Oral Presentations
Ventilatory strategies in acute lung injury – 725-730

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EFFECTS OF LUNG RECRUITMENT MANOEUVRES ON OXYGENATION AND CIRCULATION IN ENDOTOXIN INDUCED ALI

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INTRODUCTION. Recruitment manoeuvers (RM) to open up alveoli and to keep the lungs open are parts in lung protective ventilation. However, RM may have serious circulatory side effects. We have studied the acute effects of two different RM on oxygenation, central and regional circulation and oxygen delivery in an endotoxin induced acute lung injury (ALI) model and the impact of volume expansion (VE).

METHODS. In six anaesthetised pigs, endotoxin induced ALI was established. PaO_2, descending aortic blood flow (ABF), portal venous and renal blood flow were monitored. Global, mesenteric and renal oxygen delivery (DO_2) were calculated. After initial volume resuscitation, two RM were performed before and after VE with dextran 60, 8 mL/kg. One vital capacity manoeuver with sustained inflation 40 cm H_2O (ViC 40) and one manoeuver in pressure control using peak airway pressure of 40 cm H_2O, PEEP 20, I:E 1:1 and RR 40 were used.

RESULTS. PaO_2/FiO_2 at baseline, 164±76 mm Hg was improved by recruitment using ViC40 (291±75) and PC40/20 (401±47). During recruitment, following VE, PaO_2/FiO_2 was 351±65 and 398±73 respectively. RM induced pronounced circulatory depression with a decrease in ABF of 82±7% (ViC40) and 57±8% (PC40/20, p<0,05 vs ViC40). This effect was attenuated by VE to 66±9 and 44±11% respectively.

		Baseline	ViC40 1 min	PC40/20 1 min
DO_2 global mL/min	normovolemia	405±72	91±42	141±48
DO_2 global mL/min	vol. expansion	481±50	211±66 *	301±61 *
DO_2 mesenteric mL/min	normovolemia	101±11	30±13	40±14 #
DO_2 mesenteric mL/min	vol expansion	123±8	51±11 *	76±9 * #
DO_2 renal mL/min	normovolemia	20±6	9±8	11±8
DO_2 renal mL/min	vol expansion	18±4	10±6	15±6

*Values are mean±SEM (n=6) at baseline and 1 min. * p<0,05 vs normovolemia. # p<0,05 vs ViC40*

CONCLUSION. Lung recruitment maneuvers in endotoxin induced ALI resulted in marked decreases in oxygen delivery partICUlarly in ViC40 compared to PC40/2O. This effect could partly be counteracted by volume expansion. The circulatory effects seemed more pronounced in this model of ALI compared to lavage induced ALI (ref).

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ARDS NETWORK VERSUS VOLUME-PRESSURE BASED LUNG PROTECTIVE VENTILATORY STRATEGY IN EXPERIMENTAL ARDS

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INTRODUCTION. The ARDS Network (ARDSNet) protocol provides a lung protective ventilatory strategy through a tidal volume (VT) of 6 ml/Kg (Predicted Body Weight) and a PEEP/FiO_2 combination table whose goal is 55 < PaO_2 < 80 mmHg. Another physiological approach for lung protection in ARDS patients is to set the PEEP level above the Lower Inflection Point (LIP) of the inspiratory static volume/pressure (V/P) curve of the respiratory system.

METHODS. In six pigs ARDS was induced by oleic acid and three experimental conditions were studied in random order: a) baseline after injury (ZEEP, VT 10 ml/kg); b) ARDSNet protocol; c) PEEP 2 cmH2O above LIP and VT 6 ml/Kg. At the end of each experimental condition we measured respiratory mechanics, hemodynamics, gas exchange and quantified tidal recruitment with spiral CT scan (difference between expiratory and inspiratory non aerated tissue) and alveolar overinflation (alveolar dead space) and shunt, using the multiple inert gas elimination technique (MIGET).

RESULTS. Data are Mean ± SD

	Baseline	ARDSNet	PEEP>LIP
PEEPtot (cmH2O)	0.35 ± 0.31	5.15 ± 2.28 *	21.41 ± 5.25 * #
CO (L/min)	3.9 ± 0.8	4.2 ± 0.9	2.9 ± 0.7 * #
PaO_2/FiO_2 (mmHg)	112 ± 47	165 ± 39 *	475 ± 55 * #
Shunt (% Qt)	32 ± 0. 1	21 ± 0.06 *	1 ± 0.05 * #
Dead Space (% Ve)	35 ± 3	38 ± 3.6	48 ± 4.7 * #
Esp Non aerated (g)	26 ± 8	17.1 ± 4.7 *	2.2 ± 0.6 * #
Insp Non aerated (g)	14 ± 5 §	8.9 ± 5 * §	1.8 ± 0.6 * #

** = p < .05 vs Baseline; # = p < .05 PEEP>LIP vs ARDSnet; § p<.05 Esp vs Insp Non Aerated tissue*

CONCLUSION. As compared with PEEP>LIP, the ARDSNet strategy results in less recruitment of collapsed lung units, higher shunt, lower PaO_2/FiO_2 ratio and a significant intratidal alveolar opening/collapse. However PEEP > LIP setting together with complete lung recruitment induces CO reduction and dead space increase, suggesting lung overdistension.

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DYNAMIC AIRWAY PRESSURE/TIME CURVE (STRESS INDEX) IN EXPERIMENTAL ARDS

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INTRODUCTION. Tidal alveolar collapse and overinflation mechanically stress the lung. During constant flow ventilation, the analysis of the inspiratory airway opening pressure/time (Pao/t) using the power equation: [Pao = a*t b + c] allows detection of recruitment/de-recruitment (downward concavity, b<1), overinflation (upward concavity, b>1) and absence of tidal recruitment and/or overinflation (straight line, b=1).

METHODS. In 8 pigs lung injury was induced with lung lavage. Each animal was ventilated in random order with 3 setting a) low PEEP/High VT (LP/HV) (tidal recruitment; b<1); high PEEP/high VT (HP/HV) (tidal overinflation; b>1) and c) low VT and PEEP level titrated in order to obtain a straight Pao/t profile (b= 1) after a lung recruitment maneuver (LRM) (40 cm H2O X 40 sec). At the end of each experimental condition we measured respiratory mechanics, gas exchange and quantified tidal recruitment with spiral CT scan (difference between expiratory and inspiratory non aerated tissue) and alveolar overinflation (alveolar dead space) and shunt, using the multiple inert gas elimination technique (MIGET).

RESULTS. Data are Mean ± SD

	LP/HV	b = 1	HP/HV
b value	0.78 ± .1	1.09 ± .05 *	1.37 ± .07 § #
VT (ml/kg)	12.7 ± 2	6.9 ± .8*	12.7 ± 2 #
PEEPtot (cmH2O)	1.4 ± 1	15.4 ± 3.5 *	14.6 ± 1.6 §
PaO_2 (mmHg)	112 ± 68	492 ± 33 *	519 ± 76 §
Shunt (% Qt)	30 ± 10	3 ± 3 *	1 ± 1 §
Tidal recruitment (g of tissue)	14.1 ± 6	0.8 ± 1 *	1 ± 1.4 §
Alveolar Dead Space (ml)	60 ± 10	50 ± 10	125 ± 11 § #

**) p< .05 LP/HV vs b=1; § p< .05 LP/HV vs HP/HV; #) p< .05 b=1 vs HP/HV*

CONCLUSION. Lung mechanical stress in terms of intratidal alveolar collapse and/or overdistension is mirrored by the inspiratory Pao/t profile. A ventilatory strategy based on LRM and subsequent PEEP titration in order to obtain a straight Pao/t profile significantly reduces indices suggesting lung mechanical stress.

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SPONTANEOUS BREATHING IMPROVES LUNG VOLUME AND AERATION IN OLEIC ACID LUNG INJURY

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INTRODUCTION. Spontaneous breathing with airway pressure release ventilation (APRV) as compared with pressure controlled ventilation (PCV) has been previously shown to improve oxygenation and reduce ventilation/perfusion mismatch in animal models and in patients with acute lung injury (1,2). The mechanisms of this findings are not known. We hypothesized that spontaneous breathing with APRV results in recruitment of essentially non-ventilated lung regions.

METHODS. 24 anaesthetized and mechanically ventilated pigs with oleic acid induced lung injury were randomly assigned to receive either PCV, or were allowed to breath spontaneously with APRV at equal airway pressure limits in supine position. Four hours after randomisation dynamic CT scans of two slices located at apex or 1-2 cm above the diaphragm were performed, and distribution of lung density were analysed at end-expiration. End-expiratory lung volume (EELV) was measured by N2-washout. Statistical analysis was performed using analysis of variance (ANOVA) with subsequent post-hoc testing (Tukey HSD) if appropriate.

RESULTS. Arterial oxygenation and EELV were comparable between the groups at Entry but increased significantly in the APRV but not in the PCV group (APRV: 134 ± 60 mmHg and 786 ± 320 ml; PCV: 91 ± 50 mmHg and 384 ± 148 ml, p<0,05 respectively). Mean CT densities in the apical and diaphragmatic slices were –577 ± 90 HU and -515 ± 86 HU in the APRV group versus –466 ± 83 HU and -381 ± 79 HU in the PCV group (p<0.05), respectively. Continuous distributions of HU indicated less atelectasis and a higher amount of normally aerated tissue with spontaneous breathing in both slices.

CONCLUSION. In this lung injury model spontaneous breathing with APRV in contrast to PCV resulted in better aeration of apical as well as juxtadiaphragmatic lung regions and was associated with a markedly higher EELV. Improved aeration of perfused lung regions may at least partially explain the observed increase in arterial oxygenation by spontaneous breathing in acute lung injury.

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Grant. Swedish Research Council

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EFFECTS OF TRACHEAL GAS INSUFFLATION IN PATIENTS WITH SEVERE HEAD TRAUMA AND ACUTE LUNG INJURY

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INTRODUCTION. Patients with severe head injury (SHI) are normally ventilated with low PEEP and high tidal volume to maintain a $PaCO_2$ < 35 mmHg. Tracheal gas insufflation (TGI)is an adjunct to mechanical ventilation that allows ventilation with small tidal volumes while CO_2 is satisfactorily cleared. Patients with SHI are commonly excluded from lung protective strategies because of the need to maintain $PaCO_2$ < 35 mmHg. We hypothesized that TGI in patients with acute lung injury (ALI) and SHI will allow a protective ventilation at normal values of $PaCO_2$.

METHODS. We prospectively analyzed six patients with SHI and ALI (LIS 2,75) mechanically ventilated in volume assist/control mode. All of them were monitored by using a parenchyma catheter-tip transducer (Camino), a fiberoptic catheter for jugukar oxyhemoglobin saturation (SjO_2)and intermittent monitoring of cerebral circulation by transcranial Doppler. During the study we have continuosly measured pH, PO_2 and $PaCO_2$ with the Paratrend continuous blood gas analyzer. Data were collected at baseline, 90 min after the application of expiratory TGI at flow rate 8 liters/min (Nellcor prototype). During the application of TGI, tidal volume was reduced to maintain isocapnia. Statistical analysis was done by one way ANOVA witha a significance of p < 0,05.

RESULTS. Results are shown in the following table:

	BASAL	TGI	POST-TGI	P
PaO_2 (mmHg)	36±1	35±1	35±2	NS
PaO_2/FiO_2	156±47	169±35	180±33	NS
Vt (ml/Kg)	8.4±0.4	6.5±0.5	8.4±0.4	0.007*
total PEEP (cm H_{2O})	9.6±2.8	12.8±3.7	9.6±2.8	NS
Driving P (cm H_{2O})	17.4±3.2	12.9±2.2	16.4±3.2	0.06
ICP (mmHg)	19±6	18±5	16±3	NS
CPP (mmHg)	77±11	79±11	73±10	NS
SjO_2 (%)	71±11	71±12	71±11	NS

CONCLUSION. TGI is a safe adjunct to mechanical ventilation in patients with SHI and ALI, allowing ventilate patients with a more protective strategy (low tidal volume and lower driving pressure) avoiding the resultant increase of $PaCO_2$ and without any deletereous effect in the cerebral pressure and perfusion.

Grant. Fondo De Investigaciones Sanitarias 01/1036

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EFFICACY OF RECRUITMENT MANOEUVRES IN A MODEL OF LUNG INJURY INDUCED BY ALVEOLAR LAVAGE

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INTRODUCTION. Alveolar recruitment manoeuvres (RM) in acute respiratory distress syndrome (ARDS), using elevated pressures, can provide a more homogeneous ventilation, optimising gas exchange and avoiding mechanical ventilation-associated injury. We assess the efficacy of MR in a porcine model of alveolar lavage-induced ARDS.

METHODS. ARDS was induced by saline serum in 10 pigs that were randomly assigned to one of two ventilation regimens. Group I (n =5) underwent volume-controlled ventilation with tidal volume of 10 ml/Kg, breathing rate of 15 rpm and PEEP of 10 cmH2O at FiO_2 of 1. Group II (n=5) underwent a single RM by pressure-controlled ventilation, with a staged increase in PIP and PEEP to 60 and 40 cm H2O, respectively. The same regimen as for Group I was then applied. Haemodynamic and respiratory variables were recorded. Finally, both lungs were extracted for histological and histomorphometric analyses

RESULTS. PaO_2 increased by 166+44% in Group I and by 275±160% in Group II. Compliance increased by 52±44 in Group I and 71±35% in Group II. The mean alveolar area was greater in Group I than Group II (751 vs. 486), with a smaller coefficient of variation in Group II (47 vs. 26). There were no differences in histological lesions between the groups

CONCLUSION. The application of a single RM generated a greater alveolar volume with a more homogeneous distribution of the ventilation, without causing haemodynamic deterioration or additional lung injury

Grant. FISS

Oral Presentations
Ethical issues in research and clinical work – 731-736

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VALUE OF INFORMED CONSENT FOR RESEARCH IN INTENSIVE CARE

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INTRODUCTION. For clinical studies the declaration of Helsinki states that «after ensuring that the subject has understood the information, the physician should then obtain the subject's freely given consent, preferably in writing » (1). Because of the unforeseen character of the complications leading to the intensive care unit (ICU), informed consent can be obtained only after admission. However the severity of illness, the multiple treatments, the psychological status and the stressful environment may impair the competence of patients. The aim of this study was to investigate the value of written informed consent in ICU. We hypothesized that many ICU patients will be unaware of the study, its objectives and the imposed burden after ICU discharge.

METHODS. Patients with SIRS score >1, but no septic shock, after major surgery or trauma, Glasgow coma scale (GCS) 15, fully oriented, non intubated and judged competent to give their informed consent were considered for inclusion to a study on inflammatory mediators (2). Patients were informed about the study objectives and the imposed burden during a 20 min oral protocolled presentation and received a written leaflet of 1 page. We noted if the patient read the leaflet and/or asked questions about the study before giving consent. 10 days after ICU discharge, we asked patients about their awareness of a study, its objectives and the burden.

RESULTS. We obtained 68 informed consents for this study, 20 from next-of-kin and 48 from patients themselves. Of those, 44 survived ICU. 10 days after ICU discharge, 35 were aware about their study participation, 20 about the objectives, 22 about the burden. Only 14 (32%) were aware of all 3 points, 9 (20%) could not mention any. There was no difference in age, sex, SAPS score, diagnosis, temperature, GCS, renal and hepatic function, glycemia, natriemia, psychotropic drugs use except morphine between patients totally aware of the study and the others. Patients who read the leaflet and asked at least 1 question before signing the consent form were more likely to mention their participation, the objectives and the burden (OR 4.9, 95% CI 1.1-21.7). Patients who were completely unaware of their study participation had previous history of alcohol abuse (OR 13.3, 95% CI 2.3-78.2) or had received more morphine during the last 24 hours than the remaining (22±20mg vs. 9±16mg, p<0.05).

CONCLUSION. Even if patients seemed competent, the majority were unaware of participation to a study, its objectives and their burden after ICU. History of alcohol abuse, morphine administration of >10 mg/24h, lack of reading the written leaflet or asking question, were factors which favored incorrect answers regarding the study for which patients had given their consent. The value of consent for research given in ICU setting is questionable.

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IMPACT OF ETHICS STUDIES ON END OF LIFE DECISIONS

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INTRODUCTION. Conducting studies on end of life (EOL) decisions may alter physician behaviour. Although assessment of a such influence is diffICUlt, we attempted to obtain a picture of the possible impact of ethics studies on end of life decision.

METHODS. We compared EOL decisions during two periods of time. During the first period an observational ethics study was conducted. The ICU physicians responsible for EOL decisions were very much involved in that study as they had to fill in a thorough questionnaire. The second period started after the ethics study; during that period the ICU physicians responsible for EOL decisions were not involved in the questionnaire. They were just questioned about the limitation decision and the reason for limitation. Statistical analysis were processed using Chi square test for contingency tables and ANOVA when applied.

RESULTS. From January 1999 to June 2000 (Ethics study period, 18 month), 2017 patients admitted in the ICU were screened. Among them 148 patients had limitation of life support. From July 2000 to February 2002 (Post Ethics study, 19 month), 2326 patients were screened. During that second period, 203 patients had limitation of life support. Case mix was comparable in both periods for all demographic parameters but not for mean APACHE II score (p < 0.0001). One major observation was the differences in limitation of life support. There were more decision of withdrawal plus lethal sedation during the Ethics study period (p < 0.001). We also observed differences in the main reason for limitation support. In the Post Ethics study period age was a more frequent reason while poor quality of life was less frequent (p < 0.0001).

	Ethics Study	Post Ethics study
CPR	27 (18.2 %)	37 (18.2 %)
Withholding	52 (35.1 %)	93 (45.8 %)
Withdrawal	14 (9.5 %)	39 (19.2 %)
Withdrawal+lethal sedation	55 (37.2 %)	34 (16.7 %)

Limitation of life support decisions

	Post Ethics study	
Neurological	40 (29.9 %)	53 (37.3 %)
Chronical disease	10 (7.5 %)	--
Family request	1 (0.7 %)	1 (0.7 %)
Quality of life expentency	18 (13.4 %)	9 (6.3 %)
No response to maximal therapy	61 (45.5 %)	51 (35.9 %)
Age	4 (3.0 %)	28 (19.7 %)

Main reason for limitation of life support

CONCLUSION. Ethics studies are an important source of information to improve the knowledge on end of life care. However researchers should be aware that such studies may have an impact on limitation therapy and may turn out to be an ethical issue.

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A 12-MONTH OBSERVATIONAL STUDY OF POTENTIAL ORGAN DONORS IN 12 AUSTRALIAN HOSPITALS

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INTRODUCTION. At an average of 10 donors per million population (pmp), the Australian organ donation rate is amongst the lowest in the Western world. To understand why the Australian rate is persistently low we undertook a 12 month observational study of all hospital deaths in 12 hospitals in the Australian state of Victoria.
METHODS. All deaths in 12 hospitals were assessed over a 12 month period by medical record review. Potential donors were defined as patients with actual or potential brain death and who were medically suitable for organ donation. Data was collected on the number of requests, consents, organ donors, refusals, failed physiological support, and possible unrealised donors. This last group were reviewed by an independent panel of intensivists who categorised them as follows: Category I – formally diagnosed brain death, Category II – likely to progress to brain death < 24 hours, Category III – likely to progress to brain death > 24 and < 72 hours, and Category IV – unlikely to progress to brain death < 72 hours (therefore not a potential organ donor).
RESULTS. Of the 5551 deaths, 156 patients were identified as possible potential donors. Of these, organ donation was requested in 66 and consent obtained in 39 (59% of requests). Organ retrieval occurred in 37 (0.7% of hospital deaths), two donors had failed physiological support. The panel of intensivists classified the remaining 90 cases: Category I: 3, Category II: 24, Category III: 19 (Cat I to III = unrealised potential donors) and other patients either as Category IV (42) or not medically suitable (2). Two of the patients in Category I were suitable for multi-organ donation however consent was not requested. Of Cat II patients, treatment was withdrawn either in the ICU or the emergency department and half of the patients had clinical features consistent with brain death, though formal testing had not been performed. The median age of Category II patients was 56 (range: 2-72), intracranial haemorrhage the most common cause of brain injury and 9 patients would have been suitable for multi-organ donation. An improvement on the current rate of 10 donors pmp up to 21 pmp may be practically achievable through additional detection and support of potential donors and an improved consent rate of 80%. The theoretically maximal potential donor rate, which assumes detection and support of all potential donors and no refusals, is estimated to be between 26 and 30 donors pmp. This is lower than the often quoted maximum theoretical rate of 50 donors pmp and the actual organ donation rate achieved in Spain (33.6 donors pmp in 1999). This may be due to differences between Australia and other countries in the incidence of head trauma, intracranial haemorrhage and other causes of brain death, and in the management of patients with these injuries/illnesses.
CONCLUSION. The rate of confirmed brain dead missed potential donors is low compared with other studies. There is potential to improve the organ donation rate through improving the detection and support to organ donation of potentially brain dead patients, and in improving the consent rate.

Grant. Victorian Department of Human Services

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SYMPTOMS OF ANXIETY AND DEPRESSION IN RELATIVES OF ICU PATIENTS

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INTRODUCTION. The prevalence of symptoms of anxiety and or depression in family members of ICU patients has been the focus of only few studies. What has not been examined though is whether the family members perceive the atmosphere of ICU as a stressful or traumatic experience, with the result symptoms coinciding with an acute stress reaction. More over we examined, we believe for the first time in this population, the impact of the ICU itself on the family members and searched for correlation with symptoms of anxiety and depression.

METHODS. We have studied in a group of 45 family members visiting their patients in ICU the prevalence of symptoms of anxiety and depression and looked for associations with demographic and clinical variables of the patient and the family members. As family members were defined all the individuals who visited the patient in the ICU, regardless of their relationship to him. The participants were informed about the purpose of the study and were asked to complete a questionnaire. They were visiting the ICU for at least one week. We used as tool the Hospital Anxiety and Depression Scale (HADS). HADS is 14-item self administered questionnaire. Seven items evaluate depression and seven items evaluate anxiety. Each item is scored on a 4-point scale (ranging from 0-3). A cut off point of 11 on the anxiety or depression was chosen as reliable for discriminating between persons with and without anxiety and depression. For each patient the following information was recorded: age, gender, marital status, and occupation, reasons for ICU admission and clinical status including APACHE II and GLASGOW SCALE. For the family members we recorded age, sex, relationship to the patient and frequency of visits

RESULTS. Regression analysis show that there is a strong significance between HADS, apache ii (p=0.000), gender (P=0.02) and age (P=0.047) of the patient. y=40.4+ 14.5 apache II-8,41gender-.18 age

	n	%	p	% CI
prevalence of anxiety and or depression (cut off point >11)				
depression	30/45	62	0.000	-9.20 -6.13
anxiety	38/45	84	0.000	-8.23 -5.56

CONCLUSION. 1.The prevalence of symptoms of anxiety and depression in family members of ICU patients are high 2.Severity of the condition, age and gender of the patient are associated with symptoms of anxiety and depression

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PREDICTED SURVIVAL AND INTENSIVE CARE UNIT ADMISSION DECISIONS

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INTRODUCTION. The introduction of the Human Rights Act[1] in October 2000 and the associated advice given in the Joint Statement[2] has further complicated decisions surrounding intensive care admission. We sought the views of intensive care clinicians based on a real patient scenario.
METHODS. A questionnaire was circulated through the Intensive Care Society Linkmen detailing an 88 year old who arrested after arrival in hospital. Following resuscitation her Glasgow Coma Score was 5 and she scored 2 APACHE II[3] points for heart rate, blood pressure and haemoglobin concentration. Respondents were asked to predict likelihood of survival, their view on her admission to intensive care, what action they would take if she arrested again and the role of her family in the decisions.
RESULTS. APACHE II predicted mortality was 85%, analysis of our own database of 215 similar cases showed a predicted risk of death of 91%. There were 169 replies (86% consultants). Of the 22% who felt her chance of survival was 1% or less, 26% would admit the patient. Overall, 63% would admit, 11% would resuscitate, 10% thought the views of the family of no importance, 4% thinking them vital. Trainees' averaged estimate of her survival was 9%, 71% admitting the patient and 14% resuscitating again.

Estimated chance of survival (%)	Number of Consultants (%)	Average Years experience in ICU	Would admit (%)	Would resuscitate again (%)	View of family 'Not Important' (%)
0-4	43 (30.1)	12.6	23.8*	0	23.3
5-9	40 (28.0)	12.3	65.0	7.5	2.6*
10-14	34 (23.8)	9.8	72.7*	6.1*	5.9
15-19	2 (1.4)	6.5	50.0	0	0
20-24	12 (8.4)	9.8	91.7	25.0	0
>25	12 (8.4)	12.7	100.0	45.5*	8.3

*Summary of consultants' questionnaire responses, *Denotes denominator change because of missing fields*

CONCLUSION. Some estimating survival at 1% or less were prepared to admit the patient, some predicting survival above 15% were prepared to refuse. Vincent[4] reported 73% of responding European intensive care units admitted patients with no hope of survival, a situation likely to worsen with the new roles given to patients and their families[2]. Our survey illustrates the diffICUlty in establishing a consensus regarding which intensive care admissions might be futile[5].
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PROGNOSTIC FACTORS IN PATIENTS REFUSED ADMISSION TO ICU

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INTRODUCTION. Triage of admission to ICU should be based on potential benefit. In terms of survival, benefit is the increment in probability of survival attributable to ICU admission. In order to estimate benefit it is necessary to estimate both the probability of survival if admitted to ICU and the probability of survival if refused admission. As there are no studies of prognostic factors in patients refused admission it is diffICUlt to estimate the probability of survival if refused admission.

METHODS. Prospective cohort study of patients refused emergency admission to a 22 bed general ICU over a 9 month period. Sex, delay between hospital admission and ICU referral, APACHE II diagnostic coefficient, whether the patient had undergone emergency surgery and the data required to calculate MPM II0 were collected for all patients. The study end-point was hospital survival. Univariate analysis was carried out to determine which variables were significantly associated with hospital survival. These variables were then entered into a multiple logisitic regression analysis to determine the variables that were independently associated with survival. Internal validation of the logistic regression model was carried out using the bootstrap technique.

RESULTS. Two hundred and sixty two patients were analysed. 50% of patients survived to hospital discharge (SMR 1.1 based on MPM II0). Those factors independently associated with hospital survival, with their adjusted odds ratios are given in the table. Calibration (Hosmer and Lemeshow C= 4.13, p=0.845) and discrimination (area under receiver operating characteristic curve=0.86) of the model was good. Bias corrected 95% confidence intervals for calibration were 1.68-12.4 (p=0.13 to p=0.99) and for discrimination were 0.80-0.88.

	Adjusted odds ratio	95% confidence intervals
Coma	0.268	0.096-0.744
Metastatic neoplasm	0.205	0.045-0.933
Gastrointestinal bleeding	0.042	0.005-0.381
Need for immediate mechanical ventilation	0.402	0.199-0.81
APACHE II coefficient -0.282 or less	4.0	2.01-7.958
Age 65 years or less	3.205	1.585-6.484

Table Factors independently associated with hospital survival.

CONCLUSION. Our data indicate that coma, metastatic neoplasm, gastrointestinal bleeding, need for immediate mechanical ventilation, age >65 years and a disease category with a high APACHE II diagnostic coefficient are independently associated with poor outcome in critically ill patients who are refused admission to ICU.

Oral Presentations
Antibiotic usage and resistance – 737-742

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CONTROL OF ANTIBIOTIC USAGE AND PRESCRIBING IN EUROPEAN ICUS: A ESICM SURVEY

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INTRODUCTION. Antibiotics are largely and often inappropriately prescribed in ICUs, which may increase resistance rates. Organisation and structure to improve antibiotic prescribing at the hospital and especially the ICU level may help improve these problems.

METHODS. The ESICM Infection Section performed a survey of organisation for and actual antibiotic prescribing in volunteer ICUs across Europe. ICU physicians recorded existing organisation and structures, at their institution and ICU level, implemented for control of antibiotic prescribing and counselling; actual antibiotic use in ICU patients on a given day (prevalence study) was also recorded, followed by a two-week incidence study.

RESULTS. Of 44 units participating in 8 countries, data on 31 units have been analysed so far. These 31 units belonged to university (n=20) or affiliated (n=8) hospitals, were medical (n=8), surgical-trauma (n=11) or mixed (n=12) ICUs, and included 495 beds. Eight hospitals (26%) had no full-time pharmacist, 4 (13%) no full-time microbiologist, and an infectious diseases (ID) unit was present in only 16 (51%) institutions. A hospital formulary existed in 19 (61%), and antibiotic prescribing guidelines in 22 (71%); guidelines specific to ICUs existed in 18 units. A microbiological consultation was available in 27 hospitals, but daily ICU consultation was available in only 17 (55%) ICUs. Pre-approval of prescriptions by a pharmacist, a microbiologist, or an ID consultant was operating in 15 institutions, but relied on a dedicated ICU physician in 6 ICUs; renewal of prescriptions was controlled in only 16 hospitals and ICUs, and automatic stop-orders in only 5 (16%). Summary reports of antibiotic use and resistance were available at the hospital level to 68% institutions; however, such data were available at the ICU level in respectively 68% and only 19% of ICUs. Of the 31 ICUs, 24 (77%) had experienced at least one outbreak of multi-drug resistant organism, including MRSA in 18 (75%). On the first-day prevalence survey in ICUs, 259 of 469 ICU patients (55%) were receiving antibiotics for prophylaxis or therapy of infection. During the 2-weeks incidence study, there were 1084 patients admitted, of whom 677 (62.5%) received antibiotics during their ICU stay.

CONCLUSION. This study confirms the high exposure of ICU patients to antibiotics, and the high prevalence of multi-drug resistance problems in these high-risk areas. Although most hospitals have implemented some measures to improve antibiotic use, many hospitals and even more ICUs do not have appropriate structures for monitoring antibiotic usage and prescribing stewardship, or follow-up of antibiotic use and resistance.

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MOLECULAR CHARACTERIZATION OF GLYCOPEPTIDE-RESISTANT ENTEROCOCCUS FAECIUM (GREF) ISOLATES IN ICU

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INTRODUCTION. Glycopeptide-resistant enterococci are a growing clinical problem with a complex epidemiology that varies in different countries. They have an increasing rate of spread within hospitals, especially in ICUs(1).We investigated the dissemination of GREF during its emergence in a 26 bed multidisciplinary ICU.

METHODS. All GREF isolates recovered from ICU patients between February 1999 and April 2001 were studied. Clinical data from all ICU patients with GREF infection were collected. Identification of strains and antibiotic suscebtibility testing by MIC were performed. All the isolates were examined for the presence of *vanA* and *vanB* genes by polymerase chain reaction (PCR) analysis. Pulsed-field gel electrophoresis (PFGE) of *Sma*I digested genomic DNA of GREF strains was performed with a countour-clamped homogeneous electric field apparatous (CHEF DRIII Bio-Rad Lab).

RESULTS. A total of 21 multiresistant enterococci strains were isolated from a same number of ICU patients. The majority of isolates were obtained from surgical patients (n=17). The specimen sites of GREF isolation were surgical drainage (n=9), blood (n=7), peritoneal fluid (n=3), iv catheter (n=1) and urine (n=1). The preinfection mean length of ICU stay was 40±31 days. All patients had a long duration therapy with vancomycin prior to GREF isolation. The phenotype of all GREF isolates was vanA. The *vanA* glycopeptide resistance genotype was found in all isolates.The GREF isolates exhibited 5 distinct banding patterns. The majority of isolates (67%) were distributed in two PFGE patterns.

CONCLUSION. GREF infections in our ICU have been emerged in patients with a long ICU stay and surgical procedures.All GREF isolates showed *vanA* genotypes. The major two PFGE patterns of the GREF isolates suggest possible transmission within the ICU.These results indicate the need for continuous surveillance, prudent use of antibiotics and effective infection control measures.

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RISK FACTORS FOR ACQUISITION OF MULTIRESISTANT PSEUDOMONAS AERUGINOSA IN ICU PATIENTS

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INTRODUCTION. The emergence of strains of P. aeruginosa (Pa) resistant to antipseudomonal antibiotics cause therapeutic problems. Our aim was to study risk factors for acquisition of multiresistant Pa (MRPA) in ICU patients

METHODS. During a 2-year period, MRPA (i.e. resistant or of intermediate sensitivity to imipenem [Imi], ceftazidime [Cef], piperacillin [Pip] and ciprofloxacin [Cip] was acquired (> 2 d. after admission) by 37 patients (cases: C) from 3 ICUs of a single 1200-bed University Hospital. The time to acquisition was (mean ± SD [median]) 29.5 ± 4.3 (26) d. A case-control study was performed. Controls (Ct) were patients in whom no Pa has been isolated. Matching criteria were the gravity score (SAPS II) upon ICU admission and a length of ICU stay at least as long as time to MRPA acquisition in C (exposure period [EP]). C and Ct were compared for baseline characteristics, use and duration of invasive procedures (ventilatory support, urinary, central venous and arterial catheters, hemodiafiltration, pulmonary-artery catheter) and antimicrobials (>48 hours) during EP.

RESULTS. No adequate control was found for 3 C. Gravity scores upon ICU admission (SAPS II, APACHE II, OSF), baseline characteristics, immunosuppression, McCabe score, use and duration of invasive procedures and ICU mortality were not significantly different between the 34 C and 34 Ct, except for the use of hemodiafiltration. In the univariate analysis, significant differences were: duration of Cef (mean duration [days] in C and Ct, 2.0 vs 0.1, P= 0.05), Imi (6.2 vs 2.6, P= 0.006), Pip (with or without tazobactam) and ticarcillin (3.4 vs 0.9, P= 0.03), all antipseudomonal drugs together (16.1 vs 5.2, P= 0.001), whereas a trend was observed for Cip (4.5 vs 1.7, P= 0.11), and non antipseudomonal drugs conferred "protection" (3.8 vs 9.1, P= 0.002). In the multivariate analysis (conditional logistic regression), the use of antimicrobials was categorized in three groups: no use, and use for less or more than the median percentage of days (MPD) with the antimicrobial during EP. Only Cip given for more (>34%) than the MPD was associated with MRPA acquisition (OR, 13.7; 95%CI, 1.65-114; P= 0.015).

CONCLUSION. After adjustment for length of exposure period and gravity score, only previous Cip use was associated with acquisition of MRPA, a variable amenable to intervention.

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EVOLUTION OF MARKERS OF MULTIRESISTANCE TO ANTIBIOTIC IN ICU-ACQUIRED INFECTIONS

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NTRODUCTION: Objetive: To determine the time-course of markers of multiresistance to antibiotics in ICU-acquired infections.

METHODS. Cohort, prospective, multicenter study. Patients admitted to the participating ICUs from 1994 to 2000 were included in the study. Patients 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, catheter-related urinary tract infection, and primary bacteremia. Markers were defined according to CDC criteria (Am J Infect Control 1999;27:279). Data are expressed as percentage of resistant isolates to the antibiotics selected.

RESULTS. A total of 3555 infections occurred in 27,756 patients and were caused by 3855 multiresistant pathogens, with the following evolution of markers of multiresistance:

	1995	1996	1997	1998	1999	2000
E coli-R a cefotaxima	0	0	0	2,7	4,7	2,7
E coli-R a ciprofloxacino	6,3	9,8	10,7	8,1	10,9	29,0
P aeruginosa-R a ceftazidmia	17,6	17,5	25,8	11,1	19,1	11,0
P aeruginosa-R a ciprofloxacino	14,7	21,7	29,0	11,1	14,7	23,6
P aeruginosa-R a imipenem	26,5	15,8	25,8	7,4	16,2	11,3
A baumannii-R a imipenem	7,1	19,3	23,1	21,7	57,5	25,0
S aureus-R a meticilina	19,2	17,8	9,4	15,6	44,0	30,1
CNS-R a vancomicina	0	0	0	0	0	1,3

CONCLUSION. There has been intermittent increases of markers of multiresistance.

REFERENCES. Envin-Uci Study

Grant. Aventis

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TREATMENT OF VENTILATOR-ASSOCIATED PNEUMONIA (VAP) DUE TO MULTIRESISTANT *ACINETOBACTER BAUMANNII*

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INTRODUCTION. To assess the efficacy and toxicity of intravenous colistin in the treatment of VAP due to multi-drug resistant *Acinetobacter baumannii* (Ab) comparing with imipenem, the standard antimicrobial of choice.

METHODS. Prospective study of 37 episodes of VAP (CDC criteria) due to multiresistant Ab. Microbiologic diagnosis was performed by quantitative tracheal aspirate or by protected specimen brush. Cases due to strains only sensitive to colistin, were treated with i.v. colistin methansulfonate (3-5 mg/Kg/day). Doses were adjusted to renal function. If other antimicrobial treatments were possible, antibiotherapy was chosen according to the antibiogram. Evaluated variables: APACHE II and SOFA score; clinical picture; treatment duration; clinical improvement; microbiologic eradication; renal, hepatic, hematologic, and neurologic toxicity. Renal toxicity was defined as an increment of serum creatinine greater than 2 m/dL or a fall in urine output greater than 50%. Chi-square and T-student tests were used. Results were considered statistically significant when p<0.05.

RESULTS. Colistin was used in 21 cases (Group C), Imipenem in 14 cases (Group IM) and others (2 cases). APACHE II at the admission(19.6 ∂7.2 vs. 20.5 ∂7) and SOFA score at the diagnosis of VAP(10∂4,9 vs11,7∂6,6) were similar in both groups, as well as was the incidence of severe sepsis or septic shock (86% vs. 79% p=NS). Four bacteremic VAP, two in each group, were detected. Empiric antimicrobial therapy was adequate in 19% of cases of group CO and in 71% of episodes group IM (p=0.002).The mean treatment duration was 11 days in both groups. VAP was considered clinically cured in 57% of cases in both groups.The in-hospital crude mortality was 62% in group C and 64% in group IM (p=NS), and the attributable mortality 40% and 39% respectively. Three patients in group C and 5 in group IM developed renal toxicity respectively (p=NS). Electrophysiologic tests were performed in 12 cases in group C. No signs of neuromuscular blockade were noted.

CONCLUSION. Intravenous colistin appears to be, at least, as safe and efficacious as imipenem in the management of VAP due to multiresistant Ab.

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PATIENT-GUIDED VERSUS SCHEDULED ANTIBIOTIC THERAPY. IMPACT ON MULTIRESISTANT PATHOGENS EMERGENCE

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INTRODUCTION. Antibiotic cycling has been suggested as an efficacious strategy to prevent the emergence of mutiresistant pathogens. We evaluated the impact of implementing scheduled use of an antibiotic class on the emergence of multiresistant microorganisms and compared it with a previous period of patient-based antibiotic policy.

METHODS. Prospective, non-randomized study comparing two periods of empirical antibiotic policy for ventilator-associated pneumonia (VAP). Basal period (BP): 10 months using an early broad-spectrum coverage (Carbapenems, Cefalosporins, Piperacillin/Tazobactam, Ciprofloxacin) depending on patient´s previous antibiotic exposure and followed by de-escalation according with culture results. Carbapenem period (CB): Four-month period using carbapenems as first line therapy. Epidemiological (age, gender, APACHE II), antimicrobials use, and microbiological variables during the study periods plus one month were recorded. Statistical analysis: CIA package. Significant = P<0.05

RESULTS. 1010 patients consecutivelly admitted to a medical-surgical ICU during a 14 month period were included. 70.8% were males and mean age was 59.7± 16.0 years old. APACHE II was of 14±3.4. No statistical differences were found between groups. Carbapenems were the most prescribed antibiotics in the CB period (13.7 vs 9.08 in the basal period; OR 1.45). The use of Cefepime, Piperacillin/Tazobactam and Ciprofloxacin (in DDP/100 stays) was 6.0 vs 2.7 in the basal period; 9.2 vs 14 in basal period and 8.8 vs 5 in basal period, respectivelly. This was associated with an increase in the incidence of *Acinetobacter baumannii* (Table 1). The incidence of patients with Carbapenem-resistant *Acinetobacter baumannii* (CRAB)increased 20-fold during the CB period (0.3% vs 7.4%; OR 21.1 CI 95%: 5.9-75.2)

	Basal Period	CB Period		
Microorganism	% patients	% patients	OR	P value
P. aeruginosa	6.4	8.6	1.3	NS
A. baumannii	1.9	9.8	5.2	<.05
Enterobacteriacae	6.9	9.2	1.3	NS
MSSA	4.0	5.7	1.4	NS
MRSA	2.1	3.4	1.6	NS

Table. 1

CONCLUSION. A patient-guided antibiotic policy prevents the dominant use of a single class of antibiotic and emergence of resistance to that class

Grant. FIS Project: 00/1137

Oral Presentations
Neurosurgical intensive care – 743-748

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BRAIN TISSUE OXYGEN TENSION IN CEREBRAL FOCAL LESIONS

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INTRODUCTION. The position of the cerebral oxygen tension ($PtiO_2$) sensor in acutely damaged brain may affect both baseline values and the response to changes in cerebral perfusion pressure (CPP). We evaluated the relation between probe position as assessed on CT and baseline $PtiO_2$ and determined the $PtiO_2$ response to a CPP challenge according to different position.

METHODS. In 26 comatose patients (10 TBI and 16 SAH), aged 45±17, a $PtiO_2$ sensor was placed targeting penumbra-like areas. The position of the probe was subsequently assessed on CT scan and 2 groups were defined: patients with the probe inserted in normal appearing tissue adjacent to focal damage (non focal NF) and patients where the probe was within focally damaged tissue (focal F). In those patients who underwent a CPP increase test the $PtiO_2$ response was measured as Delta$PtiO_2$/$PtiO_2$baseline.

RESULTS. There were no differences between NF and F group in CPP, $PaCO_2$, PaO_2 and Temperature while $PtiO_2$ baseline values were 33±19 and 19±11 mmHg respectively (P < 0.05). On average CPP changed from 65±10 to 86±13 mmHg (P<0.001) and caused a change in $PtiO_2$ from 24±16 to 28±17 mmHg (P<0.001). In the NF group the $PtiO_2$ response was 0.18 while in the F group $PtiO_2$ response was 0.57.

CONCLUSION. $PtiO_2$ is lower at the margin of a focal lesion compared to $PtiO_2$ measured in normal appearing cerebral tissue. In focal lesions capillary density is reduced by edema or CBF may be compromised: both mechanisms may explain the critical $PtiO_2$ values detected in these regions. Furthermore while the change in CPP in non focal tissue does not improve the $PtiO_2$, in the focally lesioned tissue CPP increase is associated with a $PtiO_2$ increase probably due to CBF improvement. Focal monitoring is able to disclose volumes of damaged tissue that can benefit from therapeutic maneuvers. The benefits of increasing $PtiO_2$ are still to be demonstrated

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BRAIN TISSUE PO_2 VALUES ACCORDING TO TYPE OF LESIONS AND PROBES LOCATION IN HEAD INJURY PATIENTS

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INTRODUCTION. Although brain tissue oxygen pressure monitoring ($PtiO_2$) is a local measurement it seems to be useful in the management of head injured patients when the probe is located in a healthy brain area. The aim of this study was to investigate the relationship of $PtiO_2$ values and outcome (GOS) according to the type of the lesions and insertion site of the probes.

METHODS. In addition to ICP and CPP , we measured continuously $PtiO_2$ in 59 patients (GCS<9) who were classified into four groups: A (n=22), Marshall II-III with probes inserted in frontal white matter; B (n=20) Marshall V: in 8 of them a probe was inserted in apparently frontal healthy area in the side of the hematoma and in 12 in the undamaged hemisphere; C (n=8) with probes in "pericontusional" area and D (n=8) Marshall V with bilateral $PtiO_2$ monitoring.

RESULTS. In group A, the median percentages of time that $PtiO_2$<20mmHg in patients with GOS:4-5 was 3,5% (0-11,5 hours) and GOS:1-3= 76%(0-100h) (p<0,001,U Mann-Witney). However, there were neither differences in group B (GOS:4-5 =15%(0-87h); GOS:1-3= 27% (0-100h) nor group C (GOS:4-5=39% (20-93h); GOS: 1-3= 79 (40-86h). In the group D $PtiO_2$<20 mmHg was in the side of the hematoma 55%(24-100 h.) and in the opposite 11% (0-78 h.) (p<0,01, Wilcoxon test).

CONCLUSION. Our results suggest that $PtiO_2$ seems to be useful for predicting outcome in patients with diffuse injury. By contrast, patients with Marshall V or with unilateral contusions low $PtiO_2$ values in damaged hemisphere or surrounding contusion do not indicate a worse prognosis, therefore, in these cases bilateral $PtiO_2$ monitoring could be considered.

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COMPARISON OF THE EFFECTS OF NORADRENALINE VERSUS NORADRENALINE/DOBUTAMINE IN NEUROSURGICAL PATIENTS

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INTRODUCTION. Vasopressors are widely used in neurosurgical patients to improve cerebral perfusion. There is considerable data on vasopressors in septic patients but not in this patient population.[1] Data in septic patients suggests that dobutamine maintains tissue perfusion when noradrenaline is used. Dobutamine, however increases $CMRO_2$. We compared the effects of Noradrenaline versus Noradrenaline/Dobutamine on haemodynamics, cerebral perfusion and splanchnic circulation in Neurosurgical patients. Design :Prospective, randomized, cross-over trial

METHODS. Patients: Mechanically ventilated adult Neurosurgical patients requiring vasopressor therapy to increase cerebral perfusion pressure. Intervention: Patients received Noradrenaline for 4 hours, and Noradrenaline /Dobutamine 5ug/kg/min for 4 hours to achieve a target blood pressure. The order of drug administration was randomized. We measured baseline and hourly heart rate, mean arterial pressure, intracranial and cerebral perfusion pressures, lactate and gastric intramucosal pH (pHi) and CO_2 gap (via gastric tonometry). Statistical analysis: Random effects model.

RESULTS. 20 patients (mean age 42), male: female; 4:1.Mean heart rate was higher (91.7±SD vs76.9±SD)($P<0.05$), and mean arterial pressure was lower (93.6±SD vs 98.3±SD)($P<0.05$) with Noradrenaline / Dobutamine , despite the use of higher doses of Noradrenaline in conjunction with Dobutamine. Target Blood pressure was achieved , irrespective of the therapy used. Lactate levels were within normal range (1.17 ±SD vs1.15±SD) during both therapies.Four patients had lactate levels above 2. Intracranial pressure was higher (21±SD vs 19±SD)($P<0.05$) with Noradrenaline/Dobutamine. Cerebral perfusion pressure did not differ significantly (72.3±SD vs 71.1±SD). pHi was lower (7.27 vs 7.29)($P<0.05$), and CO_2 gap was higher (2 vs 1.8) ($P<0.05$), with Noradrenaline/Dobutamine.

CONCLUSION. Gastric mucosal ischaemia occurs in neurosurgical patients receiving vasopressors as reflected by pHi and $PgCO_2$ (normal pHi>7.3, PgCO<1.1Kpa)[2].Ischaemia is greater when Noradrenaline/Dobutamine is infused. Heart rate was higher and mean arterial pressure less with Noradrenaline/Dobutamine. Intracranial pressure was also higher. This study suggests that Noradrenaline should be used alone rather than in combination with Dobutamine in Neurosugical patients.

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SYSTEMIC AND CEREBRAL RESPONSE TO HYPEROXIA IN ACUTE BRAIN DAMAGE

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INTRODUCTION. Although increasing FiO_2 has been suggested as a manoeuvre for determining cerebral regulation or even as a therapeutic tool in acutely brain damaged patients, the mechanisms and the factors affecting this response are not fully understood. Aim of this study is to describe both the systemic and the cerebral effects of a rapid increase of FiO_2 to 100% in acutely brain damaged patients.

METHODS. Twenty-seven patients (14 Females, 43 ∂17 years old) suffering from TBI (12) or SAH with a median motor GCS of 5 have been studied. All of them were monitored with ICP, MAP, SjO_2 for $AVDO_2$ calculation and Tissue oxygen tension ($PtiO_2$) catheter (Licox GMS, Germany and Neurotrend, Codman UK). Sixty-three hyperoxia tests have been performed. Data about physiological variables were collected both at baseline and at the end of tests.

RESULTS. While ICP, MAP, CPP did not significantly change, PaO_2 increased from 136 + 25 to 403 + 73 mmHg ($P<0.001$) and $PtiO_2$ significantly increased as well (from 26 ∂ 15 to 81 ∂ 52 mmHg; $P<0.001$). $AVDO_2$ significantly ($P< 0.001$) decreased from 3.88 ∂ 1.12 to 3.45 ∂ 1.01 vol%, while $PaCO_2$ did not change. $PjCO_2$ significantly increased from 37 ∂ 5 to 38 ∂ 5 mmHg, determining a significant change in Jugular-arterial pCO_2 difference (DCO_2 from 7.35 ∂ 3.2 to 8.37 ∂ 3.3 mmHg; $P<0.05$).

CONCLUSION. Hyperoxia induces dramatic changes in arterial and cerebral oxygen tension but little is known about its cerebral metabolic and vascular consequences. Our data seem to indicate a reduction in cerebral metabolism as measured by $AVDO_2$ decrease. Since cerebral blood flow has not been measured, we can only hypothesise that the DCO_2 increases as consequence of hyperoxia-induced vasoconstriction leading to reduced CO_2 washout, even if other mechanisms, like the Haldane effect, have to be considered.

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EARLY ANTITHROMBOTIC PROPHYLAXIS WITH LOW MOLECULAR WEIGHT HEPARIN IN NEUROSURGICAL PATIENTS

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INTRODUCTION. Despite the moderate to high risk of deep vein thrombosis (DVT) and venous thromboembolic events (VTE) in neurosurgical patients, prophylaxis with heparin has not been established routinely because of the deleterious effects of bleeding complications. After initiating low molecular weight heparin (LMWH) prophylaxis pre-operatively since 1997, we retrospectively reviewed our patients in order to examine this procedure.

METHODS. Over a 3 year period, the records of patients of the Klinikum Dessau with elective intracranial surgery (ES), head injuries (HI) or intracranial haemorrhages (ICH) were analysed. Prophylaxis was performed with CertoparinR (3000 I.E./3ml sc) on the evening before elective surgery, and within 24 hours after surgery or admission whenever the control CT did not show a progressive or post-operative hematoma. Excluded were patients with coagulation abnormalities (prothrombin time <70%, partial thromboplastin time >40s, platelet count <100.000/ml, platelet aggregation test sum <60%). The incidence of bleeding complications, DVT, VTE and resulting morbidity and mortality was assessed.

RESULTS. During the study period, 964 patients were admitted for intracranial lesions. A total of 24 records were excluded for incompleteness. Of the 940 analysed records, 294 were admitted for ES, 344 for HI, and 302 for ICH. As primary contraindications against LMWH we found oral anticoagulation (8.1%), antiplatelet agents (6.7%), and thrombocytopenia (2.8%). Intracranial bleeding complications were recorded in 4.5% (ES 1.4%, HI 7.3%, ICH 4.3%), extracranial bleeding in 0.5% (ES 0%, HI 1.2%, ICH 0.3%). Operative revision was necessary in 2.9% (ES 0.4%, HI 4.4%, ICH 1.5%). Fifteen of 44 patients with bleeding complications had not been treated with LMWH because of coagulation abnormalities. In five patients, bleeding complications led to neurologic deterioriation, resulting in a LMWH-associated bleeding morbidity of 0.5% (ES 1.0%, HI 0.1%, ICH 0.1%), whereas the LMWH-associated bleeding mortality was 0.4% (ES 0%, HI 0.2%, ICH 0.2). DVT occured in 0.2% (ES 0%, HI 0%, ICH 0.7%), VTE in 0.7% (ES 1.0%, HI 0.3%, ICH 0.7%), with an associated mortality of 0.4% (ES 1.0%, HI 0%, ICH 0.3%). Heparin induced thrombocytopenia was excluded in all patients by platelet count on the 5th postoperative day.

CONCLUSION. Despite pre-operative initiation of LMWH prophylaxis in ES respectively within 24 hours after admission in HI and ICH, the 0.4% mortality rate caused by LMWH-bleeding complications was identical to the fairly low 0.4% mortality rate caused by VTE. Overall, the 0.5% LMWH-associated morbidity rate seems acceptable. In patients with intracranial lesions, antithrombotic prophylaxis with Certoparin was assertained to be safe and efficaous when contraindications by coagulation abnormalities are carefully considered and a 12-hour time interval before and after surgery was guaranteed. This retrospective analysis should encourage a prospective trial of LMWH prophylaxis in neurosurgical patients.

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FEVER CONTROL IN NEUROINTENSIVE CARE UNIT PATIENTS USING A NOVEL CATHETER-BASED HEAT EXCHANGE SYSTEM

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INTRODUCTION. Fever (>37.9 ^{0}C) rates of 40-80% have been reported amongst neuro-critically ill patients[1-4]. Standard fever management includes the use of oral antipyretics and if needed, topical cooling blankets. A recent study[5] demonstrated that in spite of utilizing these agents, 57% of febrile episodes lasted longer than 4 hours and 5% lasted longer than 12 hours. Having shown the safety and tolerability of catheter based thermoregulation[6] we now present the results of a phase 3 multicenter, randomized controlled clinical trial.

METHODS. Adult febrile patients having either intracerebral hemorrhage (ICH), subarachnoid hemorrhage (SAH), ischemic stroke (IS) with an NIHSS>8 or traumatic brain injury (TBI) patients with a GCS score of <10 were elligible for this study.Patients received either conventional management of fever, including antipyretics and, if necessary topical cooling blankets or intravascular cooling catheter and if necessary, antipyretics and topical cooling blankets. Core body temperatures were recorded hourly by rectal and bladder probes for 72 hours in all subjects. Fever burden (FB) was defined as the product of time and temperature (degree-hours, ^{0}C-hrs). Safety was evaluated by closely monitoring for all adverse events including an infection surveillance program.

RESULTS. We randomized 296 patients. Final results will be subsequently presented. We are reporting the results of a preplanned interim analysis performed after 198 patients were randomized. The final results are not expected to differ significantly from those of the interim analysis. Of the 198 patients randomized there were 44 with with ICH, 79 with SAH, 23 with CI and 52 with TBI. The two treatment groups were evenly matched by age, presenting illness, baseline Glasgow Coma Scale score, and body mass index. Patients assigned to the heat exchange catheter had a 54% reduction in 72-hour fever burden (catheter patients 3.01 (95%C.I. 2.26-3.93) v.s. controls 6.61 (95%C.I. 5.08-8.54). Other benefits noted were a 65% reduction in the use of cooling blankets, a 72% reduction in the use of other physical means of cooling and a 25% reduction in the use of antipyretics among cather patients compared to control patients (p-values all <.0001). No statistically significant differences were found in death or medical complications between the two groups.

CONCLUSION. Intravascular thermoregulation is a highly effective and safe method of managing fever among patients with neurological critical illness. Compared to conventional medical methods, significant advantages were demonstrated in this trial.

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Grant. Alsius Corporation, Irvine California

Oral Presentations
Monitoring – 749-754

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PROGRESSIVE EEG-FREQUENCY DECELERATION DESPITE CONSTANT DEPTH OF PROPOFOL-INDUCED SEDATION

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INTRODUCTION. It could be of considerable benefit to monitor the depth of sedation on ICU. It is not known, however, whether prolonged sedation possibly influences the EEG activity independent from the level of sedation. To investigate a possible time dependent effect of prolonged sedation on EEG activity we analyzed the EEG frequency in a prospective controlled trial while keeping the patients at a constant level of prolonged sedation.

METHODS. In 20 patients necessitating postoperative sedation for at least 48 hours a bifrontal EEG was recorded. During sedation using propofol (1-4mg/kg/h) and fentanyl (1.5-2.5 mg/kg/h) the depth of sedation was kept constant at a level according to Ramsay Scale 3 while adjusting the dosage of propofol given per hour. The depth of sedation was monitored hourly by a physician. At hour 6, 18, 30, and 42, blood samples were taken to assess the plasma concentration of propofol. From the raw EEG data the relative band power of the beta-, alpha-, theta-, and delta band, median frequency (SMF), and spectral edge frequency (SEF) -90, and -95 were computed. The EEG data obtained during one hour before blood sampling was performed were considered for analysis. For statistical analysis a polynomial one-factorial repeated measures analysis of variance with covariates was performed.

RESULTS. The aimed level of sedation at Ramsay Score 3 was maintained in 84% of all measuring points. Relative power of beta- and alpha-wavebands showed a constant and significant decrease over time whereas relative delta-power increased (Table 1). The theta-waveband remained unchanged. Accordingly, SEF-90, -95, and SMF decreased significantly. From hour 6 to hour 18 a significant increase of the plasma propofol concentration was found. Subsequently, the level remained constant.

	relative band power [%] beta-waveband	relative band power [%] alpha-waveband	relative band power [%] teta-waveband	relative band power [%] delta-waveband
6 h sedation mean (± SD)	15.5 (± 2.3)	14.8 (± 2.0)	13.3 (± 1.2)	56.4 (± 3.5)
18 h sedation mean (± SD)	10.3 (± 1.7)	13.4 (± 1.6)	12.8 (± 2.9)	63.4 (± 3.1)
30 h sedation mean (± SD)	10.3 (± 1.9)	10.0 (± 1.2)	14.1 (± 1.2)	70.7 (± 5.1)
42 h sedation mean (± SD)	7.6 (± 1.2)	8.3(± 1.1)	11.8 (± 1.4)	72.3 (± 3.1)

Relative band power presented for all wavebands, separately

CONCLUSION. Despite constant depth of sedation a longer period of propofol application induces a time dependent EEG frequency deceleration. The use of EEG derivatives to monitor the depth of sedation on ICU during prolonged sedation should thus be regarded cautiously.

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COMPARISON OF TISSUE METABOLISM DURING ENDOTOXEMIA AND HEMORRHAGIC SHOCK

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INTRODUCTION. Tissue hypoperfusion and ischemia during different conditions of shock is known to contribute to the pathogenesis of multiorgan failure (1). Hemorrhagic shock and endotoxemia have been suggested to cause profound changes to the cellular metabolism, partICUlarly by maldistribution in tissue microcirculation, which is often diffICUlt to detect by routine clinical monitoring. Aim of the present animal-experimental study was to ob-jectify the effect of different etiologies of shock states to cellular metabolism by using in vivo microdialysis.

METHODS. After approval by the local ethics committee 10 female pigs (33+7kg b.w.) were involved in this study: after induction of general anaesthesia and controlled ventilation (FiO_2 0.3) 5 animals (ES) were challenged with endotoxin infusion (S. fried. H909, 1mg/kg b.w./hr), while 5 animals were exposed to hemorrhagic shock (HS) by induction of acute blood loss (25ml/kg b.w.). Haemodynamic parameters (MAP, HR, PAP, CO), SvO_2 and blood gas analysis including lactate (ABL, Radiometer/ Copenhagen)) were determined in intervals of 30 min during an observation period of 5 hours. Additionally microdialysis catheters (CMA 60, Microdialysis/Sweden)were inserted into the intramuscular (im), subcutaneous (sc) and intrahepatic (hep) tissue to determine the interstitial concentrations lactate and glycerol.

RESULTS. Induction of HS resulted in significant lower values for MAP (30+18 mmHg vs. 64+26 mmHg) and CO (1.5+0.5 vs. 3.2+1.7 l/min) than endotoxemia did ($p<0.05$). SvO_2 after HS remained at significantly higher levels (69+10 %) than after endotoxin infusion (30+7 %; $p<0.05$). Arterial pH and pO_2 were significantly higher in the HS group ($p<0.05$), while blood lactate did not show any significant differences. In contrast interstitial concentrations for lactate after ES rose to significantly higher levels than after HS (im: 4.1+1.1 vs. 7.4+1.9 mM, sc: 8.4+2.3 vs. 4.8+1.3 mM, hep: 7.3+1.4 vs. 5.6+1.3 mM; $p<0.05$). Endotoxin infusion induced 5fold increase and significant higher glycerol concentrations of im, sc and hep than after HS ($p<0.05$).

CONCLUSION. Using microdialysis we were able to objectify the effects of different shock states onto metabolic changes in various tissues. Despite significantly better hemodynamic values for the ES group, more profound tissue effects like lactate accumulation and membrane damage (glycerol-increase) were observed after endotoxemia. Our data recommend the relevancy and necessity for biochemical tissue monitoring. Tissue metabolism objectified by microdialysis, more than hemodynamic parameters might be another target the therapy should be focussed on.

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NON-INVASIVE DETECTION OF INDOCYANINE GREEN KINETICS IN LIVER TRANSPLANTATION

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INTRODUCTION. The plasma disappearance rate of indocyanine green (PDRICG) using a new developed non-invasive digital pulse ICG densitometry was compared to simultaneous invasive fiberoptical dye dilution in the abdominal aorta in patients undergoing orthotopic liver transplantation (OLT).

METHODS. 14 patients undergoing OLT for end-stage liver cirrhosis without venovenous bypass and in 1 patient undergoing intrahepatic caval resection on venovenous bypass were investigated. Pulse-dye densitometry using a fingertip sensor and a prototype of the corresponding LiMON device (PULSION Medical Systems, Munich, Germany) was used to detect PDRICG non-invasively. Therefore, bolus injections of ICG were performed intra-veneously. PDRICG was then derived from the exponential decay of the ICG concentration time course. The COLD System (PULSION Medical Systems, Munich, Germany) was used as reference method. It also calculates PDRicg from downslope time of the ICG concentration measured invasively by a fiberoptic-catheter technique. Observers were blinded to the nonivasive results.

RESULTS. 71 simultaneous measurements widely spread over the clinically interesting range of PDRICG (no error alerts of both devices, no artefacts) were taken into statistical analysis (see Table 1). Linear regression analysis showed a very close correlation between the two methods ($r=0,941$, $p<0,0001$). Bias was not correlated to cardiac output (CO, $r=0,008$, $p=0,95$).

Period	n	CO (l/min)	PDRICG (%/min) invasive	PDRICG (%/min) noninvasive	Mean between methods	Bias
All	71	8.5±2.9	11.8±9.8	10.5±7.8	11.1±8.7	-1.3±3.6
Preparation	40	7.8±2.8	6.3±4.9	5.9±4	6.1±4.2	-0.4±2.6
Reperfusion	15	10.2±3.9	23.7±6.7	20.1±5.6	21.9±5.9	-3.6±4
Postoperative	16	8.9±1.1	14.5±10.6	12.9±7.8	13.7±9	-1.6±4.5

Table 1. Data are presented as mean ± SD.

CONCLUSION. PDRICG has been shown to be a reliable prognostic indicator in patients with sepsis, before liver resection and after OLT, but not widely applicated by clinicians due to the time consuming and/or invasive measurement methods. During and after OLT, non-invasively detected values of PDRICG were comparable to the reference method despite substantial changes in liver function and hemodynamics. We conclude that non-invasive digital pulse ICG densitometry is as accurate as, as invasive fiberoptic measurement of PDRICG and easily clinically applicaple.

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PRELIMINARY RESULTS OF A CONTROLLED TRIAL ON THE USE OF HEPATASSIST IN FULMINANT HEPATIC FAILURE

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INTRODUCTION. The HepatAssist® bioartificial liver support system (BAL) is an extracorporeal circuit comprised of a hollow fiber cartridge containing primary porcine hepatocytes coupled with plasmapheresis and charcoal in a plasma perfused circuit.

METHODS. The BAL was tested in a prospective randomized, controlled trial to treat patients with fulminant hepatic failure (FHF) in Stages III and IV hepatic encephalopathy (n=147) and primary graft non-function (n=24) at 20 U.S. and European sites from 1998-2001. Patients were randomized to either standard of care (SOC) or SOC + BAL treatments (BAL group) with randomization stratified for etiology, stage of hepatic encephalopathy and geographic site. Patients were treated for 6h daily until transplantation, neurologic recovery to stage I encephalopathy for 72h, a maximum of 14 BAL treatments, or any serious adverse event (SAE) that prevented further treatment. The primary endpoint was 30-day survival with or without transplantation; time-to-death was a secondary endpoint.

RESULTS. A total of 171 patients, 86 SOC, 85 BAL were enrolled. Efficacy: 30-day survival was 62% for SOC and 71% for BAL (P=.28) in the complete study population and 59% SOC and 73% BAL group for FHF patients alone (n=147; P =.10). Transplantation had a powerful impact on survival. Overall 30-day survival with transplantation was 84% (n=94); 80% SOC and 89% BAL compared with 46% (n=77) if not transplanted; 37% SOC and 51% BAL group. A covariate time-dependent proportional hazard model with time-to-death as endpoint was employed to account for the impact of transplantation and other factors predictive of survival. This analysis showed a 31% reduction (0.69 risk ratio) in mortality for the BAL group (p=0.15). Analysis of the FHF group only (n=147), revealed a 41% reduction in mortality (0.59 risk ratio) favoring BAL treatment (P=.06). A reduction in mortality of 67% (0.33 risk ratio) was seen for drug toxin etiology (n=53) favoring BAL treatment (p=.01). Additionally, for patients developing encephalopathy within 2 weeks of jaundice (n=121), there was a 47% decrease in mortality (0.53 risk ratio) favoring BAL treatment (p=.04). Safety: SAEs were balanced in each group. The most frequent SAEs were thrombocytopenia (30% each group), sepsis (12% SOC, 11% BAL group), renal failure (20% SOC, 13% BAL), and hypotension (14% SOC, 14% LAS).

CONCLUSION. This is the first randomized, prospective, controlled trial demonstrating a survival advantage for a liver-assist system in fulminant hepatic failure. These survival advantages viewed with the safety data support a risk-benefit ratio favoring the use of the HepatAssist Liver Support System for the treatment of fulminant hepatic failure.

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LIVER DYSFUNCTION/FAILURE IN PATIENTS WITH CARDIOGENIC SHOCK: ASSOCIATION WITH ICAM-1 LEVELS AND OUTCOME

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INTRODUCTION. Liver dysfunction (LD)/ liver failure (LF) is a common complication in pts with septic shock (SS) and is associated with further elevations in plasma levels of ICAM-1 (sICAM-1). Little information is available on the incidence of LD/LF in pts with cardiogenic shock(CS).

METHODS. We studied 51 pts with CS on admission to the ICU (median 16hrs after shock onset) with respect to LD/LF, sICAM-1, and their respective impact on survival. 25 pts with SS and 14 non critically ill pts served as controls. Organ dysfunction/failure was assessed via SOFA-score but CS-pts with acute ischemic hepatitis (LDH>1000U/L + SGPT >200U/L) and an acute decrease in prothrombin time + elevations in serum bilirubin received also a liver subscore of 3 (= LF).

RESULTS. Pts with CS (525ng/ml [482-575 95% CI]) had higher sICAM-1 levels than controls (332ng/ml[271-408],p<0.001) but lower levels than pts with SS (812ng/ml[700-939],p<0.001). 10 pts with CS (19.6%) exhibited LD at time of admission and LF was present in another 10 pts with CS, as compared to 40 and 20% with LD/LF respectively in pts with SS (p=0.14). Both LD and LF, but not renal or respiratory failure, were associated with significant elevations of sICAM-1 in pts with CS and in pts with septic shock. The 9 pts with CS who exhibited a further decrease in liver function within 24hrs after admission did not exhibit higher sICAM-1 levels. Concomitant renal failure was present in 70% of the CS-pts with either LD or LF whereas respiratory failure was present in 30% of pts with LD but in 80% of pts with LF. Per se LD/LF was not associated with an increased ICU-mortality (64.5 vs. 70 %) although a trend for an increased 24h-mortality was observed with decreasing liver function. Renal failure in patients with LD/LF increased the ICU-mortality from 33% (LD/LF with renal dysfunction) to 85.7% (p=0.04) and 24h mortality from 17 to 43% (p=NS) whereas respiratory failure predominantly increased 24h-mortality.

CONCLUSION. LD/LF in pts with CS is associated with elevated plasma levels of sICAM-1 and seldom occurs without simultaneous dysfunction of other organs. When associated with renal failure LD/LF is associated with a significant increase in ICU-mortality.

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A FAST IMAGING TECHNIQUE TO STUDY VENTILATION DURING EXPERIMENTAL CPR

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INTRODUCTION. Dynamic CT (dCT) imaging allows visualization and quantification of ventilation and recruitment processes in healthy and ARDS lungs [1, 2]. Aim of this study was to use this technique to investigate the effect of different ventilatory strategies during CPR on lung aeration.

METHODS. Technical developments for the experimental setup included (1) design and construction of an external chest compression device, which does not interfere with CT imaging, and (2) development of a software tool to automatically detect lung parenchyma and to calculate radiological density parameters from a large stack of images [3]. (3) In an IRB-approved feasibility study, fibrillatory circulatory arrest was induced in three anesthetized pigs (25-27 kg). After one minute of arrest, external chest compressions were started with a rate of 100 cycles/min, and either volume constant ventilation (VCV), no ventilation (NV) or continuous airway pressure (CPAP) was established in one animal each. One minute later, epinephrine was administered (0.04 mg/kg i.v.), and 6 min later, dCT acquisition was started at a temporal resolution of 100 ms. Simultaneously, arterial blood gases, acid base status and hemodynamics were recorded. After 7 min of CPR defibrillation was attempted.

RESULTS. Using a modified chest compression device, artifact-free dCT acquisitions are feasible during closed chest CPR. The pilot experiments demonstrated that different functional lung compartments (i.e. ventilated, atelectatic and overdistended lung parenchyma) can be identified and quantified during basic and advanced cardiac life support sequences. CPR with VCV resulted in a mean atelectatic fraction of 39% of the total cross-sectional lung area, with ventilation-induced oscillations between 30% and 50% (collapse / recruitment). NV caused a constant fractional atelectasis of 73%, whereas CPAP generated the least amount of fractional atelectasis (23% of total cross-sectional lung area).

CONCLUSION. We demonstrate a novel CT-based technique to investigate direct effects of different ventilatory strategies on lung aeration during CPR. This technique may help to evaluate the usefulness of ventilatory strategies discussed in the literature (e. g., CPAP, oxygen insufflation or no ventilation) for Basic and Advanced Cardiac Life Support.

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Grant. German Research Council (DFG: Th315/9-2, DFG: Ma2398/2-1)

Oral Presentations
Metabolic control and markers – 755-760

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GLUCOSE LEVELS IN CONVENTIONALLY TREATED PATIENTS AT A SURGICAL ICU

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INTRODUCTION. For complex reasons, careful regulation of glucose is believed to contribute to better outcome. The landmark study by Van Den Berghe et al. (1) on patients from a predominantly cardiosurgical ICU showed that glucose regulation to 4.4 to 6.1 mmol/l resulted in improved morbidity and mortality. The protocol used in that study allowed very high insulin infusion rates, as well as the initiation of concentrated glucose infusion directly on admission. We evaluated our past performance with regard to levels that are now considered desirable. We focused on patients with a prolonged ICU-stay, where regulation appears most relevant.
METHODS. Patients admitted to our 12-bed surgical ICU for > 3 days were studied for a 7-year period. Less than 5% of the admissions concerned cardiac surgery patients. Glucose regulation was done by a simple sliding-scale regimen, with a maximal insulin infusion of 10 units/hour. Enteral nutrition was administered as soon as feasible. However immediate administration of concentrated glucose or TPN was *not* routinely performed. For each patient the mean glucose level was calculated. To determine the quality of regulation the percentage of glucose measurements between 4 and 6 mmol/l was calculated for each patient. Groups were compared with c^2 and Mann-Whitney U tests.
RESULTS. 25641 glucose measurements were analyzed in 1101 patients. 202 (18 %) patients died within 30 days after ICU admission. The mean glucose level was 6.9 ± 1.7 (SD) and 8.1 ± 2.0 mmol/l in survivors and non-survivors respectively (p < 0.001). Abnormal glucose levels were related to mortality (table 1). The effectiveness of glucose regulation was poor, especially in non-survivors (table 2).

	Survivors (n=899)	Non-survivors (n=202)	p
Patients with 1 or more values < 4 mmol/l	165 (18 %)	71 (35 %)	< 0.001
Patients with 1 or more values > 11.5 mmol/l	303 (33 %)	113 (56 %)	< 0.001

	Non-survivors	p	
Mean percentage of measurements between 4 – 6 mmol/l	34 %	23 %	< 0.001
Mean percentage of measurements > 11.5 mmol/l	6 %	13 %	< 0.001

CONCLUSION. The conventional treatment failed to regulate glucose to desired levels. Non-survivors were significantly worse regulated, as reflected by raised glucose levels in general as well as an increased incidence of abnormally low glucose levels. Thus considerable room for improvement of glucose regulation exists, with the potential to improve survival of patients treated at our ICU.
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GLUCOSE METABOLISM AND TUMOR NECROSIS FACTOR-ALFA IN GRAM-NEGATIVE SEPTIC SHOCK PATIENTS

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INTRODUCTION. Correlation has been described between tumor necrosis factor-alfa (TNF-alfa) and insulin resistance. The greatest serum levels of TNF-a are described in gram-negative infections.

METHODS. We performed a randomized double-blind study with 16 gram-negative septic shock patients, treated with b-lactamic antibiotics. Seven patients received human polyclonal immunoglobulin G, M and A (Pentaglobinâ-Biotest Pharma), and nine patients received a 3% albumin solution. We evaluated kinetic of serum TNF-a and Homeostasis Model Assessment (HOMA), a mathematical relation of glucose and insulin, that measure insulin resistance (IR) and pancreatic beta-cell function (PCF), at the moment of septic shock diagnosis and after 24 hours. Statistical analysis was performed by ANOVA and significance level of 5% was considered.

RESULTS. APACHE II score didn't differ in both groups.

	Immunoglobulin	Control	p-value
TNF-alfa	Decrease 31.49%	Increase 46.90%	< 0.05
IR	Decrease 20.57%	Increase 95.09%	< 0.05
PCF	Decrease 13.53%	Increase 61.06%	< 0.05

Kinetic of TNF-alfa, IR and PCF (comparison of initial levels –0 hour)

CONCLUSION. Insulin resistance had an inverse relation with pancreatic b-cell function. Human polyclonal immunoglobulin patients, decrease TNF-a, and improve glucose metabolism. We don't know similar studies in humans, comparing acute variations of TNF-a and glucose metabolism.

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HYPERCHLORAEMIC ACIDOSIS AT ADMISSION IN CRITICAL CARE UNIT

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INTRODUCTION. Recently at least four major journals have published about hyperchloraemic acidosis. These include two editorials, one original paper and one review. 1,2,3,4 It appears that hyperchloraemic acidosis may be of no known pathologic or physiologic consequence in human, the greatest danger lies in inappropriate diagnosis of worsening metabolic acidosis leading to inappropriate treatment.

METHODS. The audit period was for four weeks. We prospectively collected following data with in first 24 hours of admission in all new patients. Age, sex, type and reason for admission, APACHE II score, type of intravenous fluid administered prior to admission, arterial blood gas and electrolytes analysis, serum lactate, total intake and output.

RESULTS. We collected data on 24 patients. Mean age and APACHE II were 61 years and 16 respectively. There were equal numbers (n=12) of male, female, operative and non-operative patients. Hyperchloraemic acidosis was identified in seven (29%) patients. In this group mean pH, serum chloride, base excess, serum lactate and Cl:Na were 7.31, 115, -5.1, 1.3, and 0.89. Mean volume of fluid administered prior to admission was: Normal saline (0.9% NaCl) -1945 mls, Hartmann's solution-1250 mls, gelofusine-1250 mls, 10% hetastarch-625 mls, 6% hetastarch – 375 mls.

CONCLUSION. Hyperchloraemic acidosis is a common acid-base disorder in critical care unit. If not monitored can lead to inappropriate diagnosis and treatment. Intravenous infusion of normal saline and colloids suspended in saline solution are the major contributing factors in the development of this abnormality. Frequent monitoring of chloride concentration should become routine in all relevant areas of critical care.

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TEMPERATURE SENSITIVITY OF GLYCOLYSIS DURING SEPSIS

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INTRODUCTION. Temperature variations may affect energy metabolism. Despite the well-known temperature sensitivity of biochemical processes (Arrhenius activation law) and the frequent temperature variation during sepsis, no study has focused on the real effects of temperature on the overall glycolytic pathway, and on the potential interest of homeothermy maintenance during sepsis. The goal of this experimental animal study was to assess the temperature sensitivity of glycolysis during sepsis.

METHODS. ten Sprague-Dawley male rats, weighing 400-500 g, were dedicated to either a septic or a sham-control group. Sepsis was induced by a cecal ligation and perforation. The Lateral gastrocnemius was sampled on the left leg before sepsis induction (H0), and on the right leg, four hours after sepsis induction (H4). The anaerobic glycolytic flux (JB) and the transition time (t99: the time required for the transition from aerobic to anaerobic metabolism) were measured by spectrophotometry [1] at seven different temperature levels, ranging from 32 to 42°C. For each measured variable, the temperature sensitivity of glycolysis was assessed by computing the Q10 values, which is the variation ratio of the measured parameter, due to a 10°C temperature variation. The results are expressed as mean ± SEM. Statistical significance was assessed using a Student-t-test, at the 5 % level.

RESULTS. in control rats, anaesthesia and surgical procedures induced a JB increase (7.9 ± 1.6 at H0, vs. 11.9 ± 2.1 mmol.min-1.g tissue-1 at H4, $p<0.05$), without any t99 variation. Whatever the group (sham-control or septic), the same temperature variation induces an effect which is approximately 3 times higher in the hypothermia (<37°C) than in the hyperthermia range (>37°C; $p<0.05$). Moreover, a loss of thermal sensitivity was observed in septic rats in the hyperthermia range (Q10= 1.2 ± 0.1 for septic animals, vs. 2.3 ± 0.4 for sham-control animals; $p<0.05$).

CONCLUSION. Glycolysis thermal response is not linear, more sensitive to temperature variations in the hypothermia than in the hyperthermia range. The loss of thermal sensitivity above 37°C in septic animals suggests a direct sepsis-induced glycolysis dysregulation. From an energetic point of view, hyperthermia may by itself impair energy metabolism, and should so be corrected during sepsis.

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EFFECTS OF HAEMODILUTION AND SUBSEQUENT HYPEROXIA OR NOS-INHIBITION ON ERYTHROCYTE DEFORMABILITY

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INTRODUCTION. Erythrocyte deformability (ED) is a key determinant of microcirculatory perfusion and thus tissue oxygenation. Haemodilution (HD) might impair the ED by increasing shear forces affecting the erythrocytes, or by metabolic stressors, e.g. decreased oxygenation or excessive nitric oxide (NO) levels. We speculated that those factors during severe HD may impair ED, and attempted to restore the latter by increasing oxygenation (normobaric hyperoxia) or by decreasing NO-levels (NO-synthases inhibition).

METHODS. Pigs (n=6, ~25 kg) were anaesthetised and ventilated to maintain normoxia and normocarbia. Stepwise normovolaemic haemodilution (HD) was performed with hydroxy ethyl starch (HES 6%) to total exchange volumes of 0 ml/kg (=baseline), HD 40 ml/kg, and HD 90 HD ml/kg. After completion of HD (i.e. HD 90 ml/kg), we attempted to restore ED by hyperoxia (FiO_2=1.0) or by NO-synthase inhibition (L-NAME, 10 mg/kg i.v.). ED was measured at both high and low shear stresses (30 and 3 Pa respectively), the latter regarded the more sensitive marker of ED [1]. ED was measured by the "Laser-assisted Optical Rotational Cell Analyser" (LORCA®, Mechatronics, Hoorn, NL [1]). ED is expressed as the Elongation Index (EI). Statistics: ANOVA for repeated measurement, *$p<0.05$.

RESULTS. Data are presented as mean ± SD. HD decreased haemoglobin concentration from 8.1 ± 0.3 (baseline = HD 0 ml/kg) to 3.9 ± 0.2 (HD 40 ml/kg) and finally 2.2 ± 0.1 g/dl (HD 90 ml/kg). The Elongation Index (EI) measured at the unsensitive high shear stress (30 Pa) was unaltered by stepwise HD (0.562±0.02, 0.568±0.01 and 0.571±0.01) for the conditions: baseline, HD 40 and HD 90 ml/kg respectively. In contrast, EI measured at the sensitive, low shear stress (3 Pa) decreased significantly (*$p<0.05$) already at an exchange volume of 40 ml/kg (from 0.407±0.01 to 0.369 ± 0.03, *$p<0.05$) and decreased further at HD 90ml/kg (0.358±0.02, *$p<0.05$). Neither normobaric hyperoxia nor NO-synthases-inhibition (L-NAME) restored the EI.

CONCLUSION. Erythrocyte deformability is impaired during progressive haemodilution. Resuscitation of erythrocyte deformability in the state of impaired microvascular oxygenation by normobaric hyperoxyia or inhibition of NO-synthases failed. The causes and relevance of the observed significant "stiffening" of the erythrocytes during haemodilution are subject of further studies.

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EFFECTS OF A THREE-FOLD HIGHER VITAMIN D SUPPLEMENT ON BONE TURNOVER IN PROLONGED CRITICAL ILLNESS

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INTRODUCTION. We documented dramatically increased breakdown and impaired synthesis of bone tissue in prolonged critical illness (1). Impaired synthesis appeared in part due to hyposomatotropism. Concomitantly low serum concentrations of 25(OH)vitaminD [25(OH)D] were present. To determine the extent to which lack of nutritional vitamin D (vitD) contributes to bone loss, we investigated the impact of a three-fold higher vitD supplement in a prospective, randomized, controlled trial.
METHODS. Patients with an anticipated ICU stay of >10 days were randomly allocated to daily intravenous vitD (Cholecalciferol) supplement of either 220 IU or 600 IU as long as parenteral nutrition was given. Of the 33 patients included, only 22 remained in ICU for >10 days and were analyzed. Blood was sampled daily at 06:00h for determination of serum concentrations of 25(OH)D, 1,25(OH)2D, parathyroid hormone, ionized calcium, phosphate, and biochemical markers of different maturational stages of osteoblast (type-I procollagen, bone-specific alkaline phosphatase, osteocalcin) and osteoclast (urinary excretion of collagen cross-links) function. On-admission values were compared with 64 healthy matched controls. Group comparisons were done using ANOVA and Mann-Whitney-U test when appropriate.
RESULTS. Twelve patients received 600 IU and 10 patients 220 IU vitD per day. The two groups were comparable for age, BMI, reason for ICU admission and severity of illness. At baseline, serum concentrations of 25(OH)D, 1,25(OH)2D, and osteocalcin were lower ($P=0.0004$) than in healthy controls; bone-specific alkaline phosphatase, parathyroid hormone and ionized calcium levels were normal; serum type-I procollagen as well as urinary excretion of collagen cross-links was several-fold elevated ($P<0.0001$). The 600 IU vitD supplement significantly increased serum levels of 25(OH)vitD3 during the first week of intensive care ($P<0.03$ vs. 200 IU vitD) but normal levels were never reached. This resulted in higher serum osteocalcin ($P=0.04$) and lower serum type-I procollagen ($P=0.03$) compared with the 220IU-treated patients. Bone-specific alkaline phosphatase increased over time similarly in both studygroups. Urinary excretion of collagen cross-links, parathyroid hormone and ionized calcium remained unaltered.
CONCLUSION. During critical illness, accelerated bone loss occurs because of stimulated osteoclasts in the presence of defective maturation of osteoblasts. Part of this disturbance is explained by lack of nutritional vitD. Commercially available preparations for IV supplementation of lipid-soluble vitamins should increase the vitD content in order to prevent the nutritional component of accelerated bone loss. Serum IGF-I and members of the cytokine family (TNF-alfa, IL-1, IL-6, sRANK-ligand and osteoprotegerin) measurement will further clarify non-nutritionally mediated bone loss (data yet unavailable but will be presented).
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