222.8±53.9
VO2 (ml/min)	297.9±57.5	302.6±56.2	306.1±54.9	310.4±51.4
EE (kcal/24 h)	2006±394	2189±880	2056±381	2086±334
RQ	0.75±0.10	0.75±0.11	0.74±0.11	0.75±0.11

CONCLUSION. Pressure support ventilation and airway pressure release ventilation both produced similar results in terms of oxygen cost of breathing and other metabolic variables.

REFERENCE(S). 1. Mitsuoka M, Kinninger KH, Jacobson KL, et al. Utility of measurements of oxygen cost of breathing in predicting success or failure in trials of reduced mechanical ventilatory support. Respir Care 2001; 46 (9): 902-910.

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A COMPARISON OF AIRWAY PRESSURE RELEASE VENTILATION AND PRESSURE CONTROL VENTILATION IN ACUTE RESPIR

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INTRODUCTION. The Acute Respiratory Distress Syndrome(ARDS) still presents high mortality, besides the advance in the last years with the protective strategy. The aim of this study is to compare the effectiveness of the Airway Pressure Release Ventilation (APRV),with ratio of inspiration to expiration between 2:1 to 2.5:1, as opposed to Pressure Control with conventional ratio ventilation(PCV) in patients with ARDS and Lung Injury Score(LIS)>3.25

METHODS. We evaluated 36 patients with ARDS, according to the following criteria: acute onset, bilateral chest radiographic infiltrates, pulmonary artery occlusion pressure<18 mm Hg and PaO2/FiO2 ratio<200.The patients were randomized in two similar groups one with 19 patients, that received APRV and the other group with 17 patients, that received PCV. All patients were initially sedated and paralyzed and submitted to recruitment manoeuvres with continuous positive airway pressure of 35 to 40 cmH_2O. Positive end expiratory pressure(PEEP)was preset at 2 cm H_2O above the lower inflection point. The days in mechanical ventilation, in control mechanical ventilation and for weaning, LIS, mortality and other variants were compared between the two groups through the Mann-Whitney test. Decrease in LIS at day seven after the randomization and other variants in the same group was evaluated through the Wilcoxon test

RESULTS. The mortality was not different, although was lower in APRV group(42.1% x 47.1%-p=0.76).The LIS decreased more at day seven in APRV group(2.07 + 0.27 x 3.13 + 0.52;p=0.0001). The days in mechanical ventilation, in control mechanical ventilation and for weaning were lower in APRV group (17.53 + 10.97, 13.84 + 7.20, 4.25 + 1.04 x 28.12 + 15.10, 24.41 + 14.78, 9.6 + 2.3;p=0.015;p=0.004;p=0.003 respectively)

CONCLUSION. Although the mortality did not differ, APRV was effective in decreasing the LIS and the days in mechanical ventilation, compared to PCV and it may be used as an alternative ventilatory strategy in ARDS

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HEMODYNAMIC RESPONSES TO HELIOX IN MECHANICAL VENTILATED PATIENTS WITH OBSTRUCTIVE LUNG DISEASE

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INTRODUCTION. Dynamic hyperinflation and intrinsic positive end expiratory pressure (PEEPi) are very common in intubated COPD patients with mechanical ventilation. PEEPi and trapped lung volume (Vtrapped) may impede venous return and cardiac performance, which can be observed in pulse pressure difference between insufflation and expiration. Heliox (helium-oxygen mixture) can reduce airways¡_ resistance to flow markedly because of its low density.

METHODS. We investigated the cardiopulmonary mechanic change between air-O2 and heliox in 25 consecutive mechanically ventilated COPD patients with pulsus pressure greater than 15 mm Hg.

RESULTS. During heliox insufflation, there were decreased PEEPi (13 ¡Ó 4 in air-O2 vs. 5 ¡Ó 2 in heliox, p< 0.05) and trapped lung volume (362 ¡Ó 67 in air-O2 vs. 174 ¡Ó 86 in heliox, p< 0.05). There was significant reduction in peripheral pulse pressure difference between insufflation and expiration (€ GPP) (29 ¡Ó 5 in air-O2 vs. 13 ¡Ó 7 in heliox, p< 0.05) from air-O2 to heliox. For the 10 patients with pulmonary arterial catheter monitor, the mean pulmonary arterial pressure (26 ¡Ó 4 in air-O2 vs. 24 ¡Ó 5 in heliox, p < 0.05), mean right atrial pressure (10 ¡Ó 3 in air-O2 vs. 8 ¡Ó 2 in heliox, p < 0.05) and pulmonary arterial occlusion pressure (14 ¡Ó 2 in air-O2 vs. 11 ¡Ó 2 in heliox, p < 0.05) have shown statistically significant reduction from air-O2 to heliox. The cardiac index has shown a statistically significant improvement from air-O2 to heliox (3.0 ¡Ó 0.7 in air-O2 vs. 3.7 ¡Ó 0.4 in heliox , p < 0.05).

CONCLUSION. We conclude that the use of heliox can markedly reduce trapped lung volume, intrinsic positive end-expiratory pressure in mechanically ventilated severe COPD patients. The reduction in PEEPi and hyperinflation may contribute to decreased pulmonary arterial pressure, pulmonary arterial occlusion pressure, right atrial pressure and increased cardiac index.

REFERENCE(S). 1) Tassaux D, Jolliet P, Roeseler J, Chevrolet J-C. Effects of helium-oxygen on intrinsic positive end-expiratory pressure in intubated and mechanically ventilated patients with severe chronic obstructive pulmonary disease. Crit Care Med 2000; 28:2721-2728
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PATIENT-VENTILATOR INTERACTION DURING NON INVASIVE VENTILATION: ROLE OF VENTILATOR INTERFACE

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INTRODUCTION. Non invasive ventilation (NIV) provides a safe and effective ventilatory support in patients with acute respiratory failure. Despite improvements in facial mask characteristics, pain, discomfort, skin necrosis or claustrophobia may limit the use of NIV and eventually leads to endotracheal intubation. In alternative to face mask, a transparent helmet, has been proposed as ventilator interface. Recent data showed that NIV by helmet may successfully treat hypoxemic non-hypercapnic acute respiratory failure, with better tolerance and fewer complications than facial mask. In this study we compared efficacy of face mask and helmet interfaces to deliver NIV. The study tested the hypothesis that physical characteristics of the ventilator interface may influence efficacy of PSV to unload the respiratory muscles.

METHODS. Tidal volume (Vt) -pneumotacograph, index of inspiratory effort, pressure time product per minute (PTP/min)-transdiaphragmatic pressure, and patient-ventilator synchrony – triggering delay, was measured in five healthy volunteers at different (5-10-15 cmH20) levels of PSV delivered by face mask (Mirage ResMed, Australia) and helmet (Castar StarMed, Italy), randomly applied. PEEP was set at 5 cmH20. To simulate conditions of increased ventilatory requirements a fixed resistor (endotracheal tube 5 mm internal diameter) was placed at the airway opening.

RESULTS. Results are expressed as means+SD.

	Mask PSV5	Helmet PSV5	Mask PSV10	Helmet PSV10	Mask PSV15	Helmet PSV15
Vt(l)	0.62 (0.40)	1.15 (0.41)	0.84 (0.42)	1.46 (0.14)	0.98 (0.55)	1.78 (0.13)
PTP/min	192.1	351.9	132.8	268.4	101.5	185.6
cmH20·s·min¯1	(52.9)	(94.8)*	(45.9)	(77.7)*	(43.9)	(103.1)
Delay(s)	0.17 (0.06)	0.40 (0.11)*	0.20 (0.04)	0.47 (0.15)*	0.20 (0.05)	0.46(0.07)*

** P<0,05 ANOVA for repeated measures with Bonferroni correction: mask vs. helmet*

CONCLUSION. Our data show that as compared to standard face mask helmet interface guarantees that ventilatory support is adequately provided; however helmet interface substantially impairs patient-ventilator interaction leading to an increase in muscle load

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Molecular biology – 472-477

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CLONING AND EXPRESSION OF BETA-DEFENSIN-2 GENE IN E.COLI.

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INTRODUCTION. Defensins, which represent peptides with braod antibiotic activity, are classified into α- and β- defensins. β-defensins eliminate or prevent the colonization of pathogenic organisms at a variety of anatomic sites, while they stimulate chemotaxis of monocytes and dendritic cells, may play a pivotal role in the innate and acquired immune responses. In order to investigate the role ofβ-defensin 2 in the pathogenesis of sepsis, genetic engineering method was employed to produce recombinantβ-defensin 2 peptide.

METHODS. Complete coding sequence of RBD2 was amplified with RT-PCR from pulmonary tissues, amplified DNA fragment was ligated into pET-32 vector. The expression plasmid was transformed and fused peptide was expressed in E Coli. Matured peptide was obtained with chemical cleavage and further purified on ÄKTA Purifier system.

RESULTS. The expressed fused peptide was above 40% of total cell protein. The characters of DNA and peptide were verified by sequencing and western blotting analysis respectively. The recombinant β-defensin 2 peptide showed high antimicrobial activity against E.coli.

CONCLUSION. The successful expression of recombinant β-defensin 2 peptide as intracellular fusion protein in E. Coli offers a fast system for the bioengineering production of small cationic peptide, provide the opportunity to receive high amounts of antimicrobial peptides, might be beneficial to the investigating the role of β-defensin 2 in the pathogenesis of sepsis and the treatment of sepsis.

REFERENCE(S). 1.Durr M, Peschel A. Infect Immun 2002;70: 6515-6517
2.Biragyn A, Ruffini PA, Leifer CA, et al. Science 2002;298:1025-1029
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NON-INVASIVE VENTILATION (NIV) IN ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) PATIENTS.

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INTRODUCTION. Avoiding intubation and mechanical ventilation could be a major objective in the management of Acute Respiratory Failure (ARF) patients with ARDS criteria. Nevertheless, there are only limited data on the efficacy of NIV in these hight-risk patients (1). The aim of this prospective, randomized, controlled and bi-center study, was to evaluate if NIV could improve the prognosis of ARDS patients.

METHODS. Prospective inclusion of 84 immunocompetent patients, with ARDS caused by pulmonary disease (community-acquired pneumonia, nosocomial pneumonia, aspiration pneumonia, or post-extubation pneumonia), randomized between standard treatment and standard treatment plus NIV. NIV was delivered through a face mask connected to a ventilator set in the pressure support mode with positive-end-expiratory-pressure, and with a sequential mode (2).

RESULTS. The base-line characteristics of the two groups were similar ; PaO2/FiO2 : 128±38 for NIV group (n=42) vs. 133±27 for standard-treatment group (n=42). At the 45th minute, the improvement of Pa02/FiO2 was significant only in NIV group (166±44, vs. 142±32 in standard group). Fewer patients in the NIV group than in the standard-treatment group required endotracheal intubation (40% vs. 69%, p=0.02), died in the intensive care unit (17% vs. 38%, p=0.03), or died in the hospital (24% vs. 45%, p=0.04).

CONCLUSION. In selected ARF patients with ARDS criteria, early initiation of NIV is associated with significant reductions in the rates of endotracheal intubation and an improved likelihood of survival to hospital discharge.

REFERENCE(S). (1)Rocker GM et al. Non-invasive positive pressure ventilation successful in patients with acute lung injury / ARDS. Chest 1999;115:173-177.
(2)Hilbert G et al. Non-invasive ventilation for treatment of acute respiratory failure in immunosuppressed patients with pulmonary infiltrates and fever, a randomized trial. N Engl J Med 2001;344:481-487.

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ALTERNATIVE COMPLEMENT CASCADE FACTOR B REGULATION IN SEPSIS IN HUMANS.

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INTRODUCTION. Complement factor B (Bf) is a component of the alternative pathway of complement activation. Bf is induced during the acute phase response of sepsis resulting in alternative complement cascade activation. Complement activation is an important component of the innate immune response to invading microorganisms; however, complement activation may also be an important contributor to shock in sepsis. The main mediators of acute phase proteins are inflammatory cytokines including TNFa and IFNg and bacterial products such as LPS. We have previously mapped the IFNg-responsiveness of the Bf promoter to consist of an ISRE site (at -130 bp) and a GAS site (at -90 bp) in murine macrophages. We have also identified a TNFa and LPS responsive element consisting of an NF-kB cis binding site between -423 and -433 bp of the Bf promoter. We now question the mechanism of Bf gene regulation by TNFa, IFNg and LPS in human peripheral blood monocytes (PBMC) and whether PBMC's from patients with septic shock induce Bf.

METHODS.

RESULTS. (1) We investigated Bf mRNA expression by RT-PCR. Like murine macrophages, TNFa stimulation induced a low level of Bf mRNA expression by itself but TNFa acted synergistically with IFNg to induce Bf mRNA expression in PBMC's. (2) Co-stimulation with IFNg and TNFa demonstrated time- and dose-dependent induction of Bf expression in PBMC's from human volunteers. (3) LPS showed a time- and dose-dependent induction of Bf expression in PBMC's from human volunteers. (4) PBMC's isolated from ICU patients with septic shock showed increased Bf mRNA expression by RT-PCR when compared to control patients in the ICU. (5) We have cloned the human Bf promoter and show identical ISRE and GAS cis-binding sites as well as two putative NF-kB cis-binding sites similar to the murine promoter. (6) Using a number of human Bf promoter luciferase-reporter constructs to map the human Bf promoter, we show identical IFNg promoter responsiveness but TNFa promoter responsiveness is different than the mouse Bf promoter. TNFa appears to activate the NF-kB binding site at –586 bp on the human promoter which is different than that seen in the mouse.

CONCLUSION. Although similar, there are differences in Bf induction in human PBMC's when compared to murine macrophages. Thus, Bf is induced in sepsis in human monocytes and may contribute to shock in sepsis.
Grant acknowledgement: Funded by the Canadian Intensive Care Foundation; the Heart and Stroke Foundation of Canada; the CIHR and the AHFMR

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THE RELATIONSHIP BETWEEN JAK/STAT PATHWAY AND HEPATIC GENE EXPRESSION OF HMGB-1 IN SEPTIC RATS

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INTRODUCTION. The discovery of a cytokine activity for high mobility group box-1 protein (HMGB-1) raises several important questions, including the potential mechanisms underlying signal transduction related to HMGB-1 formation during sepsis. The current study was to investigate the role of Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway in mediating hepatic mRNA expression of HMGB-1 in septic rats.

METHODS. Using a sepsis model by cecal ligation puncture (CLP), 98 male Wistar rats were randomly divided into normal control group (n=10), CLP group (n=40), AG490 (an inhibitor of JAK2) treatment group (n=24), rapamycin (RPM, an inhibitor of STAT3) treatment group (n=24). At serial time points animals in each group were sacrificed, and blood as well as hepatic tissue samples were harvested to determine HMGB-1 mRNA expression and serum aspartate transaminase (AST) as well as alanine transaminase (ALT) contents.

RESULTS. Compared to normal controls, HMGB-1 mRNA levels significantly increased in the liver during 6~48h after CLP (P<0.05 or 0.01); and serum AST and ALT contents significantly elevated at different time points respectively (P<0.05 or 0.01). Treatment with AG490 and RPM could markedly inhibit hepatic HMGB-1 mRNA expression at 24h (AG490 vs. CLP: 0.584 vs. 0.865, P<0.05), 48h (AG490 vs. CLP: 0.534 vs. 0.752, P<0.05) and 6h (RPM vs. CLP: 0.552 vs. 0.802, P<0.01), 24h (RPM vs. CLP: 0.447 vs. 0.865, P<0.01) following CLP, respectively. In addition, compared to CLP group, serum AST and ALT content in both treatment groups could markedly reduced at various intervals following CLP (P<0.05 or 0.01).

CONCLUSION. These data suggested that the activation of JAK/STAT pathway might be involved in mediating up-regulation of hepatic HMGB-1 mRNA expression in CLP-induced sepsis. Treatment with inhibitors of JAK/STAT pathway could markedly down-regulate HMGB-1 mRNA expression and attenuate acute liver injury associated with sepsis.
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ROLE OF HIGH MOBILITY GROUP BOX-1 IN THE DEVELOPMENT OF MULTIPLE ORGAN DYSFUNCTION SYNDROME IN RATS

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INTRODUCTION. Recent studies implicated high mobility group box-1 (HMGB-1) protein as a late mediator of endotoxin-induced lethality in mice, the present experiments were performed to investigate the potential role of HMGB-1 in the pathogenesis of sepsis-induced multiple organ dysfunction syndrome (MODS) in rats.

METHODS. Using a sepsis model by cecal ligation and puncture (CLP), 80 male Wistar rats were randomly divided into four groups as follows: normal control group (n=10), sham operation group (n=10), CLP group (being further divided respectively into 2, 6, 12, 24, 48 and 72 hours post-CLP subgroups, n=60), and sodium butyrate (an inhibitor for HMGB-1 expression) treatment group (being further divided respectively into 12, 24 hours post-CLP subgroups, n=20). At serial time points in each group, animals were sacrificed and samples from liver, lungs, kidneys and intestine were harvested to measure organ function parameters and HMGB-1/TNF-alpha mRNA expression. Additional experiments were performed to observe the effect of treatment with sodium butyrate on survival rate in septic rats (n=57).

RESULTS. Compared with normal controls, HMGB-1 mRNA levels significantly increased in liver, lungs as well as intestine at 6 hours and in kidneys at 12 hours after CLP respectively (P<0.01-0.05), keeping high values during the observation period. HMGB-1 mRNA levels were markedly inhibited at 12 and 24 hours in various tissues by sodium butyrate treatment group compared to CLP controls (P<0.05-0.01). Also, significant correlations were found between hepatic/pulmonary HMGB-1 mRNA expression and corresponding tissue TNF-alpha levels as well as organ function parameters. Treatment with sodium butyrate could markedly reduce serum alanine aminotransferase, creatinine levels at 12 hours and pulmonary myeloperoxidase activities at 24 hours. Furthermore, treatment with sodium butyrate significantly reduced the 1- to 6-day mortality compared with those without treatment (day 1: 13.6% vs. 40.0%, P=0.032; day 3: 36.4% vs. 77.1%, P=0.005; day 6: 59.1% vs. 94.3%, P=0.003).

CONCLUSION. These data demonstrated that HMGB-1 mRNA expression including liver, lungs, kidneys and intestine, were up-regulated at late phase and prolonged in CLP-induced sepsis. HMGB-1 might play an important role in development of excessive inflammatory response and subsequent MODS.
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TOLL-LIKE RECEPTOR 4 AND MACROPHAGE MIGRATION INHIBITORY FACTOR POLYMORPHISMS AND SIRS

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INTRODUCTION. The systemic inflammatory response syndrome (SIRS) is a major cause of morbidity and mortality, and is characterised by altered amplification of the innate immune system. It has been postulated that distinction between survivors and non-survivors may be genetically determined. The lipopolysaccharide (LPS) sensing complex is fundamental to innate immunity to Gram-negative bacteria. Genetic variation in the LPS receptor complex and downstream effectors may modify the severity of SIRS. We evaluated the association between the severity of SIRS and genetic polymorphisms in Toll-like receptor 4 (*TLR4*, pattern recognition receptor for LPS) and macrophage migration inhibitory factor (*MIF*, macrophage proinflammatory mediator).

METHODS. 104 patients (mean age 57y, mean APACHE II score 21, 63% with sepsis) with SIRS were recruited from the General ICU. DNA was genotyped using tetra-primer amplification refractory mutation system PCR (*TLR4*) or restriction fragment length polymorphism (*MIF*). Genotypes were compared to measures of SIRS severity (survived ICU, length of stay, APACHE II score, PaO_2/FiO_2 ratio and sequential organ failure assessment score (SOFA)).

RESULTS. Minor allele frequencies were *TLR4* Gly299 5% and *MIF* -173C 18%. The frequencies of the LPS-hyporesponsive *TLR4* Gly/Gly or Asp/Gly genotypes were increased in patients who died in ICU, compared to those who survived (*TLR4* 22% vs 5%, odds ratio 5, 95% C.I. 1.2 to 20.5, P=0.029, Fisher's exact test, n=99). There was no association between *TLR4* genotypes and measures of SIRS severity or presence of positive cultures. No associations were found with *MIF* polymorphisms.

CONCLUSION. These findings suggest that genetic variation leading to impaired host defence may result in increased severity of SIRS. Recruitment is ongoing to confirm these findings and explore gene-gene interactions in innate immunity.

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IMPACT ON THE OUTCOME OF TWO TNF POLYMORPHISMS IN PATIENTS ADMITTED TO THE HOSPITAL WITH SEPSIS

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INTRODUCTION. Our primary objective was to determine the association between two TNF polymorphisms and in-hospital mortality in patients admitted to the Hospital with sepsis. The secondary aims were to evaluate the association of these two polymorphisms with the development of septic shock and the severity of the MODS (measured by the SOFA score).

METHODS. Patients admitted to the Hospital that fulfilled criteria of sepsis (ACCP/SCCM definitions) were enrolled in this prospective study. After obtaining written consent, genomic DNA from peripheral blood was extracted by standard procedures. Two TNF polymorphisms were determined: one located at position -308 of the promoter region of TNFa (TNF1/TNF2) and the mutation of the first intron (-NcoI polymorphism) of TNFb (TNFB1/TNFB2). DNA was amplified using polymerase chain reaction, enzymatic digestion, and analyzed by gel electrophoresis. The following data were noted: Demographic variables, underlying diseases, clinical presentation, APACHE II, SOFA, site of infection, microbiological documentation, adequacy of empirical antibiotic therapy, and in-hospital mortality. Researchers that performed TNF polymorphisms were blinded to the patients' outcome. Statistical analysis was done with by Fisher´s exact test and t-Student test (A two-tailed p<.05 was considered significant).

RESULTS. Seventy-five patients were included (58 in the ICU and 17 in the ward). Only one patient received inadequate empirical antibiotic therapy. The sites of infection were abdomen (27), lung (19), urinary tract (17), and others (12). In-hospital mortality was similar for homozygous subjects for TNF1 and for TNF2 (21.5% vs. 23%; p>0.05) as well as the rate of patients with septic shock (54% vs. 53%; p>0.05). In-hospital mortality was greater in patients homozygous for the TNFB2 allele than in TNFB1 subjects (30% vs. 8%; p<0.05) and the presence of septic shock (65% vs. 36%; p<0.05), being comparable the groups in relation to the site of infection and underlying diseases. However, the worst SOFA score did not differ between TNFB2 and TNFB1 subjects: 7.1 (5.7) vs. 6.4 (5.2); p>0.05.

CONCLUSION. TNFB2 homozygous individuals that are admitted to the hospital with sepsis have a higher mortality rate and a greater risk to develop septic.
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Evaluation of prognosis and outcome – 478-483

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FEMALE GENDER IS ASSOCIATED WITH WORSE ICU OUTCOME; RESULTS OF THE SOAP STUDY

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INTRODUCTION. Gender may be a determinant of outcome in critical illness. We investigated the association between gender and outcome in the various disease subgroups reported in the SOAP study.

METHODS. In this cohort, multicentric, observational study, all adult patients admitted to the participating centers (198 centers participated from 24 countries) between May 1 and May 15, 2002. Patients were followed up until death, hospital discharge, or 60 days. We examined the gender differences in outcome in the whole population, patients with acute lung injury (ALI), sepsis, shock due to any cause and septic shock

RESULTS. The male population represented almost the 2/3 of the 3147 patients (61.7 %, p<0.001). All reported subgroups had a higher rates of male gender (p<0.001). ICU mortality rates were higher in females than in males in the whole population (20.6 vs. 17.4, %, p=0.026), in patients with ALI (46.5 vs. 34.2 %, p<0.01), in sepsis (30.9 vs. 24.2 %, p=0.013), in shock due to any cause (43.5 vs. 35.0, p=0.006), and septic shock (55.6 vs. 42.0, p=0.036). Moreover, in a multivariate analysis, female gender was an independent risk of ICU mortality in patients with sepsis (odds ratio=2.1; 95% confidence interval; 1.04-2.14, p<0.5), and those with septic shock (odds ratio=1.7; 95% confidence interval; 1.04-2.82, p<0.5).

CONCLUSION. In this large European cohort, female gender was associated with a higher risk of death.
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PERFORMANCE OF PROGNOSTIC SCORES IN PREDICTING OUTCOME FOR CRITICALLY ILL CANCER PATIENTS

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INTRODUCTION. Studies addressing usefulness of prognostic scores in cancer patients are insufficient. Moreover, the Cancer Mortality Model (CMM)[1], a specific score for these patients, has not been validated in another population. Our objective was to analyze the performance of 7 models (APACHE II[2], SAPS II [3], MPM II_0, MPM II_{24} [4], LODS[5], ODIN[6] and CMM[1]) in predicting hospital death for Brazilian cancer patients.

METHODS. Data were collected from a prospective cohort of 1216 patients. Discrimination was assessed by area under ROC curve (AUROC) and calibration by goodness-of-fit C-test.

RESULTS. The ICU and hospital mortality rates were 19.7% and 29.0%. Mean age was 56.2±16.8 years. Medical, scheduled and emergency surgical patients were, respectively, 31.8%, 57.2% and 10.9%.

Performance of Prognostic Scores

Prognostic Score	AUROC ± SE	AUROC (CI 95%)	C-Test (p-value)	Predicted Mortality	SMR
APACHE II	0.850 ± 0.012	0.823 - 0.876	31.564 (p<0.001)	22.44 ± 24.59	1.29
SAPS II	0.883 ± 0.012	0.861 - 0.906	30.585 (p<0.001)	22.56 ± 27.56	1.28
MPM II_0	0.829 ± 0.014	0.801 - 0.856	64.392 (p<0.001)	13.35 ± 18.74	2.17
MPM II_{24}	0.865 ± 0.012	0.840 - 0.889	58.915 (p<0.001)	18.61 ± 23.55	1.56
LODS	0.851 ± 0.013	0.826 - 0.877	47.362 (p<0.001)	18.59 ± 23.09	1.56
ODIN	0.854 ± 0.013	0.828 - 0.881	60.856 (p<0.001)	14.73 ± 19.10	1.97
CMM	0.883 ± 0.011	0.862 - 0.904	12.900 (p=0.115)	38.95 ± 31.24	0.74

SE=standard error; SMR=standadized mortality rate; CI=confidence interval

CONCLUSION. All models had good discrimination, however, solely the CMM showed good calibration. CMM can help physicians caring cancer patients in providing a better use of ICU resources.

REFERENCE(S). 1) Groeger et al. J Clin Oncol 1998;16:761; 2) Knaus et al. Crit Care Med 1985;13:818; 3) Le Gall et al. JAMA 1993;270:2957; 4) Lemeshow et al. JAMA 1993; 270:2478; 5)Le Gall et al. JAMA 1996;276:802; 6) Fagon et al. Intensive Care Med 1993;19:137.

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TISS ON ADMISSION AND AT DISCHARGE AS OUTCOME PREDICTOR IN CRITICALLY ILL PATIENTS

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INTRODUCTION. The Therapeutic Intervention Scoring System (TISS), allows assessment of workload and intensity of treatment in intensive care. TISS on admission in the ICU can also be used as an index of disease severity, and is also a predictor of nosocomial infection risk. TISS at discharge from the ICU has recently been shown to be a good predictor of post-ICU mortality in the ward (1). We studied the influence of TISS on admission and at discharge from the ICU on ICU and post-ICU mortality, and the relationship of TISS on discharge with nosocomial infection after discharge to the wards.

METHODS. We studied prospectively 205 consecutive patients admitted to the ICU. TISS was evaluated at 24 hours after admission and before discharge from the ICU. On the basis of TISS patients were delegated to one of four classes: class I (TISS < 10), class II (TISS 10-19), class III (TISS 20-39) and class IV (TISS ≥40). The outcomes we evaluated were a) mortality in the ICU and b) mortality post-ICU, during stay in the ward. Additionally, patients were evaluated daily in the ward for the presence of nosocomial infection.

RESULTS. A) On admission, 2,9% of patients belonged to class II, 61,5% to class III, and 35,6% to class IV. Mortality during ICU stay was respectively 0%, 17% and 42,5% and differences in ICU mortality were statistically significant among different classes (p<0,005). B) At discharge to the ward, 1% of patients belonged to class I, 26,8% to class II, 53,7% to class III and 18,5% to class IV. Mortality in the ward was respectively 0%, 3,6%, 23,6%, 97,4% and differed significantly among patients belonging to different TISS classes on discharge. Nosocomial infection appeared in 34,6 % of patients in the ward and was respectively 0%, 0%, 44,8% and 78% for each TISS class. The incidence of infection was significantly different among TISS classes.

CONCLUSION. High TISS on admission is associated with increased ICU mortality. TISS on discharge from the ICU is associated with nosocomial infection and death in the ward. Patients with TISS ≥40 at discharge have a uniform dismal prognosis.

REFERENCE(S). 1. Beck DH, et al. Intens Care Med 2002 ; 28:1287-93

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MORTALITY PREDICTION IN CARDIAC SURGERY: PERFORMANCE OF EURO-SCORE IN CORONARY AND VALVULAR SURGERY

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INTRODUCTION. The aim of this work was to assess and to validate the performance of European System for Cardiac Operative Risk Evaluation or Euroscore to predict mortality in coronary and valvular cardiac surgery.

METHODS. Prospective observational study of 1000 cardiac surgery patients - 500 consecutive coronary surgery and 500 consecutive valvular surgery -, in a tertiary referral center. Probabilities of hospital death for patients were estimated by applying the model and were compared with actual mortality rates. The performance of the system was assessed by evaluating calibration with Hosmer-Lemeshow goodness-of-fit test, and discrimination with receiver operating characteristic (ROC) curve.

RESULTS. Chi-square was 5.04 for coronary surgery, 5.91 for valvular surgery and 5.68 for overall cardiac surgery. The area under the ROC curve was 0.827 for coronary surgery, 0.804 for valvular surgery and 0.811 for overall cardiac surgery.

CONCLUSION. In our experience Euroscore performs well to predict overall mortality in cardiac surgery, with high calibration and discrimination, and it is an appropriate tool to assess this mortality. Euroscore performs better in coronary surgery than in valvular surgery. Predictive models originally developed in another country should be validated in the population to which they are finally applied.

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INFLUENCE OF DATA COLLECTION RELIABILITY IN MORTALITY RISK PREDICTION FOR APACHE II, III AND SAPS II

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INTRODUCTION. Validity and exactness of APACHE II, III and SAPS II might be affected by collection data reliability and its influence on mortality risk calculation.

METHODS. The present study tried to evaluate the reliability in data capture and its influence on the calculation of the APACHE II, APACHE III and the SAPS II severity scores and their mortality risk prediction. 1,210 patients were included in a general study to evaluate models above cited. Data were prospectively hand collected by physicians and residents of the ICUs participating from the patients' medical charts. Ten percent of the patients were selected by simple random sampling and three independent ICU physicians manually collected the same data retrospectively. The data and the calculations were compared. The distance between the diagnoses and its repercussion on the mortality risk calculation for APACHE II and III was evaluated.

RESULTS. The correlation between two groups was good. The agreement between two groups (paired t-test) was good for age, APS APACHE II, APACHE II severity score, APACHE II and APACHE III mortality risk; however, it was not for APS APACHE III (p=0.001), APS SAPS II (p =0.001) , SAPS II severity score (p=0.001) and SAPS II mortality risk (p=0.02). The agreement on the admittance diagnosis was 50 % for the APACHE II and III. However, the maximum difference of the mortality prediction was 10 % in 76.58 % of the patients for the APACHE II and in 79.82 % for the APACHE III.

CONCLUSION. The variables used for the calculation of the APS proved to be the most influential in the reliability of mortality risk and the different severity scores. Nevertheless, the low agreement in the admission diagnosis had no significant influence on the reliability of the mortality risk.

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PERFORMANCE OF INTENSIVE CARE UNITS: UPDATING THE SIMPLIFIED ACUTE PHYSIOLOGY SCORE II

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INTRODUCTION. Risk adjustment is one of the main tools for assessing clinical performance of Intensive Care Units (ICUs). However numerous factors, notably case-mix or pre-admission conditions, perturb the uniformity of fit of predictive models thus the use of standardised ratios to compare ICUs. The aim of this work is to investigate and validate an updating of the simplified acute physiology score (SAPS) II.

METHODS. Our study is a prospective, multicenter study involving 26 ICUs located in the Paris area participating in the Cub-Rea performance research project and more than 30000 stays upon two years. Models were built on 1999 data. Prognostic models for ICU mortality and hospital mortality are based on logistic regression analysis. For each outcome four models were developed : (1) the reference model (A) had only SAPS II score as an independent variable. (2) Points corresponding to age, surgical status and chronic illness were subtracted from the SAPS II score, the remaining score was called naked SAPS II. Model B had naked SAPS II, age, surgical status and chronic illness as independent variables. (3) Model C added to the preceding the admission diagnosis. (4) Model D, in addition to naked SAPS II, age, surgical status and chronic illness comprised all the recorded diagnosis grouped by means of a classification tree program. Internal validation was performed on 1999 data by resampling procedures. An external validation was also performed.

RESULTS. All new models had good calibration (p-value of the Hosmer-Lemeshow goodness of fit test are 0.98, 0.81, 0.42 and 0.74 for model A, B, C and D respectively) and similar or better discrimination compared with the SAPS II (area under the ROC curve are 0.89, 0.89, 0.91 and 0.93 for model A, B, C and D respectively). Uniformity of fit was obtained by inclusion of diagnostic information.

CONCLUSION. The SAPS II can be improved by integration of diagnostic information, thus gaining uniformity of prediction across various conditions.
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Oral Presentations
Preventing nosocomial infections – 484-489

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IMPACT OF SCHEDULED REPLACEMENT OF CENTRAL VENOUS CATHETERS ON THE RATE OF INFECTIOUS COMPLICATIONS

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INTRODUCTION. The aim of this study was to assess whether scheduled replacement of central venous catheters (CVC) every 7-10 days decreases the rate of infectious complications

METHODS. Prospective randomized trial in ICU patients requiring CVC for more than 7 days. Patients were assigned to undergo new-site replacement of the CVC every 7-10 days (group A) or when clinically indicated by unexplained fever, catheter malfunction, signs of insertion site infection (group B). All catheters were triple lumen. Catheter tips were semiquantitatively cultured and peripheral blood cultures were performed within 24 hours from catheter removal.

RESULTS. Group A consisted of 40 patients in whom 74 catheters were inserted at femoral (31), internal jugular (22) and subclavian vein (21). Group B consisted of 51 patients with 107 catheters inserted at femoral (45), internal jugular (29) and subclavian vein (33). Duration of catheterization was 7.5±2.4, 7.9±2.1, 8.6±1.7 days for group A and 12.6±5.2, 13.4±5.4, 13.5±5.1 days for group B for each site respectively (p<0.001). There was no significant difference in the rates of catheter-related infection (CRI) and catheter-related bacteraemia (CRB) between the groups for all three insertion sites (CRI: 19.3% vs 28.8%, p=0.5, 41% vs 38%, p=0.9, 9.5% vs 18%, p=0.5, CRB: 0% vs 2.2%, p=0.9, 4.5% vs 0%, p=0.4, 0% vs 3%, p=0.9). Within groups the rate of CRI was highest for internal jugular vein, while CRI rates for femoral and subclavian catheters were similar.

CONCLUSION. Scheduled replacement of central venous catheters every 7-10 days does not decrease the rate of infectious complications irrespectively of the insertion site.

REFERENCE(S). 1. Cobb DK, et al. N Engl J Med 1992;327:1062-8
2. Cook D, et al. Crit Care Med 1997;25:1417-24

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MRSA CARRIAGE IN ICU: MUPIROCIN DECONTAMINATION AND LONG-TERM FOLLOW-UP

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INTRODUCTION. MRSA carriers decontamination with nasal mupirocin, patients isolation and cohortation remain the proposed strategies to avoid cross-contamination in the ICU. Nasal decontamination with mupirocin (MU) together with chlorhexidine washing and shampooing was prospectively evaluated in MRSA carriers.

METHODS. All consecutive patients (pts) admitted with, or acquiring MRSA in the medical-surgical ICU were treated with nasal MU for 5 days and washing and shampooing was performed daily with chlorhexidine soap for the entire ICU stay. If MRSA was still cultured, a second treament was applied. Nasal, oro-tracheal and wound swabs were performed at regular intervals.

RESULTS. 74 pts were enrolled in the study. Age (mean+/SD): 63.1+/-14.4, SAPS II (mean+/-SD): 39+/-18.3. In 27 pts (A), the first treatment was completed in the ICU and in 47 pts, the treatment was initiated but completed outside ICU (B). At the end of treatment, all A were still MRSA carriers. A second treatment was applied in 9 pts and failed to eradicate MRSA carriage. In pts B, MRSA decontamination was achieved in 19/47 (40%). Nasal MRSA was the carriage site in these 12/19 pts. Table 1 gives the short and long-term MRSA carriage and survival for the entire population

	14 days	30 days	3 months	6 months	1 y	2 y	5 y
Survivors	60/74	56/74	46/74	36/74	34/74	30/74	21/74
(%)	81	75.6	62.1	48.6	45.9	40.5	28.3
MRSA (+)	42/60	31/56	20/46	4/36	4/34	3/30	1/21
(%)	70	55.3	43.4	11.1	11.7	10	4.7

CONCLUSION. Mupirocin combined with chlorhexidine soap is unable to eradicate MRSA carriage in patients staying in the ICU. Decolonisation can be achieved in some pts, after ICU discharge and more frequently when the nose is the unique carriage site. A large proportion of pts remains MRSA carrier at long-term.

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IMPACT OF SDD ON FUNGAL CARRIAGE AND INFECTION: A META-ANALYSIS

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INTRODUCTION. Selective decontamination of the digestive tract (SDD) is an infection control regimen that employs the enteral non-absorbable antimicrobial combination of polymyxin, aminoglycoside and polyene, to prevent or eradicate oropharyngeal and gut carriage of potentially pathogenic microorganisms, including fungi. A metanalysis of randomized controlled SDD trials has been performed to assess whether the administration of non-absorbable enteral antifungals, as part of selective decontamination protocol, may control fungal carriage and infection.

METHODS. We conducted a meta-analysis of 42 randomized controlled trials from 1987 to 2002 that compared oropharyngeal and/or intestinal administration of polyenes (amphotericin B or nystatin) with no treatment in the controls. A total of 6263 critically ill patients were included: 3133 received enteral polyenes and 3130 no antifungal prophylaxis. Main outcome measures were fungal carriage and fungal infections, namely infected patients, infection episodes and fungemia.

RESULTS. Enteral antifungals significantly reduced fungal carriage (odds ratio (OR) 0.32, 95% confidence interval (CI) 0.19-0.53). Fungal infections were significantly reduced in treatment group, both for infected patients (OR 0.31, CI 0.19-0.51), and episodes (OR 0.32, CI 0.2-0.49). Fungemia was reduced, but not significantly, from 15 episodes in the controls to 7 in treated patients (OR 0.49, CI 0.13-1.95).

CONCLUSION. This meta-analysis indicates that SDD reduces fungal carriage, and infection related morbidity in critically ill patients. The low event rate of fungemia, both in treated patients and in controls, explains why the impact on fungemia was not significant, requiring a larger patient sample.

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OROPHARYNGEAL VANCOMYCIN CONTROLS ICU-ACQUIRED LOWER AIRWAY INFECTIONS DUE TO MRSA

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INTRODUCTION. Aspiration of contaminated oropharyngeal secretions is the main pathway for the development of lower airway infections in mechanically ventilated intensive care unit (ICU) patients. Prevention and eradication of the abnormal oropharyngeal carriage of microorganisms by the administration of non-absorbable antimicrobials into the oropharynx have been shown to reduce the risk of lower airway infections. The main objective of this study was to assess whether topical oropharyngeal vancomycin may control lower airway infections and oropharyngeal carriage acquired on the ICU due to methicillin-resistant *Staphylococcus aureus* (MRSA). Secondary endpoints were the emergence of vancomycin-resistant enterococci (VRE) as well as vancomycin-intermediate *S. aureus* (VISA), and vancomycin consumption.

METHODS. Eighty-four patients mechanically ventilated for > 72 h were randomly assigned to control (n=42) or test (n=42) group. Patients who were assigned to the test group received at 6-h interval 0.5 g of a 4% vancomycin gel applied in the oropharynx. The frequency of MRSA lower airway infections and oropharyngeal carriage were assessed in both groups. Emergence of VRE and VISA, and vancomycin consumption were evaluated.

RESULTS. Lower airway infections due to MRSA acquired in the intensive care unit were reduced in the test group (OR 0.26, 95% CI 0.08-0.88) as was oropharyngeal carriage (OR 0.25, 95% CI 0.09-0.69). The duration of oropharyngeal carriage was reduced in the test group (76 days vs. 508 days/1,000 ventilator-days, p<0.01). Neither VRE nor VISA were isolated from either surveillance or diagnostic samples during the study period. The vancomycin budget was lower in the test group.

CONCLUSION. Our study demonstrated that topical oropharyngeal vancomycin was effective in preventing ICU-acquired lower airway infections and carriage due to MRSA in long-term mechanically ventilated patients.

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STRESS ULCER PROPHYLAXIS (SUP): PRESCRIPTION ATTITUDES IN ICU AND INFLUENCE ON THE INCIDENCE OF VAP

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INTRODUCTION. Prescription of SUP in our ICU varied from one physician to another, mainly because of the absence of a strict protocol regarding indications, durations and specific agents. VAP is the second nosocomial infection in our ICU (21:1000 days mechanical ventilation). The aim of the study was to search the influence of SUP on VAP incidence.

METHODS. A retrospective case-control study was performed. 38 patients with VAP were defined as cases. Cases were matched to 73 control subjects (ratio: 1:2), on the basis of age and APACHE II score (+/-2). VAP in cases was documented by a blind protected telescopic catheter (Combicath, superior or equal to 10_cfu/ml) performed on clinical suspicion of pneumonia.

RESULTS. In 26 of the VAP patients (68,4%), a SUP was prescribed for at least 72 hours before VAP. On the contrary, only 26 of the control patients (35,6%) received a SUP (p<0,001). Prescription of a SUP was found to be unjustified in 34 patients (58%). Omeprazole and Ranitidine were given intravenously in most patients (82%) for a mean duration of 13,1 days. No difference was demonstrated between cases and control subjects concerning age (resp.47,55+/-18,2 vs 49,64+/-17,95, p=0.6) and APACHE II score (resp.17,11+/-5,8 vs 18,11,+/8,2, p=0.54). However, cases had a longer ICU stay (35,45+/-17,91 vs 23,39+/-12,9 respectively, p<0,001), more days on mechanical ventilation (resp. 22,5+/-12,29 vs 14,17+/-9,32, p<0,001), and received more frequently antibiotics before VAP (resp. 84,2% vs 34,2%, p<0,001). Prior antibiotic use (OR 10,2, 95% CI 3,77-27,75) and SUP for at least 72 hours before VAP (OR 3.,91, 95% CI 1,69-9,02) were identified as risk factors for VAP in a chi-square analysis. No difference in ICU mortality was recorded between the two groups (resp. 28,4% vs 23,3%, p=0,5).

CONCLUSION. Unjustified prescription of SUP in our ICU is frequent and needs to be reevaluated. SUP has possibly contributed to a relatively high incidence of VAP in our ICU. A randomised prospective study assessing the real influence of SUP on VAP is already in progress.

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CONTROL OF A LARGE OUTBREAK OF GLYCOPEPTIDE-INTERMEDIATE S. AUREUS (GISA) IN CRITICALLY ILL PATIENTS

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INTRODUCTION. From January to October 2000, 21 patients were colonized (10) or infected (11) in ICU by the same GISA strain (MIC 2mg/l Vancomycin, 4 mg/l Teicoplanin). Pulsed field gel electrophoresis of bacterial DNA demonstrated 21 cases of cross contamination. Eight patients died in ICU (5 deaths attributable to GISA infection).

METHODS. Descriptive outbreak.

RESULTS. Recognition of the outbreak in April 2000 (7 cases) led to implementation of infection control measures including enhancement of isolation procedures and barrier safety measures according to usual recommendations. Moreover, measures were extended to any new patient. Hand disinfection was performed using Hydro-alcoholic solution. GISA carriers were pooled in the same area. Particular attention was paid with external intervener, family, during patients transport outside the ICU and disinfecting rooms after discharge. Despite these measures, 4 new cases occurred in August and September. The strain was isolated on inert surfaces outside patients' rooms. Infection control measures were drastically enhanced: 1) surfaces cleaning twice daily in and outside rooms aid of increasing health care worker number, 2) limitation of admissions and closing of 5/14 beds, 3)Quarantine (8d) of rooms and reusable materials after discharge of a GISA carrier, 4) strict assignation of designated nurses and nurse assistants to GISA carriers. These measures allowed to control outbreak: no new case occurred and environmental samples remained negative for GISA since last GISA carrier discharged from ICU.

CONCLUSION. This outbreak underline the importance of systematic detection of GISA when MRSA is isolated and efficient measures to control it.

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Monitoring of preload – 490-495

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EVALUATION OF FLUID RESPONSIVENESS IN CRITICALLY ILL PATIENTS.

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INTRODUCTION. Pulse pressure variations have been reported to predict the response to fluid challenge. However these studies have been conducted in patients mechanically ventilated with tidal volumes higher than 8 ml/kg. We evaluated whether this index can also be used in patients with ventilated with variable tidal volumes.

METHODS. We investigated 23 critically ill patients mechanically ventilated on controlled mode and equipped with a pulmonary artery catheter and in whom a fluid challenge was performed. We obtained complete haemodynamic measurements before and after infusion of 1000 ml Hartmann solution or 500 ml HES solution. Pulse pressure variation was calculated. A positive response to fluid challenge was defined as an increase in cardiac index by more than 10 %. The patients were separated in 2 groups according to tidal volume (Low TV group: tidal volume lower or equal to 7 ml/kg). Data are presented as median [range] and non parametric tests were used. Relationship between the changes in cardiac index and pulse pressure was assessed by linear regression.

RESULTS. Tidal volume ranged from 4.7 to 11.8 ml/kg (median 7.3). The Low and High TV group comprised 10 and 13 patients respectively. Seventeen patients were considered as responders. Overall cardiac index increased from 2.5[1.9-3.1] to 2.6[2.2-3.7] L/min.M^2. The relationship between the pulse pressure variation at baseline and changes in cardiac index was significant in the High TV group (R^2 = 0.49, p = 0.02), but the significance was lost in the Low TV group (R^2 = 0.09, p = 0.33).

CONCLUSION. The value of pulse pressure variation to predict fluid responsiveness may be limited in patients ventilated with low tidal volumes, probably because the respiratory-induced changes in preload were too small.

REFERENCE(S). Michard et al AJRCCM162:134-138;2000

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SYSTOLIC PRESSURE VARIABILITY VERSUS RIGHT ATRIAL PRESSURE TO MONITOR A VIRTUAL FLUID CHALLENGE.

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INTRODUCTION. Systolic pressure Variability (SPV) during positive pressure ventilation has been proposed as a monitor of preload(1). SPV is available as a minimally invasive bedside monitoring. We sought to determine whether SPV tracked the changes associated with the preload challenge of a straight leg raise(3)as well as right atrial pressure(RAP).

METHODS. In 16 consented patients scheduled for elective CABG a radial arterial cannula was inserted. Following induction of anaesthesia positive pressure ventilation (tidal volumes 10mls/Kg) was initiated. An internal jugular cannula was inserted. RAP1 and SPV1 (LiDCO Ltd) were measured, the legs were then raised and after one minute SPV2 and RAP2 were measured. One minute after the legs were lowered, SPV3 and RAP3 were measured.

RESULTS. RAP1-3 and SPV1-3 were compared using paired t-tests with a hypothesized difference of 0. Significant differences are seen between pre and post leg up and non significant differences between pre and post leg down for both SPV and RAP.

Statistical analysis of SPV and RAP at times 1-3 during virtual fluid challenge

Variables	Mean Difference	t-value	p-value
SPV1-2	2.98	4.79	.0003
RAP1-2	-3.07	-6.11	<.0001
SPV2-3	-3.56	-5.14	.0002
RAP2-3	3.4	3.93	.0015
SPV1-3	-.58	-.95	.358
RAP1-3	.333	.454	.657

CONCLUSION. In ventilated patients SPV may be used instead of RAP as a value against which a fluid challenge may be given. SPV only requires a peripherally placed arterial line and as such is minimally invasive.

REFERENCE(S). (1)Rooke GA. Systolic pressure variation as an indicator of hypovolaemia. Current Opin Anaesthesiol 1995; 8:511.
(3)Boulain T, Achard JM, Teboul JL, Richard C, Perrotin D, Ginies G. Changes in BP induced by passive leg raising predict response to fluid loading in critically ill patients. Chest 2002; 121(4):1245-1252.

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ABILITY OF SUPERIOR AND INFERIOR VENA CAVA DIAMETER TO PREDICT CENTRAL VENOUS PRESSURE.

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INTRODUCTION. A recent study (1), showed that superior vena cava partial collapse during tidal ventilation reflected insufficient venous filling. We conducted a prospective study to assess and compare the respective accuracy of inferior vena cava (IVC) and superior vena cava (SVC) diameter to predict central venous pressure (CVP).

METHODS. From august to October 2002, 28 patients with circulatory failure related to sepsis were included (19 men, and 9 women), mean age 56 ± 15 yr, SAPS II 55 ± 21. All patients were under positive pressure ventilation. CVP was measured after a brief ventilator disconnection of 3 seconds. TTE subcostal view allowed measurement of IVCd and TEE measurement of SVCd. Linear correlations between SVCd and IVCd and CVP were tested. Patients with a CVP < 10 mmHg and >= 10 mmHg were separated in two groups. Diameters in the two groups were compared using an unpaired t test. Results are expressed as mean values ± SD. ROC curves were generated for SVCd and IVCd. The area under the curve (± SE) were calculated for each parameter and compared. p < 0,05.

RESULTS. The protocol was successfully completed in 20 patients. Close linear correlation was reported between SVCd and CVP (r = 0,70, p = 0,0006). Close linear correlation was also found between IVCd and CVP (r = 0,65, p = 0,0018). In group 1 : seven patients had a CVP < 10 mmHg (6 ± 4 mmHg) and in group II : thirteen had a CVP >= 10 mmHg (14 ± 2 mmHg). SVCd (13,3 ± 2,3 versus 18,3 ± 2,2 mm, p < 0,0001) and IVCd (13,7 ± 4,7 versus 17,8 ± 2,7 mm, p = 0,02). Area under the ROC curve was significantly higher for SVCd than for IVCd (0,99 ± 0,02 and 0,79 ± 0,10, p = 0,031). A SVCd <= 15 mm allowed prediction of CVP < 10 mmHg with a sensitivity of 100 %, and a specificity of 92 %, whereas an IVCd <= 17 mm allowed prediction of a CVP < 10 mmHg with a sensitivity of 85 %, and a specificity of 69 %.

CONCLUSION. SVCd is more efficient than IVCd in non-invasive estimation of CVP and in predicting a CVP < 10 mmHg.

REFERENCE(S). 1. Vieillard-Baron A & Coll. Anesthesiology 2001, 95 (5) : 1083-88.

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INITIAL DISTRIBUTION VOLUME OF GLUCOSE TO DETERMINE PLASMA VOLUME DURING A FLUID CHALLENGE

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INTRODUCTION. The quantitative assessment of intravascular volume remains elusive, although very much needed in intensive care medicine. Initial Distribution Volume of Glucose (IDVG) is based on a one compartment pharmacokinetic model of the initial rate of disappearance of an iv. glucose bolus. It reflects effective extracellular fluid volume, and may be sensitive to changes in plasma volume regardless of capillary leak (1). We thought to evaluate if IDVG may be applicable to evaluate plasma volume status of individual patients. The specific aim of this study was to determine IDVG sensitivity to volume expansion with Poly(O-2-hydroxyethyl) starch Voluven® in critically ill patients, and to compare it to standard haemodynamic measurements.

METHODS. IDVG was calculated with a one-compartment exponential model, using plasma glucose concentrations at 3, 4, 5, 6 and 7 minutes after an i.v. bolus of 5 g glucose.
13 patients after cardiac surgery requiring volume therapy were enrolled. IDVG was computed before and after infusion of 7 ml/kg of Voluven over 30 min. IDVG and CVP were compared by one way ANOVA for repeated measurements, and expressed as mean ± SD.
IDVG was determined 3 times serially in another group of 11 postoperative cardiac patients not requiring a fluid challenge. The individual coefficients of variation (CoVar = SD/mean) were computed to assess the reproducibility of individual measurements.

RESULTS. The regression coefficient (r-square) of the exponential fit of glucose versus time was 0.96 ± 0.03 before, and 0.95 ± 0.04 after starch infusion (ns). IDVG (85 ± 14 vs. 93 ± 14 ml/kg, p = 0.08) was not different, and the power of the comparison was 0.45 for a p value of 0.05. By contrast, CVP increased significantly (9.8 ± 3.4 vs. 12.9 ± 5.0 mm Hg, p<0.05) with the fluid challenge.
In the control group, IDVG was 90 ± 18 ml/kg, and the average coefficient of variation was 0.15 ± 0.8.

CONCLUSION. Although IDVG seemed to be appealing to evaluate fluid status in relatively large groups of ICU patients, its usefulness appears limited to assess the individual response to a fluid challenge, were it was less sensitive than CVP. This limitation may be related to the characteristics of the method or to specific features of the population studied.

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DO INDICATORS OF ESOPHAGEAL DOPPLER MONITORING PREDICT FLUID CHALLENGE RESPONSIVENESS ?

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INTRODUCTION. In ICU, the best indicators of ventricular preload are still debated. Dynamic parameters should be used preferentially to static ones to predict responsiveness to a fluid challenge. Oesophageal Doppler Monitoring (EDM) provides continuous cardiac output (CO), corrected systolic flow time (FTc), a good indicator of preload and allows measurement of the beat-to-beat peak velocity (PV). The aim of this present study was to assess the predicting fluid responsiveness of the respiratory changes in PV (PPV).

METHODS. We studied 15 mechanically ventilated patients (56±11 yr, APACHE II = 24±5) with septic shock. Invasive blood pressure, CO, FTc and PV were measured by EDM (Deltex, France). The respiratory changes in arterial pulse pressure (PPP), calculated as already described and PPV were determined over the same single respiratory cycle. PPV was calculated as the difference between the maximal PV and the minimal PV divided by the mean of that difference. Measurements were before and after fluid challenge (500 ml of colloids). Patients were classified as responders if the CO increased by fluid challenge > 15% and non responders if not. ROC curves were generated for PPP, PV and FTc varying the discriminating threshold of each parameter. The areas under the curves were calculated (AUC ±SE) and compared.

RESULTS. The main results are included in the table.

	FTc	PPV	PPP
Threshold	320 msec	9.3%	13.5%
Sensitivity (Se)	33 %	89 %	67 %
Specificity (Sp)	50 %	67 %	67 %
AUC±SE	0.370±0.156	0.778±0.127	0.685±0.142

CONCLUSION. These findings suggest that in mechanically ventilated patients with septic shock, PPV obtained by EDM, a reliable non invasive haemodynamic monitoring, predicts fluid responsiveness with a better sensitivity than PPP. In contrast, FTc does not predict a CO increase after fluid challenge.

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PICCO DERIVED PARAMETERS VERSUS „FILLING PRESSURES“ IN INTRA-ABDOMINAL HYPERTENSION

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INTRODUCTION. Intra-abdominal hypertension (IAH) PEEP and hypovolemia compromise cardiovascular function (1). Correct estimation of preload is crucial. This study will compare volumetric assessment with traditional „filling pressures“ in IAH.

METHODS. In total 52 measurements (13 in each stage) were performed in 8 ventilated pts. M/F ratio 1/1, age 70.3±9.3, APACHE-II 21.8±7.1, SAPS-II 49.5±9.9, SOFA 6.9±2.9. Study-stages were: Baseline (normal IAP and ZEEP); stage 1 (IAH and ZEEP); stage 2 (IAH with velcro-belt and PEEP); and stage 3 (normal IAP and PEEP). Complete haemodynamic profiles were obtained with the aid of a Swan-Ganz catheter. Volumetric (ITBVI, GEDVI, EVLWI) assessment was done with the PiCCO system (Pulsion). Statistical analysis was done with two-tailed paired student's t test. Values are expressed as mean±SD.

RESULTS. The major hemodynamic parameters are summarised in the Table.

	Baseline	p-value	Stage 1	p-value	Stage 2	p-value	Stage 3
IAP	8.6±3.6	<0.0001	14.4±3.5	NS	15.9±3.6	<0.0001	10.2±3.3
CVP	12.3±2.6	<0.0001	17.2±2.7	0.002	19.6±3.2	<0.0001	15.4±2.2
PCWP	15.4±2.6	<0.0001	20.9±2.9	0.004	24.3±2.9	<0.0001	18.7±1.9
GEDVI	871±196	0.02	918±236	0.0005	810±189	0.04	847±194
CI	3.8±1	0.04	3.6±1	0.0005	3.1±0.9	0.02	3.4±0.9

CONCLUSION. Acute IAH significantly but erroneously increases our traditional „filling pressures“ PCWP and CVP, making them unreliable markers of volume status. Volumetric assessment with ITBVI and GEDVI better reflects preload. With IAH Cardiac output and mean arterial pressure drop while PAP rises. Continuous CO measured by the PiCCO system better reflects the acute changes. PEEP-application further increases IAP and filling pressures and deteriorates haemodynamics. Abdominal decompression has beneficial effects on all study-parameters. These deleterious effects of IAH occur in a relatively short period of time (30 to 45minutes) and at relatively low pressures of 15mmHg. Surgeons and ICU physicians should be aware of the interactions between IAP, PEEP and filling pressures and the deleterious effects of IAH caused by abdominal banding. A moratorium on Velcro-belts in unstable ICU patients seems therefore warranted.

REFERENCE(S). (1) Malbrain MLNG. Current Opinion Crit Care 2000; 6:17-29.

Oral Presentations
Cardiac surgery – 496-501

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TIME TO EXTUBATION AND TRANSFER AFTER PEDIATRIC CARDIAC SURGERY IN EUROPE

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INTRODUCTION. Little is known about the current practice of respiratory support in postoperative paediatric cardiac surgical patients in Europe. In a recent multicenter cohort study in adults large differences between centres in duration of ventilation and length of postoperative stay in ICU were identified (1). The aim of this multi-centre study is to gain information about the duration of respiratory support and the time to discharge of paediatric cardiac surgical patients in order to evaluate the current practice of respiratory management and discharge of paediatric cardiac surgical patients in Europe.

METHODS. Prospective data collection was done in 21 intensive care units admitting children after cardiac surgery between July 2001 and June 2002. The study is limited to 6 representative pathologies and 10 interventions. Centre variability in Time to Extubation (TiTOEx) and length of stay in the ICU (LOSICU) was analysed with the logrank test for the two most common interventions. Only centres that performed >= 10 for a given intervention entered the analysis.

RESULTS. Information on a total of 1602 children was collected from the 21 ICU's. 1444 were included based on diagnostic criteria and 1574 based on the interventions. The most frequent intervention was the closure of ASD or VSD (n=571) followed by the correction of Fallot's Tetralogy (n=187), arterial switch (n=147), AVSD repair (n=121), coartation repair (n=108) and systemic-pulmonary shunt (n=103). The median number of children per centre was 65 (11-370). Median TiToEx after ASD or VSD Closure varied between 0-71 hours and after repair of Tetralogy between 12-108 hours (P<0.0001). Median LOSICU after ASD or VSD Closure varied between 23-117 hours and after repair of Tetralogy between 48-146 hours (P<0.0001).

CONCLUSION. The variability in two durations related to resource utilisation, TiToEx and LOSICU, is large between centres even in very narrow groups of paediatric cardiac surgical interventions. The survival analysis of the multicentre profiles allows the definition of predominant practice with confidence limits and may support centre oriented benchmarking.

REFERENCE(S). 1. Lassnigg A, Hiesmayr MJ, Bauer P, Haisjackl M. Effect of centre-, patient- and procedure-related factors on intensive care resource utilisation after cardiac surgery. Intensive Care Med 2002; 28(10):1453-61.

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PERIOPERATIVE VOLUME THERAPY IN CARDIAC SURGERY: A TWO CENTRE'S COMPARISON

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INTRODUCTION. Perioperative high volume therapy is associated either with an improvement (1) or a worsening (2) of the prognostic. The aim of the present study was to compare perioperative fluid administration in two different centres and to evaluate the consequences on complications after cardiac surgery.

METHODS. This study was prospective and observational, and included all the patients admitted after cardiac surgery in each ICU during a two months period. Pre-, intra- and postoperative variables were compared using t and Chi-2 tests. Results are expressed as mean ± standard deviation.

RESULTS. 152 patients (centre1) and 109 (centre2) including respectively 62 and 79 CABG were studied. In the centre1, patients were youngest (62±14 vs. 65±12 p=0.036) but had a highest EuroSCORE (5.8±3.7 vs. 4.5 ± 3.0, p=0.002). Centre1 used highest volume of crystalloid intraoperatively (i.op) and postoperatively (p.op, table). P.op use of intropic drugs, length of mechanical ventilation and stay in ICU, p.op PaO2/FIO2 ratio, lactate or creatinine levels, diuresis and mortality were similar in both centres.

	Centre1	Centre2	CABG1	CABG2
Cryst i.op(l)	2.5(1.3)	0.3(0.3)*	2.5(1.2)	0.3(0.3)*
Coll i.op (ml)	540(360)	615(490)	550(360)	670(530)
Cryst p.op	5.7(2.9)	0.15(0.5)*	5.4 (2.7)	0.15(0.5)
Coll p.op (ml)	315(405)	460(415)*	360(480)	440(380)
N.epinephr i.op	39%	12 %	28 %	8 %
N epinephr p.op	49 %	9 %*	36 %	8 %*
PRC (ml)	550 (1400)	220(500)*	110 (400)	30 (99)

** : p < 0.01 ; mean (SD)*

CONCLUSION. Despite major differences in fluid therapy between the 2 centres, no main differences in postoperative outcome were found. These observations are in favour of the realisation of randomised trial on volume therapy in cardiac surgery.

REFERENCE(S). 1 Sinclair S. BMJ 1997; 315: 909-912.
2 Polanczyk CA, JAMA 2001; 286:309-14.
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EFFECTS OF PROTECTIVE AND CONVENTIONAL VENTILATION ON CYTOKINE RESPONSE AFTER CARDIAC SURGERY

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INTRODUCTION. In patients with acute lung injury, protective ventilation and high PEEP induces lower cytokine release and less pulmonary injury compared to conventional mechanical ventilation (1).Cardiopulmonary bypass (CPB) initiates a systemic inflammatory response characterized by the activation of cytokines(2)and pulmonary injury is part of this syndrome. We compared TNF-alpha, IL–6 levels and pulmonary mechanics between the protective and conventional ventilation groups during and after cardiac surgery.

METHODS. Patients ventilated with 1) protective tidal volumes (6mL/kg; respiratory rate (RR):15/min, PEEP 5 cmH_2O, n=15) Group PV; 2)conventional tidal volumes (10 mL/kg; RR:9/min, PEEP 5 cmH_2O, n=14)Group CV+PEEP and 3) conventional tidal volumes (10mL/kg; RR: 9/min;n=15) without PEEP (Group CV+ZEEP). Various pulmonary parameters were determined and arterial blood samples were drawn to measure systemic TNF-alpha and IL–6 levels throughout the study.

RESULTS. There was no difference between the groups regarding the cytokine levels. Plateau pressures of Group PV were significantly lower than Group CV+PEEP (p=0.02) and Group CV+ZEEP(p=0.001) after CPB. Peak airway pressures of Group PV and Group CV+PEEP were lower than Group CV+ZEEP (p=0.001) after CPB(p<0.05). Patients in Group CV+ZEEP had significant decreases in dynamic lung compliance after CPB (p=0.002). Oxygenation was better in both Group PV and Group CV+PEEP as compared to Group CV+ZEEP after the operation (p=0.03 and p=0.05).

CONCLUSION. Protective ventilation prevents postoperative increases in plateau and peak airway pressures in CABG patients. None of the ventilatory strategies applied in this study affected the systemic cytokine levels.

REFERENCE(S). 1) Ranieri VM, Suter PM, Tortorella C,et al: Effect of Mechanical Ventilation on inflammatory mediators in patients with acute respiratory distress syndrome: a randomized controlled trial. JAMA 1999;282: 54. 2) Butler J, Rocker GM, Westaby S: Inflammatory Response to Cardiopulmonary Bypass. Ann Thorac Surg 1993; 55: 552-559.

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THE EFFECT OF CPAP AND PEEP ON OXYGENATION DURING ONE LUNG VENTILATION IN THE SUPINE POSITION.

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INTRODUCTION. It is generally accepted that, in the lateral decubitus position, the best manoeuvre to improve oxygenation is to apply differential lung continuous positive airway pressure (CPAP) / positive end expiratory pressure (PEEP) via the step by step approach.[1] Recently, more cardiothoracic procedures are performed under one-lung ventilation (OLV) in the supine position.[2] This study was performed to investigate the effect of CPAP and/or PEEP on oxygenation during OLV in the supine position

METHODS. 15 patients scheduled for Ivor-Lewis operation via a right thoracotomy approach was prospectively studied. To collapse the right lung as much as possible in the closed thoracic cavity, continuous suction was applied to tracheal lumen of double lumen endotracheal tube (Bronchocath, Mallinckrodt medical Ltd, Athlone, Ireland). Patients were mechanically ventilated with 100% O_2 to minimize hypoxemia due to OLV in the supine position. After initiation of OLV in the supine position, PaO_2 was checked at 10 min intervals until steady level of decreased PaO_2 was maintained (OLV_{last}). At the point, PaO_2 was measured while CPAP of 1, 3, 5, and 10 cm H_2O was applied step by step with or without 5 cm H_2O PEEP.

RESULTS. PaO_2 decreased in all pateints when TLV was changed to OLV_{last} (p<0.05). Without CPAP, application of 5 cmH_2O PEEP decreased PaO_2 (mean ¡_ SE; 123 ¡_ 17 vs. 88 ¡_ 15). PaO_2 increased significantly after the application of 1, 3, 5, and 10 cmH_2O CPAP when there were stepwise increase of PaO2 from 1 to 3 cmH_2O CPAP (315 ¡_ 24, 359 ¡_ 25, p <0.05), but there were no furthur increases with higher level of CPAP. In the presence of CPAP, there were no differences in oxygenation with the application of PEEP.

CONCLUSION. We conclude that the irrespective of the application of PEEP, minimum level of CPAP is effective to prevent hypoxemia during OLV in the supine position.

REFERENCE(S). 1. Benumof JL. Conventional and differential lung management of one-lung ventilation. In: Benumof JL, 2nd ed. Anesthesia for thoracic surgery. Philadelphia: W. B. Saunders Company, 406-28
2. Watanabe S, Noguchi Eiko, Yamada S, Nobuya H, Kano T. Sequential changes of arterial oxygen tension in the supine position during one lung ventilation. Anesth Analg 2000; 90: 28-34.

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MODS AFTER CARDIAC SURGERY: RISK FACTORS AND A MODEL TO PREDICT SEVERITY

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INTRODUCTION. Multiple organ dysfunction syndrome (MODS) is a severe complication after cardiac surgery carrying high mortality and dramatically increasing length of hospital stay and costs of care (1). Nonetheless, only limited data exist on the exact aetiology and specific risk factors. Therefore, this study tries to examine the influence of perioperative factors on incidence and severity of MODS after cardiac surgery. Furthermore, it seeks to find a model to predict severity of postoperative MODS in cardiac surgery patients.

METHODS. Data of retrospectively analysed cardiac surgery patients (n=1300) were used to develop a model to assess risk factors for the development of MODS and predict severity of MODS. This model was validated using prospectively acquired data from 195 patients. Data collection included pre-, intra-, and postoperative parameters. For statistical analysis a multiple, linear regression model was used. Variables that were univariately associated with MODS were entered into the final model. For both groups, coefficients of determination were independently calculated.

RESULTS. Coefficients of determination for both models were comparable (retrospective model, 52.1%; prospective model, 50.7%). Age, sex, pre-existent chronic obstructive pulmonary disease, congestive heart failure, and renal failure, ASA classification, time on cardiopulmonary bypass, need for mass transfusion and reoperation, SAPS, incidence of perioperative myocardial infarction, tachyarrhythmias, and the syndromes of SIRS or sepsis were independently associated with the incidence of MODS after cardiac surgery.

CONCLUSION. In cardiac surgery patients, incidence and severity of postoperative MODS can only be predicted in about 50% by a model using routinely evaluated clinical data. Other factors, such as genetic predisposition, may significantly contribute to aetiology of MODS after cardiac surgery.

REFERENCE(S). 1. Chernow B. Variables affecting outcome in critically ill patients. Chest 1999;115:71-76.

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THE LEUVEN "FAILURE TO EXTUBATE STUDY": PROPOFOL AS AN INDEPENDENT RISK FACTOR AFTER CARDIAC SURGERY

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INTRODUCTION. Shortage of ICU beds and economical restrains urge to enhance patient turnover without compromising on quality of care. This requires accurate identification of the avoidable reasons for prolonged intubation and ICU stay.

METHODS. In a prospective, observational clinical study, including all adult cardiac surgery patients admitted to our 56-bed mixed surgical ICU over 3 months, all pre, per- and post-operative risk factors were analysed by using a prospectively designed questionnaire. The reasons of failure to extubate at 8h, 24h and 48h postoperative and of prolonged ICU stay were identified.

RESULTS. We studied 243 patients, aged 65.1 ± 12.3 years, of which 9.9% were operated semi-urgently and 9.5% urgently. In 54% of the cases, isolated coronary surgery was performed, of which 92% off-pump. In 56% of patients, complicated valvular and combined procedures, surgery for congenital anomalies and transplantation was performed. The M±SD Euroscore (1) was 6.9 ± 4.0 and higher than the European mean of 4.1 ± 0.5 (p<0.0001). The Euroscore-predicted mortality was 5.9% whereas the observed mortality was 4.1%. The median (IQR) time to extubation was 20(14-31)h, ICU stay 2.8 (1.8-4.9)d and hospital stay 12 (10-19)d. At 8h, 96.7% of patients were still intubated; at 24h this was 35.8%; at 48h, 18.3%. Re-intubations were required in 9.5% of cases. At 8h, 24h and 48h, the cumulative dose of piritramide was 0.4 ± 0.1 mg/kg, 0.8 ± 0.3 mg/kg and 1.2 ± 0.6 mg/kg, respectively, and the cumulative dose of propofol 12 ± 6 mg/kg, 21 ± 13 mg/kg and 25 ± 20 mg/kg. Multivariate logistic regression analysis identified pre-operative infection, haemodynamic instability, excessive bleeding (OR 14, p=0.04) and propofol dose (OR 1.7 per 10 mg/kg, p=0.003), but NOT piritramide, as independent risk factors for failure to extubate at 24h. Intubation time (OR 2.6 per 10h, p=0.003) remained an independent risk factor for failure to discharge from ICU at 48h.

CONCLUSION. The Leuven ICU admits high risk patients after cardiac surgery and performs well with a lower mortality than the Euroscore-predicted rate. Intubation time is independently determined by two, possibly avoidable, factors : excessive post-operative bleeding and use of propofol. A future study will evaluate the impact of implementing a post-operative sedation/analgesia algorithm designed at limiting propofol use.

REFERENCE(S). (1) Roques F. et al. Eur J Cardiothorac Surg 16;1999:9–13
Grant acknowledgement: Belgian Fund for Scientific Research, Research Fund of KULeuven.

Oral Presentations
Antibiotic resistance – 502-506

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OUTCOME OF GLYCOPEPTIDE-INTERMEDIATE S. AUREUS INFECTION DURING AN OUTBREAK IN ICU

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INTRODUCTION. During a large outbreak (January to October 2000) 21 patients were colonized (10) or infected (11) in ICU by the same GISA strain (MIC 2mg/l Vancomycin, 4 mg/l Teicoplanin). Pulsed field gel electrophoresis of bacterial DNA demonstrated 21 cases of cross contamination (1 imported, 20 acquired). This outbreak led to perform drastic infection control measures in order to control it. All infected patients were treated using a synergic combination of Vancomycin and Cephalosporin of third generation. Mean time to colonization and infection by the GISA strain were 14.8d (1-80) and 15.6d (7-46) respectively. Infections (11 patients) were pneumonia (10), bacteriaemia (4), sinusitis (1), endocarditis (1) and cholecystis (1). Eight patients died in ICU (5 death attributable to GISA infection).

METHODS. These 21 patients were matched with 3 control each on length of exposure to risk, SAPSII (+/-5), age and sex.

RESULTS. The univariate analysis showed that colonization or infection by GISA strain increased the length of mechanical ventilation (MV) and the length of stay (LOS) in ICU and in the ward, but did not increase the mortality rate (ICU and Hospital mortality OR (95%CI): 0.82(.29-2.29)and 1.34 (.37-4.92))even after adjustment on SAPS II on admission (ICU and Hospital mortality OR (95%CI): 1.13(.33-3.82)and 1 (.33-3.06)).

Morbidity	GISA (n=21) median (Q1-Q3)	Controls (n=63) median (Q1-Q3)	p
SAPS II	53 (36-68)	53 (34-66)	NS
Length of MV	20j (8-47)	8j (3-15)	<0.01
LOS ICU	24j (16-51)	13 (7-20)	<0.01
LOS hospital	48 (28-72)	24 (15-39)	<0.01
Mortality rate (hosp)	47,6%	41,2%	NS

CONCLUSION. The GISA strain isolated in this outbreak present a significant risk of morbidity. This underline the importance to detect systematically GISA strain on admission in ICU.

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THE PREVALENCE AND PATTERN OF INFECTIONS CAUSED BY ANTIMICROBIAL-RESISTANT ORGANISMS IN A MICU

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INTRODUCTION. The aim of this study was to investigate the prevalence of infections caused by antimicrobial-resistant organism (ARO) in MICU and to identify the risk factors for the ARO.

METHODS. This is a prospective observational study performed in 28 beds MICU of a 2100-bed tertiary-care hospital in Seoul, Korea. All patients admitted to the MICU with microbiologically documented bacterial infection between November 2001 and June 2002 were evaluated. The pattern and the risk factors for the infections caused by ARO including MRSA, third generation cephalosporin resistant *Acinetobacter baumanii* (ISAB), imipenem-intermediate sensitive *A. baumanii* (IIAB), imipenem-resistant *A. baumanii* (IRAB), expanded spectrum beta-lactamase bacilli (ESBL), imipenem-resistant *Pseudomonas aeruginosa* (IRPA) and VRE were evaluated. The other bacteria's were classified by the susceptible organisms.

RESULTS. Total of 479 patients were admitted to the MICU during the study period. Among the 258 patients (324 cases) who had microbiologically documented infections, there were 137 episodes (42.3%) of infections caused by the ARO and 187 episodes (57.7%) of infection caused by the susceptible organisms. There were 61 cases (44.5%) of MRSA, 23 cases (16.8%) of ISAB, 23 cases (16.8%) of ESBL, 11 cases (8.0%) of IRAB, 8 cases (5.8%) of IIAB, 6 cases (4.4%) of IRPA, and 5 cases of (3.6%) VRE. The resistant rates of ICU-acquired and hospital-acquired infection were significantly higher than community acquired infection (51.1%, 40.9%, 8.0%, respectively; p=0.001). The rate and the duration of mechanical ventilator (MV) use were higher in patients with ARO than the susceptible organisms (91.8 % vs. 78.7 %), (24.5¡_27.7 vs. 18.1¡_28.9 days; p=0.0011), respectively. The length of ICU stay and the mortality rates were also higher in patients with ARO (26.2¡_35.7 vs. 18.2¡_36.1 days; p<0.05), (46.0% vs. 41.7 %), respectively. Risk factors associated with antimicrobial-resistant infection were pneumonia, mechanical ventilation, and stress ulcer prophylactic agents.

CONCLUSION. Infections with ARO in our MICU caused significant increase in ICU stay and mortality. The presence of pneumonia and the use of MV and stress ulcer prophylactic agents might be risk factors for the antimicrobial-resistant infection.

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OUTCOME OF ENTEROCOCCAL BACTEREMIA: A METAANALYSIS OF THE IMPACT OF VANCOMYCIN RESISTANCE

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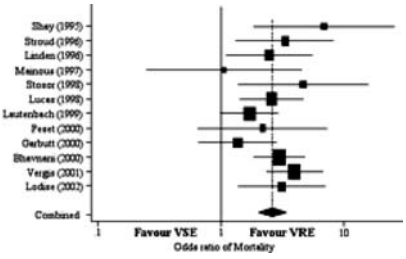
INTRODUCTION. Patients with enterococcal bacteremia (Bact) are frequently involved with severe underlying disease. The impact of vancomycin (VAN) resistance on mortality has not been clearly assessed.

METHODS. Metaanalysis of published studies between 1966 and 2002 (Pubmed) with keywords enterococcus, Bact, VAN, mortality. Odds-ratio of each study between mortality due to VAN resistant (VRE) and VAN susceptible (VSE) Bact were calculated. The analysis used inverse-variance weighting to calculate random effects summary estimates. A Q test for heterogeneity scanning and Begg's funnel plot for publication bias testing were performed.

RESULTS. 12 studies including 765 patients with VRE bacteraemia Bact (47% mortality) and 1238 patients with VSE Bact (25.6% mortality) were included. VRE Bact presented a significant increased mortality when compared to VSE Bact: OR = 2.6, 95% CI = [2.1-3.3], p<.0001 (Figure). Q test for heterogeneity (p=.28) and Begg's funnel plot (p=.92) were not significant.



CONCLUSION. VRE is associated with a significant increased mortality when compared to VSE Bact. These results are not due to heterogeneity or bias publication. The question how underlying disease may influence the prognosis of patients with enterococcal Bact remains to be evaluated.

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IMIPENEM-RESISTANT ACINETOBACTER BAUMANNII AND MORTALITY IN VENTILATOR-ASSOCIATED PNEUMONIA (VAP)

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INTRODUCTION. The prognosis of VAP in ICU may be influenced by antimicrobial resistance phenotype of nosocomial bacteria. This study compared the outcome of VAP secondary to *A.baumannii* according to their resistance to imipenem (IMP).

METHODS. From 1998 to 2003, 214 VAP were diagnosed in surgical ICU (clinical and radiological criteria associated with microbiological confirmation). *A.baumannii* were isolated in 36 cases (16.8%). The two groups (IMP resistant (IMP R) and IMP susceptible (IMP S)) were compared according to the demographic data and mortality. Mann Whitney and Fisher tests were used, p<0.05 significant. A multivariate analysis determined independent factors of mortality. Results are expressed with median [IQR] and proportion.

RESULTS. The 36 patients diagnosis were 14 peritonitis, 9 post-cardiac surgery pneumonia, 4 trauma, 4 gastro-intestinal bleeding, 3 mediastinitis et 2 pancreatitis. The delay of VAP was 23 days. The table reported data of the two groups(*p<0.05). Age, SAPS II, SOFA upon VAP and IMP resistance of *A.baumannii* were analysed by logistic regression. Only SOFA upon VAP (OR:7.6; CI95%[1.1-35]) and IMP resistance (OR:6.2; CI95%[1.5-39.3]) were independently associated with mortality.

	IMP R (n=23)	IMP S (n=13)
Age (year)	*66 [18]	49 [22]
SAPS II upon admission	48 [10]	41 [26]
SOFA upon admission / VAP	9 [3] / *8 [7]	7 [6] / 4 [6]
Length of treatment (day)	12 [5]	12 [4]
Length of ventilation (days)	39 [29]	40 [40]
Length of stay in ICU (day)	40 [27]	44 [38]
Mortality in ICU n(%)	*16 (70%)	3 (23%)
Hospital mortality n(%)	*18 (78%)	4 (31%)

CONCLUSION. Despite the small sample size of the study, the resistance of *A.baumannii* to IMP may worsen the outcome of VAP. The main hypothesis is the lack of active antimicrobial agents except colimycine. However, a relationship between IMP resistance and an increased virulence of *A.baumannii* could not be eliminated.

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RESISTANCE IN ICU ACQUIRED INFECTIONS: DOES THE FOCUS MATTER?

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INTRODUCTION. In critical patients, an adequate empirical treatment is associated with a better outcome, therefore, to know the susceptibility of the etiological agents is important. *Pseudomonas aeruginosa* (PA) and *S aureus* (SA) are the most frequent agents in ICU-acquired infections. Objective: To asses the pattern of resistance of these two micro-organisms, according the focus of infection.

METHODS. Cohort, prospective, multicenter study carried out from 1994 to 2001, for periods of 1 to 3 months. Patients admitted to the participating ICUs were included. They were followed up to discharge from the ICU or up to a maximum of 30-60 days. Infections studied included pneumonia associated to mechanical ventilation (VAP), catheter-related urinary tract infection (UTI) and primary and CVC bacteraemia (PCB). Markers of resistance were defined according to CDC criteria. Susceptibility from specimens collected from VAP were compared to the isolated from UTI+PCB. Data are expressed as percentage of resistant isolates to the antibiotic selected. Statistical analysis: Fisher test.

RESULTS. Among 32.801 patients, a total of 3.992 ICU acquired infections occurred and were caused by 4.356 organisms. In 635 cases, *P aeruginosa* was isolated (488 from VAP, 107 from UTI and 40 from PCB). *S aureus* was found in 566 episodes (500 from VAP, 8 from UTI and 58 from PCB). The rate of *S aureus* resistant to cloxacilline in isolates from VAP was 28,1%, while in specimens collected from UTI+PCB was 31%(NS).
Table 1 shows the data of P aeruginosa´s resistance

P aeruginosa resistance (%)

	Imipenem	Piper-Tz	Ceftazidime	Cefepime	Ciprofloxacin	Gentamicine
VAP	21,1	20.5	24.1	18.3	20.1	33.3
UTI+PCB	18.6	9.2	21.5	11.1	10.6	19
p	NS	0.017	NS	NS	0.019	0.008

CONCLUSION. *S aureus* showed no differences in resistance to cloxacilline in relation to the focus of the infection, while Pseudomonas aeruginosa isolated from VAP, was significantly more resistant to several antibiotics.
Grant acknowledgement: AVENTIS

Oral Presentations
NO-dependent pathways – 507-511

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NO-MEDIATED ACTIVATION OF MITOCHONDRIAL K-ATP CHANNELS IN LPS-TREATED RAT MESENTERIC ARTERIES

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INTRODUCTION. Septic shock is characterized by inadequate low vascular resistance and hyporeactivity to vasoconstrictor agents. The observed vasodilation is thought to be mediated, at least in part, by increased production of nitric oxide (NO) and activation of vascular potassium (K) channels. In the present study, we assessed the direct and NO-mediated effects of transmembrane and mitochondrial K_{ATP}-channel modulation on the phenylephrine (PE) -reactivity in rat resistance arteries with and without LPS-treatment in vitro.

METHODS. Microvascular myograph-studies were performed on incubated (20 hrs) control- and LPS (E.Coli, 50mug/ml)-treated rat mesenteric arteries. Dose-response curves to the vasoconstrictor PE (10^{-8}-10^{-5} M) were performed and contractility (E_{max} and EC_{50}) was calculated. The effects of the transmembranous K_{ATP}-channel inhibitor glibenclamide (10muM), and the selective mitochondrial K_{ATP}-channel inhibitor 5-hydroxydecanoic acid (5HD, 100muM) were assessed, both in the absence and presence of NO-precursor L-arginine (1mM).

RESULTS. 38 vessels with an internal diameter of 296±8 mum were examined. LPS diminished the sensitivity to PE: maximal contraction-responses to PE of the vessels were 7.0±0.5 for the control-vessels compared to 2.4±0.6 mN/mm^2 for the LPS-vessels (p=0.002). Contractility to a depolarizing high extracellular dose of K^+ was not changed after LPS-treatment (E_{max} controls: 7.7±0.5 vs LPS: 7.6±0.5 mN/mm^2, p=NS). The inhibitory effect of LPS on PE contraction was enhanced by L-arginine, which increased the $logEC_{50}$ from -6.05±0.07 to -5.78±0.09 (p=0.02). Glibenclamide did not have an effect on PE-reactivity in the LPS-treated vessels. 5-HD abolished the earlier seen negative effect of L-arginine on PE-contractility in LPS-treated vessels ($logEC_{50}$ -5.37±0.07 vs -5.62±0.22, p=NS).

CONCLUSION. Incubation with LPS causes a decrease in PE-reactivity in rat mesenteric arteries. The SUR-binding transmembrane K_{ATP}-channel inhibitor glibenclamide has no effect in enhancing PE-contractility. In contrast, the selective mitochondrial K_{ATP}-channel inhibitor 5-hydroxydecanoic acid abolished the negative effect of L-arginine on the contractility to PE. LPS-induced hyporesponsiveness to PE is partly caused by NO-mediated activation of mitochondrial K_{ATP}-channels.
Grant acknowledgement: PP was supported by a grant from the Dutch Scientific Organisation ZONMW

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LPS INDUCES INOS IN ALL LAYERS OF RAT MESENTERIC ARTERY IN BOTH IN VITRO AND IN VIVO MODELS

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INTRODUCTION. Vessels exposed to LPS express inducible nitric oxide synthase (iNOS) and produce nitric oxide. iNOS was thought expressed in endothelium and smooth muscle until Kleschyov (1998) demonstrated adventitial iNOS. Using models of LPS-induced hyporeactivity (O'Brien, 2000) and in vivo LPS-induced hypotension, we studied iNOS expression in rat mesenteric artery (RMA).

METHODS. RMA was incubated for 4-48 h in culture media +/- 1mg ml-1 LPS (S. Typhosa). RMA was also removed from anaesthetised rats 4 h after saline or LPS (Klebsiella 40 mg kg-1). Rings were rinsed, fixed and 7mM sections cut on a cryostat. Endogenous peroxidase was inhibited with 3% H_2O_2 and non-specific protein binding inhibited with 5% milk powder. Sections were incubated with primary antibody (monoclonal rabbit anti-mouse iNOS,1:200 dilution) and then biotin conjugated anti-rabbit antibody (1:1000 dilution). Antigen was visualised with diaminobenzidine. Sections were counterstained, dehydrated and mounted in DPX. These were graded from nil (negative controls) to +++ at microscopy.

RESULTS. LPS incubation in vitro induced iNOS in all layers. There was less iNOS in controls. The short-term in vivo model induced less iNOS mainly in endothelium and smooth muscle.

Presence of LPS-induced iNOS within RMA after in vitro or in vivo incubation

	Endothelium	Smooth Muscle	Adventitia
Cont 4h : LPS 4h	nil : +/-	+ : +	nil : +/-
Cont 24h : LPS 24 h	+ : ++	+ : +	+/- : ++
Cont 48h : LPS 48h	++ : +++	+ : ++	+ : +
Cont : LPS in vivo	+/- : +	+/- : +	nil : +/-

CONCLUSION. LPS induces iNOS in all layers of RMA. iNOS in controls in vitro presumably reflects LPS in serum in culture medium; the small amount in vivo may reflect animal instrumentation.

REFERENCE(S). Kleschyov et al. (1998) Br. J. Pharmacol., 123, 623-626. O'Brien et al. (2001) Br. J. Pharmacol., 133, 351-360.
Grant acknowledgement: Medical Research Council

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SELECTIVE INOS-INHIBITION DURING PORCINE BACTEREMIC SHOCK: EFFECTS ON GUT AND LIVER ENERGY BALANCE

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INTRODUCTION. In porcine long-term endotoxemia we recently showed that selective iNOS inhibition prevented the progressive derangement of hepatosplanchnic energy metabolism (1).Here, we investigate whether these effects can be confirmed during live bacteria-induced, hyperdynamic septic shock.

METHODS. 12h after induction of shock with continuous i.v. ps. aeruginosa (PSAE) up to now 12 pigs received either no drug (PSAE; n=6) or selective iNOS inhibitor L-NIL(n=6) titrated to maintain MAP at preshock levels (range 1.0-3.0 mg/kg/h). We measured mesenteric, hepatic and portal blood flows (Transonic), ileal microvascular perfusion (LDFgut, laser Doppler),ileal-arterial PCO2 gap(Tonocap) and liver lactate clearance (lac-clear).

RESULTS. Data are median and interquartile range, P<0.05. * vs. Preshock (ANOVA on Ranks);§ L-NIL vs PSAE (Mann-Whitney Rank Sum Test). L-NIL maintained blood pressure and regional macrocirculation did not differ between groups.

		Baseline	12 hours	18 hours	24 hours
LDF gut	PSAE	27(23;28)	14(10;21)*	14(8;15)*	8(6;9)*
units/10	L-NIL	24(20;28)	11(10;19)*	13(11;16)*	13(10;15)**
PCO2-gap	PSAE	15(14;20)	28(20;30)*	29(25;33)*	50(37;59)*
mmHg	L-NIL	16(15;19)	20(16;27)	17(14;19)	19(8;22)*
Liver Lac-Clear	PSAE	13(13;19)	5(4;14)	6(0;9)*	0(-1;10)*
umol/min/kg	L-NIL	14(7;17)	3(-1;5)*	8(7;10)	8(7;14)

CONCLUSION. Also in a porcine live bacterial septic shock selective iNOS inhibition blunted the detrimental consequences of sepsis on intestinal and hepatic energy balance. Prevention of progressive microcirculatory disturbances might contribute to these results, though improved cellular respiration cannot be ruled out.

REFERENCE(S). 1.Matejovic et al. Shock: 2001; 16:203-10
Grant acknowledgement: Supported by a research grant IGA MZ CR: ND6837-3/2001

Oral Presentations
Nephrology: Clinical investigations – 512-516

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RECOVERY FROM ORGAN FAILURE IS ASSOCIATED WITH IMPROVED MITOCHONDRIAL FUNCTION IN SEPTIC PATIENTS

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INTRODUCTION. Mechanisms underlying the sepsis associated, multi-organ dysfunction syndrome (MODS) are unclear though mitochondrial dysfunction may be an important factor. We have reported low [ATP] and mitochondrial respiratory chain inhibition in skeletal muscle of septic shock patients taken within 24 hrs of ICU admission (1). There was an associated rise in nitric oxide (NO) production and reduction in the protective antioxidant, reduced glutathione (GSH). We thus investigated whether clinical improvement was associated with resolution of mitochondrial dysfunction.

METHODS. Vastus lateralis muscle biopsies were performed in 15 septic shock patients within 24 hours of ICU admission and repeated every 5 days (max 5) until death or discharge. Samples were frozen in liquid N2 and later assayed for evidence of NO generation (nitrite/nitrate, NOx), GSH, respiratory chain complex activities (expressed as a ratio to citrate synthase activity) and [ATP]. Biopsies were obtained from 8 elective orthopaedic patients(controls).

RESULTS. Mean values (±SE) for SOFA, [NOx], [GSH] and complex I activities for the 11 septic survivors and the orthopaedic controls are shown in table 1. In comparison, septic, non survivors, (4 on days 1 and 5, 2 on day 10) showed an increased SOFA score and a smaller rise in GSH and complex I activity (data not shown). No differences in [ATP] and other Complex activities were seen.

	Controls	Day 1 n=11	Day 5 n=11	Day 10 n=8	Day 15 n=3	Day 20 n=3
SOFA	-	11±1	8±1[b]	6±1[b]	7±2	5±1[b]
NOx muM/mg prot	68±8	142±18[a] n=8	83±12[b] n=6	70±10[b] n=4	79±5 n=2	28±3 n=2
GSH nM/mg prot	9.5±0.7	5.5±0.6[a]	9.7±1.0[b]	7.9±1.1	6.9±1.7	8.9±0.4
Complex I	0.21±0.01	0.16±0.01	0.18±0.02	0.20±0.04	0.22±0.04	0.30±0.06[a,b]

ANOVA with post hoc LSD;a=p<0.05 vs controls, b=p<0.05 vs day 1

CONCLUSION. Resolution of MODS is associated with reduced nitrosative stress and less mitochondrial enzyme inhibition. This merits further investigation to establish causation

REFERENCE(S). Brealey D et al. Lancet 2002;360:219.
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CARDIAC PROTEINS ARE NITRATED BY PEROXYNITRITE & METABOLISED BY UBIQUITIN PATHWAY IN SEPTIC PATIENTS

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INTRODUCTION. Mechanisms of heart failure during sepsis are not completely known. Nitric oxide (NO) produced by inductible NO Synthase (iNOS) does not seem to be directly involved (1) but peroxynitrite produced from NO nitrates proteins and inactivates them (2). This process has never been show in human heart. Nitrated proteins are destroyed by proteolytic ATP-dependent ubiquitin pathway (3). We study iNOS expression, the amount of nitrated proteins (NT prot) and of ubiquitinated proteins (ubiq prot) in wall of cardiac ventricules, in diaphragm and in rectus abdominis muscle (RA) from patients died from septic shock.

METHODS. Biopsies from left and right ventricules (LV, RV), diaphragm (dia) and RA were performed during autopsy in patients that died from septic shock and in RA from alive non-septic patients undergoing elective surgery (control group, approved by ethical committee). Expression of iNOS, NT prot and ubiq prot was identified by Western-Blot (monoclonal antibody; arbitrary units:UA). A Kruskall-Wallis test was used.

RESULTS. given as mean±SE. *p<0.04 vs control.
The expression of iNOS, NT prot and ubiq prot is the same between LV and RV.

	Septic LV (n=7)	Septic Dia (n=7)	Septic RA (n=7)	Control (n=3)
iNOS	12.5±3.4*	10.7±4.3*	9.3±1.5*	3.6±2.7
NT prot	10.8±4.2*	9.9±4.3*	11.3±2.8*	3.5±0.5
ubiq prot	51.4±11.9*	57.2±22.7*	44.7±13.3*	21.8±6.4

CONCLUSION. This study (i) confirms iNOS expression in heart and diaphragm of septic patients and (ii) shows for the first time proteins nitration and activation of the proteolytic ubiquitin pathway in human septic heart and diaphragm. Thus, iNOS, NT prot and ubiq prot are expressed at the same level in cardiac ventricular wall and in skeletal muscles, including diaphragm, in septic patients.

REFERENCE(S). (1) FASEB J. 2001; 15: 294
(2) Biochem J. 2002; 366: 399
(3) Arch Biochem Biophys. 2000; 380: 360

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CU, SE, ZN AND THIAMINE BALANCES DURING CONTINUOUS VENOVENOUS HEMODIAFILTRATION (CVVHDF)

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INTRODUCTION. Acute renal failure is a serious complication in the critically ill patient and frequently requires dialysis. Trace element metabolism is altered in renal failure but balance data are lacking. We studied micronutrient balances during CVVHDF

METHODS. CVVHDF using alternatively commercial bicarbonate (BIC) and lactate (LAC) substitution fluids on 2 consecutive days in ICU patients with acute renal failure. Measurements during 8-hr periods. Determination of Cu, Se, Zn and thiamine in plasma and replacement solutions; hourly determination in the ultrafiltrate (=UF). The 8hr balances were calculated as the difference between fluids administered and the UF losses; The 24hr balances were compared to recommended parenteral nutrition intakes (RI).

RESULTS. 11 patients were enrolled, aged 65±10 years, with a SAPSII score of 62±22; 19 sessions were studied. The replacement solutions contained no Cu, but Se 0.01 mumol/l, and Zn: BIC 1.42 mumol/l, LAC 0.85 mumol/l. Cu, Se, Zn and thiamine were detectable in the UF of all patients: concentrations were stable over time in each patient, with little variation between patients. Balances were negative for Cu, Se and thiamine (no difference BIC vs LAC), positive for Zn (Table). Mean CRP level was 178 mg/l. Plasma concentrations: Cu was normal; Se and Zn were below ref. ranges; glutathione peroxidase (GSHPx) was in the lower range

	Zn - mol (mg)	Se - mol (g)	Cu mol (mg)	Thiamine (mg)
8hr Balances	6.9 ±5.7	-0.32 ±0.23	-2.2 ±1.3	-1.37±0.34
24hr balances	20.7 (1.3 mg)	-0.97 (-73 g)	-6.5 (-0.40 mg)	-4.12
Recomm. Intakes	100 (6.5 mg)	0.5 (40 g)	20 (1.3 mg)	3 mg

CONCLUSION. CVVHDF resulted in significant Se, Cu and thiamine losses,which were equivalent to 2 times the daily recommended intakes for Se, 0.3 times for Cu, 1.4 times for thiamine, while Zn balances are modestly positive (+0.2 times the recommended intakes). The losses and the inflammatory response explain the low plasma levels. If prolonged, CVVHDF is likely to result in selenium and thiamine depletion, and to have deleterious effects on antioxidant defences reflected by the low GSHPx

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DECREASED MORTALITY WITH THE USE OF PLASMA EXCHANGE IN PATIENTS WITH CLASS 1 HELLP SYNDROME

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INTRODUCTION. HELLP syndrome is a multisystemic disorder. It is characterized by elevation of liver enzymes, low platelets and haemolysis (1,2). Maternal mortality changes between 0-24%, and it is due to the severity of disease, delayed diagnosis, infections and renal failure (1-3). We aimed to investigate the use of plasma exchange in patients with HELLP syndrome.

METHODS. During two-year period (2000-2002) 23 patients with HELLP syndrome were treated with plasma exchange using fresh-frozen plasma (group I). All procedures were performed with Fresenius AS 200 cell separator. Control group consist of 26 patients with HELLP syndrome treated with conservatively in between 1993 and 1999 (group II). All patients have had single-or multiple-risk factors (which were suggested by Martin et al.: platelet <50.000/mm3, LDH level >1.400 IU/L or AST level >150 IU/L)(3). Maternal complications and mortality rate were the main outcomes in this study. Statistical comparisons were performed with Chi square test.

RESULTS. Median age, LDH, platelet and Hb level were not statistically different in two groups. One plasma volume corresponding to 40 ml/kg of body weight was exchanged daily until normal LDH level or platelet count were reached. Median five apheresis procedure (1-26) were performed. While maternal mortality rate was 23.1% (6/26) in control group, there was no death in group I. Patients were classified according to criteria, which were suggested by Martin et al. (Class 1 was defined as a platelet nadir <50.000/mm3, class 2 50.000-100.000/mm3, and class 3 100.000-150.000/mm3). All deaths were in control patients with Class 1 and mortality rate was significantly higher than the study group (p<0.005). The causes of mortality were infection, brain oedema and ARDS. Dialysis requirement was not statistically significant between two groups (17.4% vs 23%).

CONCLUSION. Our study showed that plasma exchange reduced mortality in high risk patients with HELLP syndrome, particularly in Class 1 patients. Therefore, we suggest that plasma exchange should be added to standard therapy in patients with Class 1 HELLP syndrome and may be considered in other high risk patients.

REFERENCE(S). 1-Weinstein L. Am J Obstet Gynecol 1982,142:159-67.2-Rath W, et al. J Perinat Med. 2000,28:249-60. 3-Martin Jn Jr, et al. Obstet Gynecol 1990, 76:737-41.

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UNFRACTIONED VERSUS LOW-MOLECULAR-WEIGHT HEPARIN (ENOXAPARIN) FOR ANTICOAGULATION IN CVVH

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INTRODUCTION. Heparin is the most frequently used anticoagulant for CRRT in European ICUs. Nevertheless, low-molecular-weight (LMW) heparins appear to possess several advantages over unfractioned heparin, such as causing less bleeding, thrombocyte activation, AT III consumption and thrombocytopenia, as well as affecting the lipid profile to lesser extent. The purpose of this study was to evaluate the efficacy and safety of the LMW heparin enoxaparin as anticoagulant in CVVH compared to unfractioned heparin.

METHODS. Consecutive adult medical and surgical ICU patients with normal anticoagulation parameters requiring CRRT were included in this randomised, prospective, cross-over study. CVVH was performed with pre-filter fluid replacement at 2500 mL/hr and blood flow rates of 180 ml/min. Filters were primed with normal saline containing anticoagulant (5000 IE heparin or 25 mg enoxaparin, respectively). Heparin-treated patients received a initial pre-filter bolus of 30 IU/kg and a maintenance infusion at 7 units/kg/hr, titrated to achieve a systemic activated partial thromboplastin time (aPTT) of 0,4 - 0,45 seconds. Enoxaparin-treated patients received an initial pre-filter bolus of 0,15 mg/kg and a maintenance infusion starting at 0,05 mg/kg/hr, which was subsequently adjusted to maintain systemic anti-factor Xa activity (anti-Xa) at 0,25-0,30 IU/ml. To adjust anticoagulation blood samples were drawn at baseline, 0.5, 1, 2, 4, 12, 24 and 48 hours after initiation and at the end of CVVH. Maximum treatment duration for each set was 72 hours.

RESULTS. 28 patients with a mean APACHE II score of 20 (range 10 to 29) were included. Mean filter life span was 21,4 h (±16,8 SD) for heparin and 26,5 h (± 22,2 SD) for enoxaparin (p=0,04, paired t-test). No correlation could be established between filter life span and either peak aPTT or steady state aPTT for heparin treatment. On the other hand, a significantly positive correlation was found between filter life span and both peak systemic and post-filter anti-Xa activity (p=0,024 and 0,004, respectively). One major bleeding occurred during heparin treatment, no bleeding event was observed during enoxaparin treatment.

CONCLUSION. Enoxaparin can be safely used for anticoagulation during CVVH resulting in slightly higher filter life span compared to unfractioned heparin. Anti-FXa activity appears to be positively correlated with filter life span in patients treated with enoxaparin.

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INTERIM RESULTS OF SHARF4 STUDY: OUTCOME OF ACUTE RENAL FAILURE WITH DIFFERENT TREATMENT MODALITIES

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INTRODUCTION. It is important for ICU physicians and nephrologists to predict mortality of acute renal failure (ARF) in the first 24 to 48 hours (h). For this purpose the SHARF II score at 0 and 48 h has been developed [1,2]. This study will look at short and long term morbidity, mortality, and quality of life with different modes of treatment in ARF.

METHODS. Prospective multicentre randomised clinical trial. Target population are 1600 adult patients with ARF consecutively admitted to ICU. Those patients needing renal replacement therapy (RRT) were randomised to either slow extended daily dialysis (SLEDD) or continuous veno-venous haemofiltration (CVVH). Randomisation was done according to SHARF II_0 score (<30, 30-60 and >60). Interim study endpoints were hospital morbidity and mortality.

RESULTS. Interim analysis after 692 patients: age 69 (16-93), 60% male, SHARF II_0: 66.8 ± 34.1, SHARF II_{24}: 64.4 ± 32.5, $SOFA_0$ 8±4, $SOFA_{24}$: 6.9±4.8, APACHE II: 22.8±10.3, ICU LOS: 13.1±14.4. Diagnosis of ARF was medical in 66.7% and surgical in 27.1%. The cause of ARF was prerenal in 46.1%, and renal in 48.9%. The cause of renal ARF was ATN in 90.5%, and AGN in 6%. There were 14.1% of patients in SHARF category 1 (<30), 26.8% in category 2 (30-60) and 59.1% in category 3 (>60). The higher the SHARF score the higher the APACHE II and SOFA score: respectively 18.9±8.8 and 5±2 for category 1, 20.4±8.8 and 7.5±3.2 for category 2 and 25±17 and 9.7±3.5 for category 3. RRT was needed in 40.8% of patients, from whom 63% were randomised. Outcome analysis on 481 patients showed a mortality rate of 56.5%, 2.9% developed ESRD, 10.2% had partial recovery and 30.4% had complete recovery of renal function. Mortality was 46% in conservative treatment versus 64% in CVVH and 68% in SLEDD. The ICU LOS was 19±16 in CVVH and 17±14 in SLEDD. Observed mortality was lower than expected in non-RRT. In RRT observed mortality paralleled the expected.

CONCLUSION. The interim results of an ongoing prospective study show that the SHARFscore, incorporating parameters at 0 and 48h has good predictive value in estimating prognosis in ARF-patients requiring intensive care. Overall mortality was 56.5% and 40.8% needed RRT. Mortality was the same regardless of RRT used. Major problems lay in recruiting centres using both techniques equally. Randomisation rate is lower than expected.

REFERENCE(S). (1) Chew S et al. Nephrol Dial Transplant 1993;8:101-7.(2) Lins R et al. Clin Nephriol 2000;53:10-7.

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PREDICITVE VALUE OF INTERLEUKINS 6. 8, AND 10 LOW HLA-DR EXPRESSION IN ACUTE RENAL FAILURE

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INTRODUCTION. Increasing evidence exists for the role of inflammatory mediators, such as cytokines, in the pathogenesis of ischemic renal failure (1, 2). In addition, decreased monocyte HLA-DR expression has been demonstrated to be associated with poor outcome (3, 4) in critical care patients. The aim of this study was to evaluate monocyte HLA-DR expression and plasma levels of pro- and anti-inflammatory cytokines (IL-6, IL-8, and IL-10) and their predictive value concerning survival of critically ill SIRS patients with and without acute renal failure (ARF).

METHODS. A total of one hundred and three consecutive adult patients with systemic inflammatory response syndrome from two intensive care units participated in the study. Laboratory data for all patients were prospectively collected on the day of admission and two days thereafter. Patients with acute renal failure (ARF) and non-ARF patients were compared by the Mann-Whitney U-test. Independent predictors of mortality were tested using forward stepwise logistic multiple regression analysis. The discriminative power of different variables was tested using receiver operating characteristic (ROC) curve analysis.

RESULTS. ARF developed in 36 patients (35%). ARF patients showed significantly lower HLA-DR expression and higher plasma levels of IL-6, IL-8, and IL-10 than non-ARF patients. Moderate discriminative power in predicting survival was observed for day 2 IL-6 and IL-10 plasma levels (AUCs 0.703 and 0.749, respectively). However, in our opinion, these AUCs are insufficiently high to be of clinical significance.

CONCLUSION. Our results do not support the use of HLA-DR expression or cytokine plasma levels in predicting survival of ARF patients.

REFERENCE(S). 1. Goes N et al. 1995 Transplantation Feb 27; 59 (4): 565-572
2. Lemay S et al. 2000 Transplantation 69; 5: 959-963
3. Van den Berk JM et al. 1997 Transplantation 63: 1846-1848
4. Allen ML et al. 2002 Crit Care Med 30: 1140-1145

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CORRECT POSITIONING OF NEP DEVICE TO ASSESS EFL DURING ASSISTED MECHANICAL VENTILATION

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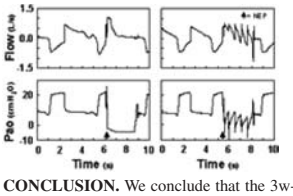
INTRODUCTION. Negative expiratory pressure (NEP) has been used to estimate expiratory flow limitation (EFL) in mechanically ventilated patients. Given that triggering systems could interfere with NEP manoeuvre if the 3-way valve (3w-v) of the NEP device is positioned on the expiratory limb of the ventilator circuit as usual (AJRCCM 1994;150:1311-1317),we hypothesized that the placement of the 3w-v at the Y-piece might avoid triggering related artifacts.

METHODS. To test this hypothesis we assessed NEP in 8 mechanically ventilated patients (age 74+/-6) under the following conditions: 1) controlled mechanical ventilation (CMV) and 2) pressure support ventilation (PSV). In both conditions the 3w-v was placed either on the expiratory limb of the ventilator (CMVE and PSVE respectively) or between the Y-piece and the orotracheal tube (CMVY and PSVY respectively).

RESULTS. In all the patients NEP was successfully maintained through the expiration at a level of -5 cmH_2O in CMVE, CMVY and PSVY (left panel) conditions. By contrast, during PSVE condition (right panel) the ventilator repeatedly switched to inspiration, making EFL assessment impossible.



CONCLUSION. We conclude that the 3w-v must be positioned between the airway opening and the Y-piece to obtain reliable EFL measurement.
Grant acknowledgement: Sensor Medics,Italy

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ASSESSMENT OF SEDATION LEVEL IN POST CARDIAC SURGICAL PATIENTS

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INTRODUCTION. Assessment of the sedation level in the ICU is a continuous challenge and relevant for ICU outcome. The aim of this study was to examine whether neuromonitors could be used as objective methods to guide the sedation regimen in the ICU.

METHODS. The study was approved by the local ethics committee and data was collected from 40 patients after elective coronary artery bypass grafting surgery on arrival to the ICU. Patients were divided into 2 groups. Group P received Placebo (NaCl 0.9%) and group C received clonidine. In addition all patients received propofol and morphine as required to achieve standardized Ramsay sedation scale (RSS) and visual analogue scale (VAS)levels. All patients were monitored simultaneously with Bispectral index (BIS A-2000, Aspect Medical Systems, Na. MA)and Auditory Evoked Potentials (AAI-Monitor, ver. 1.4, Danmeter, Denmark). AAI, BIS and Ramsay Sedation Score (RSS) were collected every 10 minutes in the first hour and subsequently every hour until 6 hours after extubation. AAI and BIS were compared to RSS using the prediction probability (Pk) analysis.

RESULTS. Basic patient characteristics did not differ between groups. There was no significant difference between the performance of AAI and BIS nor between VAS levels in both groups.

Prediction performance (Pk) in the two groups.

Group	Indicator	Pk	SE
P	AAI	0.75	0.02
	BIS	0.83	0.02
C	AAI	0.85	0.02
	BIS	0.82	0.02

CONCLUSION. Both AAI and BIS correlated well to the clinical assessment of the sedation level in the ICU. Continuous assessment of the sedation level may be beneficial in avoiding over- and under-sedation for ICU patients.

REFERENCE(S). 1. BMJ 1974; 22:656-659
2. ICM 1998; 24:1294-1298
3. NEJM 2000; 18; 342:1471-1477
Grant acknowledgement: Boehringer-Ingelheim

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USE OF THE IMAGYN PRO2 REFLECTANCE PULSE OXIMETER IN THE PICU ON CYANOTIC YOUNG CHILDREN

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INTRODUCTION. We tested a pre-release version of a reflectance pulse oximeter (PRO2) from Imagyn Medical Technologies (Irvine, CA, USA). The distinctive sensor design (3 low output central light sources encircled by 2 detector rings), results in a sensor usable on a flat skin surface with a signal capture area much larger than a transmittance sensor. The sensor is held to the skin by hydrogel. Potential advantages in paediatrics include: use of central body sites, sensitivity in low perfusion, reduced risk of adhesive and thermal injury and accuracy from low to high SpO2 values.

METHODS. 20 young children (age 3.7 ± 4.4 mos, [1 day to 16 mos]), representing 5 races and various skin colour but all with cyanotic cardiac disease were studied (9f/11m, wt. 4.57 ± 1.97 kg [2.5 to 9.8 kg]). Entry criteria were ECG for heart rate, pulse oximetry via a transmission sensor and an arterial line for blood specimens. The PRO2 pulse rate (PR) values were referenced to ECG heart rate (HP Merlin, Philips, Boeblingen, Germany) and the SpO2 values to functional SaO2 (ABL 725, Radiometer, Brønshøj, Denmark). A computer sampling at 1 Hz captured all monitoring data. The values for PRO2 bias (or mean error) and precision (or standard deviation of the error) were derived.

RESULTS. 144 datasets of SaO2 (47 to 91%) and heart rate (71 to 188 bpm) were gathered. The PRO2 bias and precision were +0.9 ± 3.2 for PR and +8.1 ± 3.9 for SpO2. PRO2 sensor sites included: abdomen, axilla, back, chest, flank and thigh. Waveform and digital display quality was excellent regardless of sensor positioning in those paralysed but the best signal with activity was with the sensor dependent, usually on the lower back. The range of mean arterial pressure was broad (47 ± 12 mmHg [22 to 82 mmHg]) and when low caused loss of transmission SpO2 signals but the Imagyn monitor was unaffected. No evidence of injury or irritation at the PRO2 sensor sites was found.

CONCLUSION. A pre-release version of the PRO2 reflectance pulse oximeter was tested without adverse effects on 20 children with cardiac disease in the PICU. PR values were highly accurate and SpO2 values exhibited a linear positive bias, which should be readily correctable. Central positioning of the reflectance sensor was very effective, particularly in those with low arterial pressure. We easily obtained reliable information over a wide range of skin pigmentation, blood pressure, heart rate, oxygen saturation and sensor sites.

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PULMONARY ARTERY CATHETER AND MORTALITY IN SHOCK CAUSED BY ACUTE MYOCARDIAL INFARCTION

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INTRODUCTION. There are important controversies about the use of pulmonary artery catheter (PAC) in ICU patients (1). Our objective is to analyse the influence of PAC insertion in mortality of patients with acute myocardial infarction (AMI) developing shock.

METHODS. Among 12,071 episodes of AMI recruited between 1995-2000 in the Proyecto de Registro de Infarto Agúdo de Miocardio de Valencia, Alicante y Castellón (PRIMVAC) (2), 11.2% developed shock defined as Killip IV. We analyse the mortality of this subgroup of patients according to the use, or not, of PAC. The statistical methods were chi squared; Student t test and logistic regression for confounders adjust. Results are showed as relative risk (RR) and p values. S-Plus statistical packet was used.

RESULTS. A total of 24.1% of the patients with shock were monitored with PAC and showed a lower age and a higher number of procedures (echocardiography, pacemaker insertion, coronariography, angioplasty and cardiac surgery) than the patients without PAC. Mortality in the group with PAC was 67.4% vs. 78.1% in the patients without PAC (RR: 0.86; p<0.001). After adjusting for age, sex, coronary risk factors, prior AMI, Q wave on electrocardiogram, trombolysis and hospital level (with or without facilities for haemodynamics), the use of PAC showed a RR of 0.64 (p=0.003).

CONCLUSION. In our population the use of PAC in patients with AMI and shock is associated with a lower mortality.

REFERENCE(S). 1)Vincent JL, Dhainaut JF, Perret C, Suter P. Is the pulmonary artery catheter misused? A European view. Crit Care Med 1998 Jul; 26(7):1283-7
2) Cabadés A, Echanove I, Cebrián J, Cardona J, Valls F, Parra V et al. Caracteristicas, tratamiento y pronostico del infarto agudo de miocardio en la Comunidad Valenciana en 1995: resultados del registro PRIMVAC. Rev Esp Cardiol. 1999 Feb; 52(2):123-33

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PRAM: A NON-INVASIVE METHOD TO MONITOR CARDIAC OUTPUT FROM ARTERIAL PRESSURE DURING CARDIAC SURGERY

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INTRODUCTION. A new method has been introduced that measures CO by arterial pressure (Pressure Recording Analytical Method [PRAM]) and without calibration by thermodilution (ThD) [1]. PRAM is based on the mathematical analysis of changes of arterial pressure profile with time. It allows beat-by-beat stroke volume (SV) assessment from the pressure signals recorded in femoral (PRAM-fem), or radial (PRAM-rad) arteries [1]. CO is obtained by SV and heart rate. A dedicated software program has been used for the continuous on-line reading of the arterial pressure profile.

METHODS. In 15 patients undergoing aortic valve replacement CO was measured before induction of anaesthesia (T1), after induction (T2), at the end of cardiopulmonary bypass (T3), at the end of surgery (T4) by ThD and PRAM-rad. CO (L/min) values obtained at the same time of the ThD dilution curve (180 paired data) were used for the comparison by linear correlation and Bland-Altman analyses.

RESULTS. See Table

Table shows the CO values evaluated at the various times of the study.

CO values	T1	T2	T3	T4
ThD (L/min) (mean ± SD)	4.5 ± 0.8	3.8 ± 0.7	3.7 ± 1.0	4.3 ± 0.9
PRAM-rad (L/min) (mean ± SD)	4.3 ± 0.6	3.7 ± 0.7	3.8 ± 0.8	4.2 ± 0.5
ThD vs PRAM-rad R (Pearson), p value	0.83, < 0.01	0.82, < 0.01	0.81, < 0.01	0.88, < 0.001

ThD, thermodilution; PRAM-rad, PRAM-radial pressure; SD, standard deviation.

CONCLUSION. In this small series of cardiac surgery patients, PRAM measurements remain reliable in any established interval of the study. PRAM allows to monitor continuously CO during cardiac surgery and offers a non-invasive approach for perioperative cardiac output monitoring.

REFERENCE(S). 1- Romano SM, Pistolesi M: Assessment of cardiac output from systemic arterial pressure in humans. Crit Care Med 2002; 30:1-8

Oral Presentations
Assessment of cost effectiveness – 522-526

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COST ASSESSMENT OF 21 INTENSIVE CARE UNITS IN THE PARIS AREA

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INTRODUCTION. The aim of the study was to evaluate if the cost blocks method (1) can reliably be used in France. This top down method has been used worldwide recently for the SAPS 3 project but the results have not yet be published. The present study is part of a retrospective multi-centre assessment of medico-economic performance of French ICUs.

METHODS. The point of view was the ICU one. A new cost questionnaire was developed by a group of French financial directors. The costs considered were the sum of the first cost block (capital equipment) and the last three ones (clinical support services, consumables and staff). The total costs were direct medical costs, excluding estates and non clinical support services as suggested by the UK working group (1).

RESULTS. 21 out of 26 ICUs (13 University hospitals, 6 general hospitals, 2 private hospitals) responded. Staff costs accounted for 62.4%, consumables for 17.3%, laboratory services for 17.8% and capital equipment for 2.5%. The answers were very variable and the staff salary taxes had often to be estimated. Existence of a High Dependency Unit (HDU) led to difficult problems.

Total direct medical costs in Euros

	ICU per year	Per patient day	Per ICU stay	Per bed per day
Mean	3,665,885	985	5,990	702
1 SD	1,109,126	257	2,740	179
minimum	1,912,812	670	3,627	481
maximum	6,425,362	1537	12,599	1,114

CONCLUSION. The values of French ICUs costs were much lower than that of UK. The data were also variable even for costs per bed per patient day or per admission. It could be due to local differences. Before using cost blocks method routinely, it needs a better definition of costs.

REFERENCE(S). D.Edbrooke et al: Anaesthesia, 1999, 54, p. 110-120.
Grant acknowledgement: PHRC AOM 98-184

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PROVISION OF CRITICAL CARE IN LARGER UNITS IMPROVES COST EFFECTIVENESS OF NURSE STAFFING.

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INTRODUCTION. In December 2002 our Trust commissioned a 21 bedded critical care facility by combining the nursing workforces from two 6-bedded units. The economic argument for this development was based on the ability to staff more beds with the same workforce in a larger facility. Increased capacity was predicted from reducing from 1 supernumerary on each unit to 1 supernumerary nurse for the whole new unit. It was also envisaged there would be increased ability to co-locate high dependency patients, facilitating 1:2 nurse to patient ratios. The estimate of the provision of 1 additional ICU bed and 0.5 HDU bed (respectively) allowed revenue savings of € 310k to be predicted, making a capital investment of € 1.1M viable even for a building with a 6 year life expectancy. The Trust runs a similar critical care unit on its other hospital site which was used as a control in this study.

METHODS. Data were collected on bed days delivered, occupancy and nursing pay spend, for 6 months pre and 3 months post amalgamation. An established unit similar to the amalgamated study unit was used as a control.

RESULTS. There was no significant difference in occupancy which remained between 92% and 95% on both units pre and post amalgamation. Other results are tabulated below as monthly mean (sem), significant differences post amalgamation (Mann-Whitney - Statview) are marked *. All data is mathematically adjusted for length of month and is presented as standard 30 day months.

	Bed days Pre	Bed days post	Nurse spend pre	Nurse spend post
Study unit	324 (14)	385* (25)	€ 195,413 (2889)	€ 205,153 (6422)
Control unit	359 (16)	339 (39)	€ 198,148 (4051)	€ 205,936 (9471)

CONCLUSION. An average of 61 bed days per month has been delivered post amalgamation without a significant increase in nursing costs. The trend to increase in nursing costs we believe to be seasonal, as suggested by a similar increase on the control site. The data demonstrate that a single facility can deliver significantly more cost effective and staff efficient care. While more work would be required to define the optimal size of a critical care unit these data should be taken into account when planning critical care services.

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CAN PRICE INFORMATION ON LABORATORY TEST ORDERING REDUCE COST IN INTENSIVE CARE UNIT?

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INTRODUCTION. The high costs of acute health care have risen over the last years. Some authors proposed a written guideline implementation to reduce the laboratory testing costs in Intensive Care Unit (ICU)[1]. The aim of our study was to asses whether daily information on the price of common laboratory tests can decrease the costs by influencing the number of tests ordered by the treating physician [2].

METHODS. The study was performed in a mixed ICU of a University Hospital during a period of 12 months: July-December 2001, July-December 2002. During the first 6 months, laboratory tests were ordered without any guideline and this time period served as a control. During the second 6 months the price of laboratory tests was added in front of each test on the form. The number of tests ordered and price during the two periods were compared. Tests were only prescribed by treating physicians, which was blinded to the study protocol.

RESULTS. A total of 380 patients were included; 182 patients in the first 6 months and 198 in the second 6 months. Severity scores SAPS II and APACHE II were not statistically different between the two groups and the patients were comparable in terms of sex, length of ICU stay, days of mechanical ventilation and reasons of ICU admission. The analysis of price in Euro showed a 6.5 % reduction between the two periods (table 1)

July-December	Laboratory test (Number)	Price (Euro)
2001	33580	73275,87
2002	29392	68551,53

CONCLUSION. Price information was associated with a decrease in the number of tests ordering by physicians and with a significant cost saving without negative effects on quality of care as shown by similar mortality and length of stay in ICU.

REFERENCE(S). 1. Seguin P, Bleichner JP, Grolier J, Guillon YM, Mallédant Y. Effects of price information on test ordering in an intensive care unit. Intensive Care Med 2002; 28:332-335
2. Civetta JM, Hudson-Civetta JA. Maintaining quality of care while reducing charges in the ICU. Ten ways. Ann Surg 1985 202:524-532

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EFFECTIVENESS AND EFFICIENCY OF TREATMENT IN GIVITI INTENSIVE CARE UNITS (ICUS)

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INTRODUCTION. We studied effectiveness and efficiency of ICU variable costs (CEA) per pathology and level of care.

METHODS. In 44 general ICUs we recorded patient (pt) admission diagnosis, daily level of treatment (high-HLT/monitoring-LT) (Iapichino: Intensive Care Med 2001), ICU length of stay (LOS), hospital outcome (effectiveness). We computed admission/following days daily variable cost, ICU cost, efficiency of treatment (ratio between mean cost for hospital alive pts and for all pts), cost for saved life and for dead pt (mean±95%CI).

RESULTS. In 570 pts ICU LOS was shorter for hospital dead pts than survivors only in Head Trauma (HT) (4.6±1.8 vs 10.7±1.8 days), Intracranial Haemorrhage (IH) (7.9±2.1 vs 11.5±2.2 days), Stroke (ST) (2.9±2.3 vs 8.6±5.6 days). First day cost varies from 885±152 ¤ for Trauma (TR) to 241±55 ¤ for ST, is different among pathologies ($p<0.001$) and is greater than mean cost of the following days for all pathologies ($p<0.01$) except Abdominal Surgery (AS) and Coronary Bypass (CB). Mean cost for the following days is different among pathologies as well ($p<0.001$). Variable ICU cost varies from 4,423±675 (TR) to 505±173 ¤ (CB) and differs among diagnoses ($p=0.000$, Sheffé for linear contrasts). Mean cost is lower for dead pts than survivors in HT (1,877±618 vs 3.225±665 ¤) and IH (2,026±592 vs 3,106±849 ¤) and greater in COPD (2,467±653 vs 1,649±347 ¤) ($p<0.05$). Mean daily cost is greater for dead pts than survivors in TR (507±172 vs 369±47 ¤), HT (645±314 vs 312±38 ¤), COPD (257±75 vs 177±22 ¤), ALI/ARDS (468±208 vs 277±53 ¤), Heart Failure (HF) (310±102 vs 201±40 ¤) and AS-SS (883±8,348 vs 268±47 ¤) ($p<0.05$). Medians of diagnosis mean variable costs (1,884 ¤) and of diagnosis mean efficiencies (62.9%) select 4 groups: low cost and efficiency (ST, HF, COPD), high cost and low efficiency (IH, AS-SU, ALI/ARDS), high cost and efficiency (HT, TR), low cost and high efficiency (CB, AS-SS, LT pts). Cost for saved life lowers from AS-SU (5,906 ¤) to ALI/ARDS, TR, IH, HT, ST, COPD, HF, LT pts, AS-SS, CB (517 ¤). Cost for dead pt lowers from AS-SU (1,633 ¤) to ALI/ARDS, IH, TR, COPD, HF, ST, HT, LT pts, AS-SS, CB (38 ¤).

CONCLUSION. CEA points out high and low cost & efficiency classes of pts, and suggests the best way to improve effectiveness/efficiency for each class. Moreover ICU variable costs depend on case-mix.

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EXTRA CHARGES AND PROLONGATION OF STAY ATTRIBUTABLE TO ICU INFECTIONS

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INTRODUCTION. Infections are a significant factor on the course and prognosis of the ICU patients. They are responsible for the increase of stay in the ICU and impose a huge economic burden. The objective of the study was the estimate of the socioeconomic impact of nosocomial infections in ICU patients: morbidity, mortality and costs of antibiotics.

METHODS. We performed in 205 ICU patients, admitted in a five months period, a pairwise-matched (1:1) case control study. ICU patients with nosocomial infection were designated as "cases" and those without infection as "controls". Matching variables were primary diagnosis for admission, age and length of stay before the day of onset of the first infection in cases, 70 matched case-control pairs were studied.

RESULTS. The results of this study showed that the crude mortality rates in cases and controls were 38,2% and 32,4% respectively. Thus, the estimated attributable mortality rate was 5,8%. The median length of ICU stay significantly differed between cases and controls (20,5 vs 12 days respectively, $p \geq 0{,}000$). Thus, extra length of stay attributable to nosocomial infection was 8,5 days. The daily cost per patient was 187,82 €. Thus, extra costs due to increase of stay in the ICU attributable to the nosocomial infection were (8,5 days x 187,82 €) 1.596,47 € per survivor.

CONCLUSION. The attributable mortality to the nosocomial infection was high. The infection is associated with a significant excess length of stay and a significant economic burden.

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REGIONAL DIFFERENCES IN BRAIN TISSUE SUSCEPTIBILITY TO SECONDARY DAMAGE AFTER TBI

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INTRODUCTION. The treatment of patients with Traumatic Brain Injury (TBI) is relying on the monitoring of global parameters such as ICP and CPP. CT is the only technique that routinely provides us with an understanding of the extent and severity of regional damage. However, none of these techniques provide information of differences in regional energy metabolism and sensitivity to secondary insults during the course of intensive care. Two new techniques for monitoring regional metabolism of the traumatized brain are now available: Tissue pO2 probes monitoring the regional availability of oxygen and Microdialysis catheters monitoring the regional availability of glucose and the effect of ischemia on local brain biochemistry. This is an account of 50 patients studied with gold tip microdialysis catheters visible on CT.

METHODS. Microdialysis catheters (CMA70) were routinely implanted in all patients with severe traumatic brain injury (GCS >9). The catheter was inserted into cerebral cortex via a separate burr hole in front of the ICP catheter ("better" position). In patients with focal brain lesions catheters were inserted into the "penumbra" defined as a region about 1 cm from the border of the lesion. Samples were analysed every hour on a bedside analyzer. The Lund University ethical committee has approved of the use of intracerebral microdialysis as a routine procedure.

RESULTS. The pathology of brain tissue was evaluated by analyzing the lactate/pyruvate ratio (ischemia, redox state) and glycerol (cell membrane degradation) in the dialysate. Our results show a pronounced difference in the sensitivity of brain tissue in the "better" as compared to the penumbra position. Changes in e.g. CPP, ICP, hematocrit and periods of seizures that had no effect on brain chemistry in the "better" position had severe pathological effects on lactate/pyruvate ratio and glycerol levels in the penumbra.

CONCLUSION. Our results demonstrate a great heterogeneity in the pathology of brain tissue after TBI. Relatively small changes in e.g. CPP may have profound effects on the vulnerable penumbra tissue. We conclude that local monitoring of strategic positions in the brain of TBI patients gives an early warning of imminent secondary damage and helps the clinician to individualize the treatment of the patient.
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Oral Presentations
Experimental aspects of severe injury – 527-531

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THE EFFECT OF FIBRINOGEN ON DILUTIONAL COAGULOPATHY - A PORCINE MODEL

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INTRODUCTION. Synthetic colloids and crystalloids are usually administered to treat hypovolaemia in severely injured patients. There is no doubt that appropriate fluid management influences final outcome of bleeding patients. However, colloids are well known to impair haemostasis, which is also crucial in these patients. Reduced clot weight and elasticity as well as impaired fibrinogen polymerisation have been reported after gelatine administration. This study was conducted to determine whether fibrinogen substitution is useful to restore haemostasis after administration of high volumes of gelatine.

METHODS. Anaesthetised pigs (n=14) were cannulated for blood sampling and haemodynamic monitoring. About 65% of the estimated blood volume was withdrawn and replaced with gelatine at a ratio of 1:1.4. After dilution, animals were randomised to receive either fibrinogen (group 1, n=7) or placebo (group 2, n=7) and the liver was subsequently injured to induce uncontrolled haemorrhaging. Thrombelastographic measurements using ROTEG (Pentapharm, Germany), measurement of blood loss as well as scanning electron microscopy (SEM) of blood clots were performed. For SEM clots were conventionally fixed and analysed. Statistics: A repeated measures ANOVA.

RESULTS. Subsequent to gelatine infusion, increased clotting times (CT) and clot formation times (CFT) were observed in the ROTEG® analysis, while the decrease in maximum clot firmness (MCF) and alpha-angle was statistically significant in both groups. After administration of fibrinogen (250mg/kg) in group 1, CFT decreased and MCF as well as alpha-angle increased significantly, achieving values similar to baseline measurements. Blood loss after liver injury was significantly less in group 1 (2.542ml +667 ml) as compared to control group 2 (3.578ml +455 ml). SEM showed a reduced reticular network, and fibrin strands appeared thinner after dilution as compared with clots after fibrinogen administration. Further, the fibrinogen-treated animals showed a trend to longer survival following liver trauma.

CONCLUSION. We conclude that fibrinogen substitution is able to compensate the consequences of dilutional coagulopathy to a certain degree.
Grant acknowledgement: The study was kindly supported by Aventis Behring, Germany

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GLIAL AND NEURONAL PROTEINS IN SERUM PREDICT OUTCOME AFTER SEVERE TRAUMATIC BRAIN INJURY.

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INTRODUCTION. To evaluate if glial (GFAP, S100b) and neuronal (NSE) proteins in peripheral blood predict neurological outcome after severe traumatic brain injury.

METHODS. In patients with severe traumatic brain injury (admission Glasgow Coma Score (GCS) < of = 8) blood samples taken at the time of hospital admission were analyzed for S100b, GFAP and NSE. Outcome was assessed using the Glasgow Outcome Scale (GOS) at 6 months.

RESULTS. In 85 patients median serum S100b, NSE and GFAP concentrations at the time of hospital admission were raised 17.5, 2.5 and 4.5 fold respectively. Serum NSE, GFAP and S100b levels were significantly higher in patients who died or had a poor outcome. A serum S100b level > 1.13 mug/l was the strongest predictor of death. Higher odds ratios were found for NSE and GFAP compared to the clinical parameters in the prediction of poor outcome. The sensitivity of brain specific proteins in predicting poor outcome were similar for NSE, S100b and GFAP (0.80, 0.88 and 0.80). The negative predictive values were between 0.73- 0.79. After multivariate adjustment S100b, NSE and GFAP strongly predicted outcome (odds ratios for death 6.38 and 5.29 respectively and for poor outcome 7.42, 4.18 and 3.65 respectively).

CONCLUSION. Determination of serum levels of astroglial and neuronal proteins in peripheral blood may add in the assessment of the primary damage and prediction of outcome after severe traumatic brain injury.

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ENDOTHELIAL OXIDATIVE STRESS IS CORRELATED WITH HEMORRHAGIC SHOCK SEVERITY IN TRAUMA PATIENTS.

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INTRODUCTION. Hemorrhagic shock in trauma patients increases endothelial oxidative stress [1]. The aim of this study was to assess if correlation between reactive oxygen species (ROS) production and hemorrhagic shock severity exists.

METHODS. This study was approved by institutional ethic committee. ROS production by perfused human umbilical vein endothelial cells (HUVEC) was studied by fluorescent microscopy [2] by using 2'7' Dichloro-dihydrofluorescein diacetate (DCFH) probe. Serum samples were collected from patients in hemorrhagic shock within the first 24 h after recovery . Endothelial cells were exposed to serum during 30 minutes. SAPS II, ISS, fluid therapy replacement, number of red packed blood cells transfused and highest rate of norepinephrine within the first hours were analysed. The worst clinical (FC, PAM, GCS, Temperature), and biological values (pH, lactate, P/F ratio, PaCO2, Bicarbonates, natremia, protidemia, calcemia, hemoglobin, leucocytemia) were recorded. Regression between DCFH fluorescence intensity and studied parameters were performed. In order to consider variation induced by hemodilution, DCFH fluorescence was normalized by protidemia. Results are expressed as mean ± SD.

RESULTS. 7 patients were studied. SAPS II 43 ± 25, ISS 41 ± 17, Hb 6.9 ± 2.2 g/dL, lactate 6.0 ± 3.7 mmol/L, pH 7.1 ± 0.1, bicarbonates 17.5 ± 3.3 mmol/L, calcemia 1.48 ± 0.09 mmol/L. Norepinephrine infusion rate was 2.8 ± 1.7 mg/h. SAPS II ($r2 = 0.85$; $p = 0.009$), norepinephrine infusion ($r2 = 0.95$; $p = 0.0009$) and lactate ($r2 = 0.67$; $p = 0.045$) was significantly correlated with ROS production. Hemoglobin ($r2 = 0.87$; $p = 0.007$), calcemia ($r2 = 0.72$; $p = 0.03$), bicarbonates ($r2 = 0.85$; $p = 0.009$) and pH ($r2 = 0.69$; $p = 0.03$) was inversly correlated with endothelial oxidative stress induced by trauma patients serum.

CONCLUSION. Serum of trauma patient with hemorrhagic shock induces an in vitro endothelial oxidative stress. This ROS production is correlated with shock severity.

REFERENCE(S). [1] Intensive Care Med 2002 ; 28 (Suppl1): S35
[2] Am J Respir Cell Mol Biol 2001 ; 24 : 762-768

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CEREBROSPINAL FLUID OF SUBARACHNOID HAEMORRHAGE PATIENTS UPREGULATES MONOCYTE HLA-DR EXPRESSION

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INTRODUCTION. Brain controls peripheral inflammation such as cytokine release in blood and modification in cell function by different pathways (1, 2). Subarachnoid aneurismal haemorrhage (SAH) creates brain injury with blood cells erupting in cerebrospinal fluid (CSF). Hypothesis: blood monocytes in CSF may acquire different phenotype for HLA-DR expression than circulating blood monocytes.

METHODS. After Ethical Committee approval, 7 females patients, Fishers grade III-IV, were enrolled within 24 hours after bleeding. An external ventricular drainage for hydrocephalus permitted blood and CSF paired sampling for: a) monocyte HLA-DR expression (AB/C) by flow cytometry, b) IL-10, IL-12, IL-6, TNF-alpha and MIF by ELISA and c) NOx by colorimetric assay. Blood parameters were compared to sex- at aged-matched controls.

RESULTS. Expressed as median (interquartile range).
[1] $p<0.02$ [2] $p<0.05$ vs patient blood, [3] $p<0.02$ vs control blood, § $p<0.05$ vs control CSF, non parametric test.
Plasma and CSF IL-10, and MIF levels did not differ in SAH patients nor compared to controls. IL-12 was not detected in plasma or CSF.

	CSF	BLOOD	CONTROL CSF	CONTROL BLOOD
HLA-DR (AB/C)	33982 (23666)[1]	9118 (2875)[3]		20832 (6282)
NOx (muM)	15.2 (6.3)[2]	19.9 (9.1)	6.36 (3)	25.2 (3.5)
IL-6 (pg/ml)	735 (982.25)[4]	16.9 (26.75)[3]	32 (13.5)	5 (0)
TNF-alpha (pg/ml)	149.3 (41.42)[1]	41.8 (16.52)	187.6 (17.45)	29.8 (4.45)

CONCLUSION. In SAH, monocyte HLA-DR expression in blood is downregulated whereas upregulated in CSF with elevated NOx and pro-inflammatory mediators. The mechanisms of CSF-induced HLA-DR expression need further investigations.

REFERENCE(S). 1)Tracey K, Nature, 420: 853-859, 2002; 2)Woiciechowsky C et al., J Mol Med, 77 (11):769-780, 1999.

Oral Presentations
Endocrinology – 532-534

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VENTILATION WITH PEEP ACTIVATES THE ACTH / CORTISOL-AXIS: EFFECTS OF EXTENDED SYMPATHICOLYSIS

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INTRODUCTION. PEEP may activate the endogenous stress-response system (SRS),e.g. by PEEP-induced impairment of haemodynamics[1].The SRS comprises of two major components, i.e. the adreno-cortical axis (mediated by ACTH/cortisol) and the sympatho-adrenomedullar system (mediated via spinal sympathetic fibres),both with complex amplifying and inhibiting interaction[2].It is unclear,if PEEP activates the ACTH/cortisol-axis and further, if inhibition of the alternative SRS, i.e. sympatho-adreno-medullar system, modifies a putative ACTH/cortisol response.

METHODS. Healthy dogs (permission of district government) were anaesthetised and mechanically ventilated. Intervention: Ventilation with zero end-expiratory pressure (ZEEP), followed by moderate PEEP ($10cmH_2O$, 15min), and again ZEEP. This protocol was randomly performed either in dogs with intact sympathetic nervous system (n=6, controls) or after inhibition of the sympatho-adrenomedullar system (n=6, extended epidural anaesthesia (lidocain), sympathicolysis verified).Plasma ACTH and cortisol were measured at the end of each intervention. Statistics:t-test, $p<0.05$. Means±SEM.

RESULTS. In the controls PEEP doubled cortisol from 56±14 to 110±16 ng/ml within 15min (correlation between ACTH and cortisol, r=0.65),whereas after PEEP-release cortisol returned to 83±19ng/ml.MAP was maintained during PEEP(64±2 vs 65±3 mmHg).Sympatholysis per se (epidural anaesthesia) did not increase cortisol,despite significant drop in MAP(from 66±2 to 60±3mmHg).During sympathicolysis, PEEP again doubled cortisol from 71±27 to 147±21ng/ml,and after PEEP-release cortisol decreased to 118±20ng/ml. In this group, PEEP significantly depressed MAP(52±4 vs 65±3mmHg in controls).

CONCLUSION. We demonstrated that PEEP reversibly activates the ACTH / cortisol-axis, indicating an endogenous stress-response. Interestingly, abolition of the alternative SRS (sympathetic nervous system) did not evoke a compensatory overshoot of ACTH/cortisol, but only maintained the „physiologic" increase in cortisol during PEEP (i.e. doubled cortisol levels).This finding surprises in view of the aggravated depression of MAP by PEEP during sympathicolysis, since hypotension appears a potent trigger of ACTH/cortisol [2].

REFERENCE(S). [1]Scheeren TWL et al.(2002) Crit Care Med 30:881-7 [2]Crozier TA(1995) in:Anaesthesiologie. Springer,Berlin Heidelberg,1186-1222

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LOW DOSE CORTICOTOPHIN TEST FOR ADRENAL FAILURE DIAGNOSIS IN ICU

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INTRODUCTION. Adrenal-axis dysfunction is acquiring evidence in sepsis due to higher mortality and multiple organ failure when it is present. Conventional (249 mug) corticotrophin test(CCT) has been greatly criticized since it underestimates this diagnosis. Low-dose(01 mug) corticotrophin test(LCT) has been suggested as a way to solve this problem. We compare the adrenal failure incidence using both low-dose and conventional corticotrophin test

METHODS. Prospective study in the 10-bed ICU at a tertiary hospital from may 2002 to March 2003.Patients admitted with septic shock, dependent on norepinephrine for more than 48h were selected for blood basal, post-LCT(60 min) and post-CCT (120 min) cortisol dosages and then classified as having primary or secondary adrenal failure, ACTH peripheral resistance or normal response(1).Adrenal failure (AF) was defined as cotisol < 25 mug/dl in the basal state or after corticotrophin test. Demographic data, APACHE II, admission diagnosis (clinical, surgical),the highest SOFA score during the first 28 days in ICU and mortality rate (MR) were matched with adrenal response. Values are expressed as mean +/-SD. Data analysis was performed on EPIINFO(version6).$p<0.05$ was considered significant

RESULTS. Fifty-two patients were enrolled but 3 excluded(without APACHE II),27 (55.1%) female. APACHE II was 16.86 +/- 4.5 (8-26) and the highest SOFA score during first 28 days in ICU 9.36 +/- 3.77.There were no differences in APACHE II, the highest SOFA score or admission diagnosis between the groups. AF was detected in 73.5% (36/49),with 4.0%(2/49)primary AF, 51%(25/49) secondary AF and 18.3% (9/49) ACTH-PR.LCT detected 22.4% (11/49)of AF compared with 4% (2/49) CCT. Corticosteroids were replaced in 36.1% (13/36) with 23% (3/13) MR. Overall and AF mortalities were 26.5% (13/49) and 22.2% (8/36), respectively. Mortality rate was lower in the ACTH-PR (11.1% - 1/9) than other AF groups(primary AF 50%-1/2 and secondary AF 24%-6/25, p=0.21) but not statistically significant.

CONCLUSION. Adrenal failure is a common entity in critically ill patients with frequency varying according to established criteria. CCT can underestimate AF diagnosis, but its clinical significance is not defined yet. There were no statistically significant differences between the groups, probably due to no uniform corticosteroids replacement

REFERENCE(S). 1) Marik PE and Zaloga GP (2002)Adrenal insufficiency in the critically ill.A new look at an old problem.CHEST 122:1784-1796.

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BRAIN NATRIURETIC PEPTIDE IN ACUTE BRAIN DISEASE – WHERE IS ITS ORIGIN?

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INTRODUCTION. Brain natriuretic peptide (BNP) was first isolated in the brain, although now it is presumed that its main production is in the heart. Its significance in acute brain disease so far remains unclear.

METHODS. We retrospectively analysed 103 blood samples for N terminal fragment pro brain natriuretic peptide (NT-proBNP) from 30 patients hospitalised at our ICU from February until May 2002. 29 patients had acute brain disease (subarachnoid hemorrhage (SAH) 9, intracerebral hemorrhage 5, tumor 9 and others 6) and 1 patient had spine disease. Patients were classified as NYHA I (n=21), NYHA II (n=8), NYHA III (n=1). Their age was between 23 and 81 years (mean age 57 years). We investigated NT-proBNP, serum osmolality (S_osm) and sodium (S_Na+) on day 1, S_osm, S_ Na+, daily urinary loss of sodium (dU_Na+), creatinine clearance (C_krea), diuresis, intake of fluids and sodium in 24 hours on day 2. Upper reference range for NT-proBNP is 150 pg/l.

RESULTS. NT-proBNP was significantly elevated in all patients. The mean value of NT-proBNP was in patients with NYHA I 999 +/- 1496 pg/l (p=0.005) and 321 +/- 244 pg/l (p=0.007) in patients with NYHA I - III. NT-proBNP correlated with S_osm on both days and with S_Na+ on day 2, but only in patients with NYHA I – III. In patients with NYHA I NT-proBNP did not correlate with other parameters measured.

CONCLUSION. In our retrospective study we found significant elevation of NT-proBNP in all patients with acute brain disease without sodium disbalance, but higher values were in patients with NYHA I -III than with NYHA I. We presume that the elevated value of BNP in acute brain disease partially originates from the brain.

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TLR 4 INDEPENDET MYOCARDIAL REGULATION OF MMPS AND TIMPS FOLLOWING LPS APPLICATION

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INTRODUCTION. Changes in the expression of myocardial Matrix Metalloproteinases (MMPs) and Tissue Inhibitors of MMPs (TIMPs) have been demonstrated in septical cardiomyopathy, a potentially fatal complication of septic shock. The precise mechanisms that cause changes in the expression of MMPs and TIMPs during a Gram-negative sepsis remain elusive. Previous studies from our laboratory and others have shown that in an in vivo sepsis model the signal transduction of Lipopolysaccharide (LPS) in the myocardium is Toll Like Receptor 4 (TLR4) dependent. However the significance of TLR4 for MMP and TIMP expression following LPS application is not known. Therefore the purpose of this study was to elucidate whether changes in MMP and TIMP expression following LPS application are TLR4 dependent.

METHODS. MMP (-1, -2, -3, -8, -9) and TIMP (1-4) gene expression were determined with an RNase Protection Assay in C3H/HeJ (TLR4-defiecient, TLR4-D) and in C3H/HeN mice (control) following 6 hrs. of intraperitoneal (i.p.) LPS- (20mg/kg) or PBS (control) application. Protein levels were determined with western blot and MMP activity was determined with zymography.

RESULTS. Following 6 hrs of i.p. PBS application gene expression of MMP-2, TIMP-2 and TIMP-3 were detectable, however following 6 hrs. of i.p. LPS application there were significant changes in gene expression of MMP-1, -2, -3 and TIMP-1, -2 and -4 compared to control ($p<0.05$). The gene expression of TIMP-3 decreased significantly ($p<0.05$) following LPS application. There were no differences between TLR4-D and control mice. There were no MMP-1 protein expression at all and no differences in the protein expression of MMP-3 regarding TLR4 and control. The zymography results showed a significant TLR-4 dependent activation of MMPs ($p<0.05$).

CONCLUSION. Following i.p. LPS application myocardial expression of MMPs and TIMPs are significantly regulated with an TLR4 independent pathway. However, as shown with zymography the activity of MMPs are significnatly regulated via TLR4.

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Cellular mechanism in septic cardiomyopathy – 535-537

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TLR 4 DEPENDET CARDIAC MYOCYTE CONTRACTILITY FOLLOWING LPS ADMINISTRATION

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INTRODUCTION. Myocardial depression is a potentially fatal complication of septic shock. The precise mediators that cause myocardial dysfunction during sepsis remain elusive. Previous studies have shown that in an in vivo sepsis model the expression of relevant mediators are related to Toll Like Receptor 4 (TLR-4). However the functional significance regarding myocyte contractility of the TLR-4 dependent signalling cascade is not known. Therefore the purpose of this study was first to elucidate whether TLR-4 deficient myocytes do show any functional changes following lipopolysaccharides (LPS) application and second to differentiate between direct myocardial effects and those of immune cells.

METHODS. Cardiac myocyte were isolated from TLR-4 deficient (TLR-4D, C3H/HeJ) and control mice (C3H/HeN). Cells were stimulated by external electrodes and with LPS (10ng/ml) for 5-8 hours. Shortening-velocity frequencies were detected at different frequencies.

RESULTS. LPS suppresses the shortening amplitude significantly at all frequencies except at 6 Hz in C3H/HeN myocytes, however there were no significant changes in TLR-4D myocytes. In contrast to TLR-4D myocytes LPS does affect the shortening-velocity frequency in C3H/HeN myocytes at all frequencies. As a consequence of the decreases in shortening- and relaxation velocities the duration of shortening is significantly prolonged by LPS in C3H/HeN cells at different stimulation frequencies in contrast to TLR-4D myocytes.

CONCLUSION. Cardiac myocyte contractility in an in vivo model of septical cardiomyopathy is TLR-4 dependent. The production of mediators by immune cells is not necessary.

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CD25 POSITIVE T-CELLS PREVENT AUTOIMMUNITY AFTER MYOCARDIAL INFARCTION

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INTRODUCTION. Myocardial infarction and heart surgery release cardiac self-proteins. Some patients develop transient myopericarditis and cardiac autoantibodies but scarcely severe myocarditis. Nothing is known about the prognostic long-term relevance of this heart specific inflammation. However, studies in mice suggest that heart specific autoimmunity finally results in cardiomyopathy. Thus, regulatory mechanisms suppressing autoimmune responses after organ damage appear to be essential for the functional preservation of the heart. CD25+ regulatory T-cells suppress autoimmune responses. We tested the role of CD25+ regulatory T-cells for the prevention of heart specific immunity after myocardial infarction.

METHODS. BALB/c mice were depleted of CD25+ T-cells by antibody injection. Controls received vehicle only. Myocardial infarction was then induced in anaesthetized and mechanically ventilated mice by ligation of the anterior descending coronary artery. Animals were killed 6 days after surgery.

RESULTS. Six days after surgery hearts of vehicle treated mice showed necrosis and scarring but only minimal cardiac inflammation. In contrast, depletion of CD25+ cells in BALB/c mice before myocardial infarction resulted in autoimmune myocarditis as early as six days after surgery. Myocarditic lesions were not located next to the infarcted area but occurred mainly in the epicardial region of the right ventricle. Moreover, injection of CD4 T–cells isolated from non-treated mice after myocardial infarction induced autoimmune myocarditis in CD25+ depleted but not wild-type recipients after in vitro expansion.

CONCLUSION. Our results demonstrate that CD25+ T-cells prevent autoimmunity after myocardial infarction in a mouse model. Further animal studies must address the mechanism which might overcome the protective effect of CD25+ T-cells. This mouse model might be of help in understanding the pathogenesis of myopericarditis after cardiac damage.
Grant acknowledgement: Swiss National Foundation

Oral Presentations
Nutrition: Clinical aspects – 538-540

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INTENSIVE INSULIN THERAPY PROTECTS THE NERVOUS SYSTEM AND IMPROVES LONG TERM REHABILITATION

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INTRODUCTION. Maintaining normoglycemia (80-110 mg/dl) with intensive insulin therapy during critical illness reduces morbidity and mortality. Effects on CNS function and long-term rehabilitation of neuro-ICU patients are unknown.

METHODS. This retrospective analysis of a large(N=1548) prospective, randomized and controlled study evaluated acute and long-term (at 6 and 12 months) effects of intensive insulin therapy in all 63 patients who were included for neurological disease or after isolated cerebral trauma, haemorrhage or brain surgery.

RESULTS. The studied subset of patients in the intensive (n=33) and conventional (n=30) insulin groups had been admitted for similar diagnoses and were comparable at baseline. Intensive insulin therapy required a median 88 units of insulin per day versus 0 in the conventional group (p=0.0001), resulting in mean±SEM blood glucose levels of 98±2 mg/dl versus 148±6mg/dl (p<0.0001). The incidence of hypoglycaemia was not different between the two groups. ICU mortality was 18% in the intensive insulin group and 23% in the conventional group (p=NS) and mortality at 6 and 12 months was also not significantly different. Patients in the intensive insulin group required a median 8 days less on the ventilator (p=0.0007), 9 days less in ICU (p=0.002) and 12 days less in the hospital (p=0.05). The reduced need for mechanical ventilation was explained by preventing critical illness polyneuropathy (63% versus 24%; p=0.002). Acute renal failure was not affected in this subset of patients, whereas blood stream infections were reduced from 47% to 12% (p=0.002) as well as inflammation (6 days less of pronounced CRP rise above 75mg/l; p=0.02). Maximal and mean intra-cranial pressure (ICP) was significantly lower in the intensive as compared with conventionally treated patients (p<0.0001 and 0.003, respectively). Seizures(p<0.001) and diabetes insipidus (p=0.06) occurred less frequent in the intensive insulin group. Between 6 and 12 months, the Karnofsky performance score improved significantly better (p=0.02) in the intensive insulin treated patients (median score of 75% versus 55%).

CONCLUSION. Intensive insulin therapy in neuro-ICU patients is highly protective for peripheral and central nervous system which reduces the need for intensive care. For the first time, a long-term benefit with better rehabilitation was shown.
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ABSENCE OF HYPERMETABOLIC STATE AND PROTEIN WASTING IN CRITICALLY ILL CHILDREN.

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INTRODUCTION. Critically ill adults are characterized by a hypermetabolic and catabolic state as the result of inflammatory process. A negative nitrogen balance is described in spite of adequate nutritional support. Our aims were to measure daily Energy Expenditure (EE) and Nitrogen Balance (NB) of critically ill mechanically ventilated children. EE was compared to the actual nutritional support (NS) and to the Recommended Dietary Allowances (RDA, 1989) for age and to the inflammatory status (C-Reactive Protein, CRP).

METHODS. EE was measured by indirect calorimetry (DeltatracII, Datex) and Total Urinary Nitrogen (TUN) by pyrochemiluminescence in mechanically ventilated children under analgesia and sedation, at 24h and then each day until extubation. NB was calculated from nitrogen intake and nitrogen urinary loss, fecal (20 mg/kg) and tegumental (10mg/kg) losses. Day to day EE and C-Reactive Protein (CRP) were analysed. For each patient, Energy Balance (EnBal) was calculated from NS and measured EE; Energy Nitrogen Ratio (ENR) was also evaluated.

RESULTS. 122 EE and 163 NB measurements were performed in 18 children (cardiothoracic surgery, burn). Population characteristics (mean±SD) were : age (months): 17±18; weight (kg) : 8.3±4.9; PRISM Score:11.0±4.8. At 24h after admission EE was 55±11 kcal/kg; VO2: 8.2±1.8 ml/kg/min; RQ: 0.8±0.1. EE was stable during the first week and ranged from 53 to 60 % of RDA despite the increase of the CRP at 67±47 mg/l at day 2. Then CRP declined exponentially. At the same time the NS increased from 34±16 kcal/kg to 63±23 at day 7. At 24h, nitrogen intake was 0.12±0.11 and reached 0.31±0.16 g/kg at day 7. TUN values were: 0.19±0.07 and 0.30±0.16 g/kg respectively. NB was –0.12±0.13 g/kg at 24h and got up to a positive value since day 4. Energy balance became positive for the majority of the children since day 5. ENR decreased from 377± 250 at 24h to 234±75 Kcal / 1g of nitrogen at day 7.

CONCLUSION. On the first week, EE was stable and ranged from 53 to 60 % of RDA and nitrogen balance were not so negative as suggested in critically ill adults, despite a moderate nitrogen intake. We did not observe a hypermetabolic state as it could be presume by the evolution of CRP values. NS cancelled out the caloric deficit at day 5. Children demonstrate clearly a different metabolic response to acute phase of critical illness.
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TRACE MINERALS IN ICU PATIENTS, A FORGOTTEN CAUSE OF DELAYED RECOVERY?

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INTRODUCTION. The aim of this prospective, observational pilot study was to assess the possible deficiency of the standard nutrition protocol, based on the daily recommended doses (DRD) in the literature for trace minerals(1).

METHODS. Thirty patients in a surgical intensive care unit of a tertiary referral center with 2 or more organ failure were included. All received total parenteral nutrition (TPN) according to standard protocol. Plasma measurements of copper, manganese, selenium and zinc were performed before and after 7 days of supplementation with a commercial formula containing one DRD of each element (Addamel®N, Fresenius Kabi, 's-Hertogenbosch, NL).

RESULTS. Copper as substantial element in the normal function of oxidative enzyme systems and in plasma bound to ceruloplasmine, an acute phase protein, is difficult to interpret in critically ill patients. However, levels before were normal (16,1 ± 4,7 mumol/l, N = 10,0-30,0 mumol/l) and could be raised significantly (18,4 ± 4,7 mumol/l, p = 0,017). Manganese is part of mitochondrial superoxide dismutase and important for the metabolic effects of vitamin K. Normal starting levels were found (32,9 ± 10,3 nmol/l, N = 2-37 nmol/l) and were raised significantly (37,2 ± 10,8 nmol/l, p = 0,049). Selenium as a co-factor in the erythrocyte glutathionperoxidase complex has a protective role against peroxides. Low baseline levels were found (0,50 ± 0,21 mumol/l, N = 0,8-1,8 mumol/l) and the supplement could not normalize this (0,65 ± 0,25 mumol/l), improvement was statistically significant (p = 0,002). Zinc deficiency is known for impaired wound healing, alopecia and immunologic dysfunctions. Almost all patients were deficient at start (8,1 ± 3,3 mumol/l, N = 11,5-23,5 mumol/l), supplementation did result in significant improvement, but only just to normal levels (10,5 ± 2,4 mumol/l, p = 0,002).

CONCLUSION. A significant percentage of ICU patients have trace mineral deficiencies. Our results support a more prominent role for detecting deficiencies and re-evaluation of the current recommended nutrition standards for ICU patients.

REFERENCE(S). 1. Shenkin A: Adult micronutrient requirements. In: Payne-James J, Grimble G, Silk D, ed.- Artificial Nutrition Support in Clinical Practice. Edward Arnold (London), 1995.

Oral Presentations
Assessment of new technologies – 541-543

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LUNG EXPANSION DURING IPPV ASSESSED WITH 8-ELECTRODE MULTIFREQUENCY ELECTRICAL IMPEDANCE TOMOGRAPHY

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INTRODUCTION. Electrical impedance tomography (EIT) is a non-invasive imaging technique that has been applied to many different tissues, originally with a 16 electrode system (1). Sixteen electrodes can present practical difficulties when using the system clinically. The aim of this study is to evaluate whether the 8 electrode multifrequency EIT system (2)can be used to quantitatively monitor changes in lung volumes in ventilated patients.

METHODS. 10 patients scheduled for elective surgery requiring intermittent positive pressure ventilation (IPPV) were studied in the anaesthetic room using the Sheffield (Mk 3.5) 8-electrode multifrequency EIT system. Measurements of chest electrical impedance lasting 60 seconds were made during spontaneous breathing, and then with the patient anaesthetised and ventilated using tidal volumes of 4, 6, 8 and 10 mls per kg respectively. Regions of interest were then analysed to assess impedance.

RESULTS. All patients were ASA 1-11, mean age 42 years (range 29-73), mean weight 76 kg (range 67-95). Linear regression applied to the relationship between tidal volume and the magnitude of the impedance changes within individual patients revealed a mean r2 of 0.95 (range 0.81-0.99). Analysis of within individual changes in impedance recorded at each tidal volume demonstrated a mean coefficient of variation of 6.3% (range 3.4-13.9). Mean between subject variability was much greater (26.1%).

CONCLUSION. The 8-electrode Sheffield Mk 3.5 multifrequency EIT system can be used to assess changes in lung expansion within individual patients, but direct comparison between subjects is compromised by between subject variation.

REFERENCE(S). 1) Barber DC, Brown BH. 1984 Applied Potential Tomography: Journal of Physics E: Scientific Instruments, 17; 723-33
2) Wilson AJ, Milnes P, Waterworth AR, Brown BH. 2001 Mk 3.5 EIT System; a modular, multifrequency successor to the Mk 3a EIT System. Physiol Meas 22(1); 49-54

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PRESERVATION OF PEEP WITH A CLOSED SUCTIONING DEVICE: A LUNG MODEL STUY

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INTRODUCTION. It has been recommended to use closed suctioning devices in patients on high PEEP(1) based on studies reporting better oxygenation(2) in the post suctioning period. The goal of this study was to determine the influence of pressure versus volume controlled mode of ventilation on the preservation of PEEP with a closed suctioning device.

METHODS. A two chamber lung model was filled with water to achieve a compliance of 40 ml/cm H_2O and connected to a Siemens Elema Servo 300™-Ventilator. A 20G-catheter with transducer under the water surface was used to simulate alveolar pressure. Suctioning was performed 10 times during inspiration using the Ballard Trach Care™ closed suctioning system. PEEP measured by the ventilator and pressure in the water were recorded with and without (=baseline) suctioning at PEEP settings of 15, 10 and 5 cm H_2O in the Volume controlled mode (VCM) and in the pressure controlled mode (PCM).
Fisher's exact test was used for statistical analysis.

RESULTS. In the volume control mode water pressure dropped between 60–85% from baseline during suctioning and the measured PEEP on the ventilator dropped from 5 to 2(+/-0,6)cmH2O, 10 to 3(+/-1,1)cmH_2O and 15 to 7(+/-1)cmH_2O. In the PCM water pressure dropped only 5-10% from baseline (p< 0,05) and the measured pressure on the ventilator dropped from 5 to 4(+/-0,2)cmH_2O, 10 to 8(+/-0,4)cmH_2O and15 to 13(+/- 0,4)cmH_2O.

CONCLUSION. In this lung model study PEEP is only mildly reduced in PCM compared to VCM during suctioning with a closed suctioning device. This explains better oxygenation results compared to open suctioning where PEEP is lost almost completely. Side effects like high intrinsic PEEP on introduction of the catheter in both modes and negative airway pressures in VCM has been demonstrated in another lung model study(3).
In assisted ventilation modes their use might be limited by inappropriate ventilator triggering(4. No hygienic benefit of their use has been shown(5).

REFERENCE(S). 1.Weitl J et al. Anaesthesist 1994;43:359-63
2.Baun MM et al.Crit Care Nurs Q 2002;25:13-26
3.Stenqvist O et al. Acta Anaesthesiol Scand 2001;45:167-72
4.Al-Khafaji A et al. Intensive Care Med 2002;28:515-9
5.Ritz R et al. Respir Care 1986;31:1086-91

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THE USE OF PULMONARY ARTERY CATHETER IS NOT ASSOCIATED WITH WORSE OUTCOME; RESULTS OF THE SOAP STUDY

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INTRODUCTION. In critically ill patients, the impact of pulmonary artery catheter (PAC) use on outcome is debatable. We investigated the epidemiology of PAC use in European ICUs and its relation to outcome.

METHODS. This cohort, multicentric, observational study included all 3147 adult patients admitted to 198 European ICUs between May 1 and May 15, 2002. Patients were followed up until death, hospital discharge, or 60 days. Patients were classified according to the use of PAC at any time during ICU stay into PAC group and others with no PAC. Propensity score case-matching was performed and matched pairs were examined for baseline characters and outcome.

RESULTS. Of 3147 patients, 481 (15.3 %) had PAC and 2666 (84.7 %) never had a PAC. Patients with PAC were older, had a higher incidence of cancer and heart failure, most commonly surgical admissions, had a higher SAPS II and SOFA scores, and higher incidence of sepsis syndromes on admission. Fluid balance was comparable between the two groups. As expected, both ICU and hospital mortality rates were higher in patients with PAC (28.1 vs. 16.8 and 32.5 vs. 22.5 %, p<0.001) than in the other patients. However, PAC use was not associated with an independent risk of ICU death in a multivariate analysis. Moreover, in a 453 matched-pairs according to a propensity score, ICU and hospital mortality rates were identical in patients with and without PAC group (26.7 vs. 26.3 and 31.4 vs. 32.8, p=NS). Survival at 30 days were similar between the two matched groups (Log Rank = 0.02; p = 0.894).

CONCLUSION. In this observational study, the use of PAC was not associated with increased mortality in a heterogeneous ICU population.
Grant acknowledgement: The study was supported by an unrestricted grant from: Abbott Laboratories, Baxter, Eli Lilly, GlaxoSmithKline,and Novo Nordisk

Oral Presentations
Acute coronary syndrome – 544-546

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NO IN ACUTE CORONARY SYNDROME: CORRELATION WITH MYOCARDIAL ISCHEMIA ASSESSED BY PERFUSION IMAGING

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INTRODUCTION. Intact endothelium (end.) releases Nitric Oxide (NO) which acts through cGMP to mediate coronary dilatation, whereas diseased end. releases less NO & poorly reduces the vasomotor tone. Diabetic patients (pts) with microangiopathy are expected to be poor secretors of NO. Release of NO is indirectly assessed by measurement of NO synthase & NO end product metabolites. Our aim is to assess serum level of NO in pts with acute coronary syndromes (ACS)in correlation with the extent of ischemic burden.

METHODS. We studied 20 pts (8 diabetics, 12 non diabetics) with ACS (18M, 2F),age ranging from 38-65y (mean 55ys),unstable angina (3pts), NSTEMI (2pts) & acute MI (15pts). Before therapeutic intervention, serum arterial NO level was measured by ELISA photometry as well as acute myocardial perfusion imaging with gated SPECT study by injecting the pt with 10 mci 99mTC SestaMIBI IV during chest pain. By acquisition the 1st set of SPECT images we assess the myocardium at risk (MAR), with estimation of the initial EF. The 2nd set acquired 72 hours later assessed extent of myocardial salvage achieved by different therapeutic modalities. Twenty segments scoring system was applied for both sets of images to estimate the salvage index(SI). SI = (MAR – 2nd score)/MAR x100. A control group of 8 pts matched for age & sex are studied.

RESULTS. Compared to control group pts with ACS had significantly lower level of serum NO metabolites (mean 27+6 vs 70+10 Ug/L, P = 0.004). The initial score ranged from (12 to 48, mean 27+15). The 2nd score ranged from 3 to 31, mean 15 & SI ranged from (14 to 71%, mean 40%). There was a weak correlation between NO level & the extent of myocardial ischemia (r= -0.5), which was still observed when the pts were divided into diabetics and non-diabetics (r= -0.5).

CONCLUSION. A significantly lower serum levels of serum NO metabolites in pts with ACS is a marker of substantial end. dysfunction with impaired coronary perfusion. Despite the key role of NO in maintaining normal vasomotor tone & coronary flow, therapeutic inhalation of NO would not be expected to improve coronary flow in ACS as extrapolated from our data showing poor correlation between serum level of NO & the extent of myocardial salvage.

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STRESS HYPERGLYCEMIA AND ACUTE CORONARY SYNDROME

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INTRODUCTION. Acute stress hyperglycemia (HG) is associated with an increased risk of in-hospital mortality and heart failure in patients with myocardial infarction (AMI) before and during the era of Thrombolysis (TL); but the relationship between HG and the severity of coronary disease is still unclear. We tried to find a correlation between a certain value of HG and the risk of coronary occlusion or multiple vessel disease occurred in patients with Acute Coronary Syndrome (ACS).

METHODS. 513 patients with ACS were included in this study. Blood glucose measurement was performed before any fluid administration after the patient's admission and fasting 24 hours later. It was considered elevated if the value was above 110mg/dl. Creatinin-Kinase (CK) and CK-MB were measured every 6 hours. Coronarography and primary angioplasty was performed in patients with anterior or other complicated AMI and it was performed within 72 hours in those patients who received TL or who had unstable angina. The global ejection fraction (EF) and the wall motion score (WMS) of 16 segments of the left ventricle (LV) were evaluated by echocardiography in the first 48 hours after ACS. Chi-square test was used for statistics.

RESULTS. In total, 408 patients had a glycaemia above 110 mg/dl and 304 were above 125 mg/dl and only 62/513 patients had a history of diabetes (12%). A HG above 125 mg/dl was significantly associated with an occlusion of one of three main coronary arteries and peak of CK and CK-MB (p<0.005), but it was not correlated with the EF and the WMS. A HG above 110 mg/dl and especially above 125 mg/dl was significantly associated with the risk of death and heart failure in hospital (p<0.005), but the mortality was lower in patients with AMI that had HG and treated by Angioplasty or TL than those were not treated (p<0.005). Coronary by-pass surgery was also more frequently performed in patients with HG due to the occurrence of multiple vessel disease (p<0.005).

CONCLUSION. In patients with ACS, stress hyperglycemia is associated with the severity of coronary artery disease and the risk of death and heart failure in hospital. A HG above 125 mg/dl is strongly associated with the occlusion of one of three main coronary arteries and the occurrence of multiple vessel disease in the acute phase.
Grant acknowledgement: Apply for Edwards

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VENTRICULAR FIBRILLATION IN ACUTE MYOCARDIAL INFARCTION IN SPANISH POPULATION.

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INTRODUCTION. The aim of this study has been to investigate the factors predisposing to primary or secondary ventricular fibrillation (VF) and the prognosis in Spanish patients with acute myocardial infarction (AMI) during their admission to the intensive care unit (ICU) or the coronary care unit (CCU).

METHODS. A retrospective cohort study including all the AMI patients listed in the ARIAM registry (Analysis of Delay in AMI), a Spanish multicentre study (119 Spanish hospitals). The study period was from January, 1995, to January, 2001. Factors associated with the onset of VF were studied by univariate analysis. Multivariate analysis was used to evaluate the independent factors for the onset of VF and for mortality.

RESULTS. 17,761 patients with AMI were included in the study. 934 (5.3%) developed VF, primary in 735 patients and secondary in 229 patients. In the multivariate analysis, the variables which continued to show an association with the development of VF were the Killip and Kimball class, the peak CK, the APACHE II score, age and the time from the onset of symptoms to the initiation of thrombolysis. The mortality in the patients with any VF was 31.8%, 27.8% in the patients with primary VF and 49.1% in the patients with secondary VF. The development of VF is an independent predictive factor for mortality in patients with AMI, with a crude OR of 5.12 [4.41 - 5.95] and an adjusted OR of 2.73 [2.12 - 3.51].

CONCLUSION. Despite the considerable improvement in the treatment of AMI in recent years, the onset of either primary or secondary VF is associated with a very poor prognosis. It is usually accompanied by extensive necrosis.
Grant acknowledgement: ARIAM group. Boehringer-Ingelheim.

Oral Presentations
Neurosurgery – 547-549

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TWO-DIMENSIONAL TRANSCRANIAL COLOR DOPPLER IN SUBARACHNOID HEMORRHAGE

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INTRODUCTION. M-Mode Transcranial Color Doppler became an important tool for neurointensivism in the follow-up of patients with Subarachnoid Hemorrhage (SH). Two-dimensional Color Doppler (TDCD) may provide the same sort of information obtained with M-Mode and additionally it is possible to visualize the anatomy of intracranial vessels. Therefore our purpose was to acquire color images from intracranial vessels, identify arterial segments under vasospasm and recognize aneurysms with the Color Doppler technique.

METHODS. We used a two-dimensional color Doppler ultrasound (Acuson - Sequoia) with a 2 MHz transducer. We obtained two-dimensional colour images from the Circle of Willis, recording vessel velocities and analyzing the flow, resistance index and pulsatility index of patients admitted in the intensive care unit (ICU) with SH. We used transtemporal, occipital and ocular windows in order to register the arterial flow. We defined vasospasm when mean velocities were higher than 120 cm/s. Images of vasospasm and probable aneurysms were recorded and compared to cerebral angiography.

RESULTS. From May 2000 to August 2001, sixteen patients were admitted with SH in our surgical ICU. Thirteen were classified Fisher IV stage after head CT scan. Three aneurysms were diagnosed by TDCD and confirmed by cerebral angiography. One was on the top of the basilar artery and two other were in the middle cerebral artery. Sixty one percent (n=8) of patients in Fisher IV stage had vasospasm initially diagnosed by TDCD and posteriorly confirmed by the angiogram. Flow and velocities were recorded; these data helped us to understand and to use appropriate therapeutic intervention.

CONCLUSION. There was technical feasibility in obtaining two-dimensional Colour Doppler images of intracranial vessels and no contrast was needed for the diagnostic procedure. Immediate better treatment of cerebral vasospasm, including percutaneous angioplasty in selected cases, was possible after TDCD. Finally, good anatomical correlation between images from TDCD and angiography were also noted, making it a suitable bedside tool in the management of patients with SH.

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CONTROL OF ICP DURING PERCUTANEOUS TRACHEOSTOMY IN NEUROSURGICAL PATIENTS: PRELIMINARY CASES

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INTRODUCTION. The intracranial pressure is modified from haemodynamic variations and increasing of paCO2.We studied in neurosurgical patients, modifications on intracranial pressure, cerebral perfusion pressure, blood gases during a technique of percutaneous dilatation tracheostomy (Percutwist).

METHODS. Thirty-five neurosurgical patients,GCS =8(19M,16W,age 49 ± 4) between May 2002 and March 2003. Admission criteria: need of mechanical ventilation and or protection of airways. Exclusion criteria: emergency conditions, difficult to perform intubation, irreversible coagulation disorders, unstable cervical spine. The standard intraoperative monitoring was EKG, IBP, MAP, SPO2, PaCO2 and continuous recording of ICP, CPP, derived through a ventricular catheter (Raumedic ® Neurovent ®) connected to a monitor Siemens SC 7000. The procedure was conducted under general anaesthesia TCIDiprifusor, fentanyl, vecuronium, mechanical ventilation(CPPV), FiO2 1, monitoring changes on PaCO2. The technique, as suggested by G. Frova, has been performed under FBS control.

RESULTS. See table 1

Results

	BASELINE	FIBEROPTICAL BRONCHOSCOPY	ROTATING DILATOR	TRACHEAL CANNULA	END OF PROCEDURE
MAP	93±12.1	95±14	97±14.4	95±12	90±15
ICP	11±4.2	14±5.2	14±4.5	13±5.4	12±3.8
CPP	80±5.6	79±6.1	77±5.2	78±4.3	77±4.4
PaO2	128±24	145±50.1	286±64	305±70	159±55
PaCO2	34±4.9	36±5.2	35±5	34±3.3	32±2.1

CONCLUSION. As demonstrated in table 1 there was stability of haemodynamic parameters (MAP). ICP was not increased because of ventilation (PaCO2), subsequently we observed stability of CPP during all the procedure. We conclude that this technique because of their rapidity, easily, safety is suggested for neurosurgical patients.

REFERENCE(S). G.Frova et al. A new simple method for percutaneous tracheostomy: controlled rotating dilation. Int Care Med 2002 March;28(3):299-303.

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CEREBRAL VASOSPASM – MORE FREQUENT FOLLOWING ENDOVASCULAR ANEURYSM COILING?

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INTRODUCTION. Cerebral vasospasm is the most common cause of morbidity and mortality in patients with subarachnoid haemorrhage. The early removal of subarachnoid blood and irrigation of the basal cisterns during surgery has been reported to reduce the incidence of vasospasm. In contrast to aneurysm clipping, endovascular treatment does not allow removal of subarachnoid blood. The present study compares the incidence and severity of cerebral vasospasm following endovascular treatment with that following aneurysm surgery in patients with aneurysmatic subarachnoid haemorrhage.

METHODS. A total of 52 patients with subaracnoid haemorrhage classified as Hunt and Hess grades I to III was included. From these, 25 patients underwent aneurysm clipping and 27 endovascular aneurysm coiling. The amount of blood on computerized tomography was classified by means of Fisher´s scale. Hypertensive, hypervolemic, haemodilution therapy was used to treat vasospasm.

RESULTS. Vasospasm occurred in 8 (35%) patients following clipping, and in 11 (41%) following endovascular treatment. The mean duration of vasospasm was 17.5 days in the coiling group as compared to 10.7 days in the clipping group ($p<0.05$). The mean blood flow velocity in the middle cerebral artery during the first 21 days following subarachnoid haemorrhage was 117.4 cm per second in the coiling group and 94.9 cm per second in the clipping group.

CONCLUSION. The incidence of cerebral vasospasm after aneurysmatic subarachnoid haemorrhage seems to be higher in patients following endovascular aneurysm coiling as compared to patients following clipping.

Oral Presentations
Nursing: Making the patient safer in the ICU – 550-554

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THE EFFECT OF GUIDELINES ON REDUCTION OF INCOMPATIBILITY ERRORS WITH INTRAVENOUS MEDICATION

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INTRODUCTION. Medication errors are still a major hazard in intensive care units (ICU). The intensive care patient frequently receives multiple drugs simultaneously by injection or infusion. In Denmark information regarding compatibility of different compounds is scarce and information in the individual product information is often inadequate. In order to reduce the risks of incompatibility reactions, we collected information from pharmacological databases, contact to the manufacturers or through own in vitro tests and draw up a guideline. The purpose of this study was to investigate the level of knowledge among ICU nurses of compatibility when co-administrating drugs by y-site infusions. Additionally we wanted to examine if the newly developed guideline could increase the knowledge and skills of the nurses and thereby reduce the number of medication errors.

METHODS. The investigation was conducted in 18 nurses who volunteered for the study in our 8 bed multidisciplinary University Hospital ICU. The investigation was divided into 3 parts: A pre-intervention questionnaire (February 2003, an intervention – introduction a guideline (March 2003) and a post intervention questionnaire. The questionnaire was self-reported with open-ended (n=3) and multiple-choise (n=7) questions. Reporting was anonymous.

RESULTS. A total of 18 nurses answered the pre-intervention questionnaire. The percentages of correct answers in multiple-choice questions were: 0, 56, 61, 61, 61, 88 and 94%, respectively. The open-ended questions revealed a high level of uncertainty of incompatibility reactions when administrating two compounds or more simultaneously. One month after implementation of the new guidelines a preliminary survey indicates that the guidelines have been well implemented and are useful in minimizing medication errors with respect to compatibility. The post-intervention questionnaire results will be presented at the conference.

CONCLUSION. The first part of the study revealed an insufficient knowledge on risks of incompatibility reactions when co-administrating a mixture of compounds intravenously in critically ill patients. Introduction of guidelines increases the knowledge and may prove to minimize the risks of medication errors.

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INFLUENCE OF THREE DRESSING REGIMENS ON PERIPHERAL INTRAVENOUS CATHETER DWEEL TIME IN CHILDREN

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INTRODUCTION. Intravascular catheters are indispensable in modern health care, particularly in paediatric intensive care units (PICU). The incidence of local or systemic infections associated with peripheral intravenous catheters (PIC) is usually low, although serious complications produce important morbidity, because of the great frequency with which such catheters are used.[1] The type of dressing has been associated with PIC dwell time, infection rate and local complication. The purpose of this study was to verify the influence of three dressing regimens on the PIC dwell time.

METHODS. A prospective, randomized, controlled study was carried out with 150 PIC inserted in 68 children with ages ranging from 0 to 12 years, submitted to surgical interventions in an university hospital in Brazil. The groups of study consisted of 50 PIC with sterile gauze dressing (EG1),50 PIC with sterile transparent film dressing (EG2) and 50 PIC with non-allergenic adhesive tape (CG). The variables selected for homogenization were related to children, professionals, and intravenous therapy characteristics. The data obtained was submitted to statistical analysis through Chi-Square, ANOVA, and Kruskal-Wallis tests with significance level of 5%.

RESULTS. There were no statistically significant differences regarding age (p=0.523), nutritional state (p=0.916), race (p=0.526), and gender (p=0.920) of the children distributed in the studied groups. The professional category, of those performing the venous puncture, presented a statistical difference (p=0.029) among the groups. The variables regarding intravenous therapy did not present a statistical difference due to catheter gauge (p=0.743), blood vessel (p=0.980) and site (p=0.960) of catheter insertion, limb immobilization (p=0.224), type of maintenance (p=0.395), and solutions used for maintenance (p=0.808). Significant differences (p=0.022) were obtained in the length of the PIC dwell time, been higher in EG1 (46.12±37.36), followed by CG (38.18±30.45) and EG2 (29.53±30.80).

CONCLUSION. According to the results the dressing regimens significantly interfered in the length of the PIC dwell time. The PIC presented an extended time of dwelling in the sterile gauze dressing group.

REFERENCE(S). 1.CDC. Guidelines for the prevention of intravascular catheter-related infections.MMWR2002;51(RR-10)

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INCIDENCE, RISK FACTORS AND MORTALITY OF VAP IN THE ICU

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INTRODUCTION. To investigate the incidence, risk factors and mortality of ventilator associated pneumonia (VAP) in ICU patients by means of a prospective, single centre study.

METHODS. All 1295 adult patients admitted to the ICU during 4 three-month periods between 1996 and 1998 were included. A set of demographic variables were collected at the day of admission. The different devices used in each patient, were recorded on a daily basis.

RESULTS. The study population (63.1% male) can be separated in patients with (n= 89) and without VAP (n= 1206). The characteristics are described in the table below.
The incidence rate of VAP was 8.4%. The mean time to the development of VAP was 9.6 days with a median of 6 days. The risk factors associated with VAP from the Cox regression were age and the time of being intubated during ICU-stay. The crude mortality rate of the population was 12.9% and the patients with the infection reached 20.2%. Factors allied with mortality are SAPS II-score, days receiving therapeutic antibiotics and total days in the ICU. VAP was not a significant variable.

Patient characteristics	VAP	non-VAP	P value
Days of ICU stay	23 ± 18.7	6 ± 6.9	<0.001
Age	55 ± 18.6	56 ± 18.0	= 0.63
Days with Ventilation	18 ± 15.7	3 ± 6.0	<0.001
Days with tracheotomy	6 ± 11.3	1 ± 4.2	<0.001
Days with therapeutic AB	15 ± 13.2	3 ± 5.9	<0.001
SAPS II-score	47 ± 16.7	31 ± 17.9	<0.001
ICU-mortality	20.2 (17/84)	12.0 (142/1185)	<0.05

CONCLUSION. We found an incidence rate of VAP of 8.4% and a crude mortality rate of 12.9%. VAP was significant in the univariate analysis of mortality, but it wasn't in the logistic regression analysis.

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EFFECT OF ADDITIONAL DISEASES ON THE DEVELOPMENT OF PRESSURE SORES IN INTENSIVE THERAPY PATIENTS

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INTRODUCTION. Patients of an Intensive Care Unit (ICU) are particularly prone to develop pressure sores (PS) because of their severe main diseases for witch they are hospitalized and because of numerous co-existing illnesses. The objective of the studies was to evaluate interrelations existing between additional diseases and PS development.

METHODS. The prospective, randomized studies were carried out in a period of 24 months in a 12-bed clinical multiprofile ICU. The therapy method (medical or surgical), type of disease according to APACHE II system and additional diseases were recorded. Subsequently, until the date of discharge from ICU, the patients were monitored regarding the presence of PS. Chi^2 statistical test, logistic regression and survival analysis (Kaplan-Meier method) were used to analyse.

RESULTS. Studies were carried out on 508 patients. Almost one half of the patients had co-existing neurological diseases 47.2%, circulatory failure 43.7%, diseases of peripheral vessels 37.8%, diabetes 13.6%, motor system failures 4.9%.The incidence of PS development for the total population of the ICU patients was 13.2%: for conservative therapy patients 13.3%, and for emergency surgery patients 23.0%. Patients burdened with co-existing diseases were characterized by higher incidence of PS. The PS occurrence for the total number of patients was from 21.7 to 18.9%, for conservatively treated patients 21.8÷13.3% and for surgical patients 40.0÷27.0%. It was found that PS risk for the total number of patients increases in case of co-existing neurological diseases (odd ratio 4.66), then in patients with circulatory failure (3.05) and in case of peripheral vessel failure (3.03). The same PS risk order was observed in the conservatively treated patients whereas the odd ratio for neurological patients was almost twice as great amounting to 8.62. For circulatory and peripheral blood vessel diseases, the risk was slightly lower (2.65 and 2.58 respectively). In surgical patients, a definitely higher PS incidence was found in patients with circulatory failure and with peripheral vessel diseases (3.52, 5.11). No significant statistical effect of the motor system diseases and diabetes on PS incidence was recorded. It was found that co-existing diseases reduced time of PS incidence.

CONCLUSION. Co-existing diseases have a significant effect on the frequency and time of PS incidence in intensive therapy patients. They constitute essential PS risk factors that should be taken into consideration in the risk prediction scales for ICU patients.

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COMPARATIVE STUDY ON THE CLOSED-24-HOUR-SUCTION-SYSTEM

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INTRODUCTION. The repeatedly performed tracheobronchial suction is an absolutely necessary and frequently used method of keeping free the respiratory tract of patients underlying mechanical ventilation by means of endotracheal tubes. Frequently new suction catheters appear on the market supposed to reduce to a minimum or even to eliminate completely such complications as hypoxia, bradycardia and RR-loss (hypotension?). The 24-hour-systems are instrumental in accomplishing this aim. They are commercialized by several companies on the market. (Several companies offer different products on the market.)

METHODS. Based on a series of tests involving 658 patients of various intensive care units, the differences between open suction and closed suction-systems were investigated. All of the patients underwent suction treatment by means of both methods for a period of 24 hours each, in accordance with a previously elaborated study- protocol.
The necessary blood-gas analyses with complete acid-base status were made after a stipulated interval.

RESULTS. In the group of open suctions we found a mean PaO2 reduction of 29,7%. In the group of closed suction a mean reduction of 7,6% was found. Initial PaO2-levels were reached 15-17 minutes after suction treatment in the open group, in the closed group initial PaO2 was achieved after 7 minutes.
Corresponding to these findings, the increase of the PaCO2 levels is markedly less (3,15%) when applying the closed-system compared to the open suction, where an increase of the PaCO2 with an average of 6,3% is to be found.

CONCLUSION. In investigating over a sequence period of 360 minutes considerably better results were measured in the closed group than with those patients who underwent suction treatment by means of the open system.