Oral Presentations
Mechanisms in acute lung injury – 001-005

001

LOW PH DECREASES LUNG LIQUID CLEARANCE

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INTRODUCTION. Acidosis is a common clinical finding in patients with cardiogenic or increased permeability pulmonary oedema. Permissive hypercapnia is also applied in mechanically ventilated patients with ARDS. Resolution of pulmonary oedema is known to be effected by the active Na+ transport across the alveolo-capillary epithelium via apical Na+ channels and the basolaterally located Na,K-ATPases which produces the gradient necessary for water to be reabsorbed.

METHODS. We examined the effect of systemic acidosis on lung liquid clearance (LLC) in the isolated perfused fluid filled rat lung model while changing the perfusate pH through pulmonary circulation from 7.00 to 7.20 and 7.40 (normal). We also examined the effects of the b-adrenergic agonist isoproterenol, which is known to increase on lung oedema clearance by increasing the abundance of Na,K-ATPases at the plasma membrane of alveolar epithelial cells.

RESULTS. LLC significantly decreased by 39% at pH 7.00 and 26% at pH 7.20 ($P<0.05$) compared to normal pH (7.40). Also, the lung liquid clearance was restored to normal levels after correcting the pH from 7.00 to normal pH. In additional experiments we observed that isoproterenol increased LLC by 90% even in the presence of acidosis.

CONCLUSION. Systemic acidosis may be a contributing factor for decreased lung oedema clearance in patients with acute lung injury and pulmonary edema. Correction of pH to normal and the use of isoproterenol may be a significant therapeutic measure to restore LLC in patients with ALI and ARDS who have impaired ability to clear edema.
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002

TEZOSENTAN PREVENTS THE INCREMENTS IN ENDOTHELIN-INDUCED FLUID FILTRATION IN ISOLATED RAT LUNGS

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INTRODUCTION. The potent vasoconstrictor endothelin-1 (ET-1) mediates pulmonary hypertension and microvascular permeability (1,2). In sheep endotoxemia, the endothelin receptor antagonist tezosentan ameliorates the increments in pulmonary capillary pressure; however its effect on endothelial integrity remains unsettled (3). Thus, our aim was to evaluate whether tezosentan attenuates ET-1-induced changes in lung microvasular permeability.

METHODS. Isolated rat lungs were perfused with whole blood. A control group (n=8) received saline only. An endothelin group (n=7) and a tezosentan group (n=7) received papaverin followed by ET-1 (1 nM). The tezosentan group 5 min later received tezosentan (Actelion Ltd., Switzerland) 30 mg/kg. Pulmonary artery pressure (PAP), airway pressure (Paw), lung fluid filtration rate (FFR), filtration coefficient (Fc) and compliance (C_L) were determined (2). Activation of protein kinase Cepsilon (PKCepsilon), an intracellular mediator of microvascular permeability (4), was assessed by translocation of PKC from the cytosole by subcellular fractionation and Western blotting. Data were analyzed by ANOVA and Scheffe's test; $p<0.05$ was regarded as statistically significant.

RESULTS. At baseline, no intergroup differences were found. In the controls, PAP increased gradually throughout the experiment. In the endothelin and the tezosentan groups, PAP remained unchanged. In the endothelin group, FFR and Fc increased 3-fold and C_L decreased 5-fold in parallel with increasing pulmonary oedema from 30 to 90 min. In the control and the tezosentan groups, all the latter variables remained unchanged. In endothelin group PKCepsilon decreased by 60% in the cytosolic fraction compared with the control group. The endothelin-induced translocation of PKCepsilon was blocked by tezosentan.

CONCLUSION. In isolated blood perfused rat lungs, tezosentan inhibits the ET-1-induced increase in microvascular permeability by preventing activation of PKCepsilon.

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003

KL-6 LEVELS ARE ELEVATED IN PLASMA FROM PATIENTS WITH THE ACUTE RESPIRATORY DISTRESS SYNDROME

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INTRODUCTION. The mucin-like glycoprotein KL-6 is expressed on type II pneumocytes and when elevated in human plasma is considered to be a highly specific marker of alveolar epithelial cell damage. Damage to, and disruption of, the alveolar epithelial lining is a key feature in the pathophysiology of the acute respiratory distress syndrome (ARDS).

METHODS. Plasma samples were collected from 28 patients with ARDS (12 non-survivors), 9 ventilated control patients and 10 healthy controls. Samples were collected from ARDS patients in the acute phase (median duration 2.5 days) and later in their illness (median interval 11 days). Illness severity (SOFA score) and tidal volumes were recorded for patients (at the time of acute sample collection) and ventilated controls. The plasma level of KL-6 was measured by ELISA.

RESULTS. Plasma KL-6 concentrations were elevated in patients with ARDS (537U/ml IQR 383-1119) compared to ventilated controls (255U/ml IQR 83-338, $p<0.001$) and non-ventilated healthy controls (215U/ml IQR 149-307, $p<0.001$). No significant difference emerged between levels in the ventilated and non-ventilated control groups. Plasma KL-6 concentrations were higher in samples taken from ARDS non-survivors compared to survivors ($p<0.05$). SOFA scores ($p<0.01$) and tidal volumes ($p<0.05$) were also elevated in non-surviving patients. KL-6 concentrations remained elevated in samples collected from patients later in the course of ARDS ($p<0.001$ compared to ventilated and non-ventilated control groups). Within the ARDS population, there was a trend towards a relationship between tidal volume at time of acute sample collection and KL-6 concentration in the initial sample ($p=0.055$) and a significant correlation between the same tidal volume and the KL-6 concentration in the late plasma sample ($p<0.01$, $r=0.59$).

CONCLUSION. Elevated levels of plasma KL-6 provide a useful marker for ARDS in ventilated patients, and have prognostic significance. Our findings support the view that alveolar epithelial cell damage is of key significance in the pathogenesis of this condition. The relationship between ventilatory strategy and plasma KL-6 concentration provides further evidence that alveolar epithelial damage is sustained during high tidal volume mechanical ventilation.
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004

ROLE OF TOLL-LIKE RECEPTOR 4 IN THE PATHOGENESIS OF LPS-INDUCED ACUTE LUNG INJURY

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INTRODUCTION. The expression of proinflammatory cytokines such as tumour necrosis factor (TNF), interleukin-1 (IL-1b) and nitric oxide plays an important role in the pathogenesis of acute lung injury (ALI) during gram-negative sepsis. However, the molecular pathways by which LPS induces an inflammatory response in the lung are unknown. It has been shown that Toll-like receptor 4 (TLR4) is critical for the expression of TNF and IL-1b during endotoxic shock. Additionally, recent studies determined that TLR4 is expressed in lung tissue. Accordingly, the purpose of this study was to determine whether TLR4 was necessary for the expression of TNF, IL-1b and other inflammatory mediators in the lung during endotoxic shock.

METHODS. Wild-type (WT) and TLR4-deficient (TLR4-D, C3H/HeJ) mice were injected i.p. with 20mg/kg E. coli 0111:B4 LPS. TNF, IL-1b and IL-6 as well as IL-1R1, IL-1R2 and TNF-Receptor II mRNA levels were assessed by RNAse protection assay.

RESULTS. Myocardial expression of TNF, IL-1b and IL-6 mRNA was significantly ($p < 0.05$) greater in WT mice than in TLR4-D mice 6h after LPS stimulation. One hour after stimulation there was no significant difference detectable. At 6h, IL-1 receptor I expression as well as TNF-Receptor II were significantly greater in WT mice than in TLR4-D mice.

CONCLUSION. Our data suggest that TLR4 plays an important role in the expression of inflammatory mediators in the lung following LPS-stimulation suggesting that TLR4 or downstream components of this signalling pathway may be potential targets for the development of novel therapies that attenuate acute lung injury.

005

CYTOLOGY OF BRONCHOALVEOLAR LAVAGE FLUID (BALF) IN CHILDREN WITH ACUTE LUNG INJURY (ALI)

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INTRODUCTION. Previous studies have shown major changes to pulmonary phospholipids(PL) in children with ALI(1). These show a decrease in the dipalmitoyl phosphatidycholine (DPPC) with concurrent increases in other molecular species. We speculate these changes are due to degradation, with the neutrophil playing a key role in this process. We studied the inflammatory cells in the BALF of children with acute lung injury.

METHODS. Children without pre-existing lung disease who developed ALI (PaO2/FiO2 <300 mm Hg [39.5 kPa] and bilateral infiltrates on chest X-ray) [2] were eligible. Following consent, BALF were collected on days 1-4, weekly and at extubation, were filtered, and centrifuged. The supernatant was frozen at 80ºC for PL analysis. The cell pellets were re-suspended in Hanks buffered saline solution (HBSS), 2 cytospins were prepared (5 min at 1000 rpm). The cells were fixed in methanol, air dried, stained with Haema-Gurr method and differential cell counts were performed. Children without lung injury acted as controls.

RESULTS. Over 22 months, 65 (5.5%) of 1165 admissions developed ALI, 18 had pre-existing lung disease and were excluded, of the 47 remaining, 18 were enrolled, 6 parents declined consent and 23 children were excluded by secondary criteria. BALF differential cell counts showed predominant neutrophils, 86.5% on Day 2 in ALI group compared to 2.3 % in the control group ($p<0.0001$,Mann Whitney U test). There is a reciprocal reduction in macrophage count (35.8 % in control to 5.8% on Day 2 of ALI, $p<0.03$) There is no significant change to neutrophils and the macrophages counts during the period of mechanical ventilation in ALI.

CONCLUSION. Neutrophils are the predominant inflammatory cells in the BALF of children with ALI. This predominance persists throughout the period of mechanical ventilation even when PL levels return towards the normal pattern and gas exchange is adequate for extubation. Activated neutrophil and neutrophil products rather than the presence of neutrophils alone is likely to account for lung PL degradation.

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007

SYNDECAN-4-DEPENDENT NEUTROPHIL MIGRATION IN RESPONSE TO ANTITHROMBIN INVOLVES SRC TYROSIN KINASES

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INTRODUCTION. Tyrosine phosphorylation is critical in the regulation of neutrophil function. Direct effects of antithrombin on neutrophils are mediated by syndecan-4-induced signalling [1]. We investigated the role of SRC –familiy selective tyrosine-kinase inhibitors on transgenic, recombinant antithrombin- or Kybernin P®-regulated neutrophil migration.

METHODS. Neutrophils were obtained from forearm venous blood. Chemotaxis assays were performed using a 48-well Boyden microchemotaxis chamber in which a 5-ìm pore sized cellulose nitrate filter separates the upper and the lower chamber. Neutrophils were pretreated by various SRC –family selective tyrosine-kinase inhibitors with or without antithrombin followed by washing and assessment of their migratory response toward antithrombin or interleukin-8.

RESULTS. Neutrophils pretreated with selective tyrosine-kinase inhibitors showed a significantly reduced migratory response toward recombinant antithrombin or Kybernin®. Pretreatment of neutrophils with antithrombin deactivates migration toward chemokines in a syndecan-4 dependent manner. Co-incubation of tyrosine-kinase inhibitors with antithrombin reversed the inhibitory effects of antithrombin in neutrophil migration. Dose dependent reversal of migration was induced with 4-Amino-1-tert-butyl-3-(1'naphthyl)pyrazolol[4,4-d]pyrimidine (PP1). Of the two other pharmacological Src tyrosine kinase inhibitors, 4-Amino-5-(4-chlorophenyl)-7-(t-butyl)pyrazolo[3,4-d]pyrimidine (PP2) and 4-Amino-7-phenylpyrazolo[3,4-d]pyrimidine (PP3) only PP2 exerted a similar effect.

CONCLUSION. SRC kinases may play an important role in regulating antithrombin-mediated neutrophil chemotaxis via syndecan-4 which is known to be linked to the focal adhesion complexes.

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Oral Presentations
Leukocyte-dependent mechanisms – 006-010

006

CD28 AND ACUTE RENAL FAILURE (ARF) - CRITICAL ROLE FOR T CELL-NEUTROPHIL INTERACTIONS

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INTRODUCTION. In sepsis, recruitment of neutrophils (PMN) is critical for organ failure [1]. Recent studies demonstrated a close association between CD28 receptor pathways and PMN recruitment into chronically inflamed tissues [2]. Here, we sought to examine the role of CD28 in a murine model of septic ARF.

METHODS. ARF was induced in wild-type mice (WT) and CD28-deficient mice ($CD28^{-/-}$) by i.p. injection of lipopolysaccharide (LPS). To evaluate the role of PMN, some WT and $CD28^{-/-}$ also received anti-PMN serum (aPMN) 24h prior to LPS. In an adoptive transfer model (AT), we also injected T cells from WT into $CD28^{-/-}$ 2h prior to LPS in order to further explore the role of T cells. Serum creatinine concentrations (Crea) served as indicators of renal function. CD28 expression was analyzed by flow cytometry. Renal myeloperoxidase activity (MPO) was measured to quantify PMN infiltration. Results were compared to untreated control mice. Data (Tab. 1) are given as mean±SEM. Statistical analysis included ANOVA, Student-Newman-Keuls test and unpaired t-test ($p<0.05$).

RESULTS. Control Crea and MPO values were not significantly different between WT and $CD28^{-/-}$. CD28 expression could only be detected on T cells. $CD28^{-/-}$ demonstrated a significant protection from ARF which was accompanied by a similar reduction in PMN infiltration. PMN-depletion did not provide any additional protection for $CD28^{-/-}$. Injection of $CD28^{+/+}$ T cells in $CD28^{-/-}$ fully restored the levels of PMN infiltration and ARF seen in WT after LPS challenge.

	WT (n=6)	CD28 (n=7)	WT/aPMN (n=6)	CD28/aPMN (=7)	AT (n=6)
Crea (mg/dl	0.95±0.06[1]	0.59±0.07[2]	0.58±0.03	0.44±0.08	1.17±0.18[3]
MPO (mU/mg)	167.5±22.5[1]	99.5±14.9[2]	42.4±8.2	55.9±9.8	222.6±40.2[3]

[1] $p<0.05$ vs. control, [2] $p<0.05$ vs. WT 24h, [3] $p<0.05$ vs. CD28 after 24h

CONCLUSION. Through regulation of PMN recruitment via CD28 pathways, T-lymphocytes play a significant and clinically relevant role in the development of LPS-induced ARF.

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008

RECEPTOR AND NON-RECEPTOR TYROSINE KINASES ARE REQUIRED FOR EPCR-DEPENDENT EFFECTS IN NEUTROPHILS

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INTRODUCTION. Protein C and activated protein C deactivate neutrophil chemotaxis via activation of the endothelial protein C receptor (EPCR) of leukocytes [1]. Src kinases play an important role in neutrophil signalling and effector's functions [2] and different Scr family members are involved in regulating cell migration [3]. Aim: We investigated the involvement of Src-family tyrosine kinases in the signalling of EPCR of neutrophils.

METHODS. Neutrophils were obtained from forearm venous blood. Leukocyte migration toward gradients of soluble attractants into cellulose nitrate micropore filters was measured using a 48-well microchemotaxis chamber. Cells were pretreated with activated protein C in presence of Src inhibitors followed by washing; then chemotaxis toward interleukin-8 was tested.

RESULTS. Activated protein C inhibits neutrophil chemotaxis toward interleukin-8. Inhibitors of Src-family tyrosine kinases reverse these migration-inhibitory effects. Dose dependent reversal of migration was induced with 4-Amino-1-tert-butyl-3-(1´-naphthyl)pyrazolo[4,4-d]pyrimidine (PP1). Of the two other pharmacological tyrosine kinase inhibitors, 4-Amino-5-(4-chlorophenyl)-7-(t-butyl)pyrazolo[3,4-d]pyrimidine (PP2) and 4-Amino-7-phenylpyrazolo[3,4-d]pyrimidine (PP3) only PP3 which is a EGF-R tyrosine kinase blocker exerted a similar effect. Neiter PP1 nor PP3 affected IL-8-induced migration.

CONCLUSION. Activated protein C inhibits neutrophil chemotaxis. The selective reduction of this effect by inhibitors of Src-family and EGF-R tyrosine kinases suggests that non-receptor and receptor tyrosine kinases are involved in the signalling of EPCR-mediated effects of activated protein C in neutrophils.

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009

INFLUENCE OF SHEAR FORCES ON LEUKOCYTE-MEDIATED INFLAMMATION

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INTRODUCTION. Although leukocyte accumulation has been repeatedly shown to impair tissue perfusion during shock, less is known on the direct effects of flow on leukocyte-mediated inflammation. Since low flow often precedes the onset of inflam- matory reactions during shock, we studied the effects of reduced shear stress on leukocyte-endothelial interactions and subsequent endothelial inflammation.

METHODS. Using a flow chamber assay, non-activated neutrophils (PMN, n=16) and monocytes (MO, n=12) were perfused over non-activated human umbilical venous endothelial cells (HUVEC) at different levels of shear stress (3-0.25 dynes/cm^2). Perfusion over LPS-activated HUVEC (lipopolysaccharide 100ng/ml, 4h) served as positive control. To examine subsequent endothelial inflammation after pre- treatment of HUVEC with PMN or MO at 0.25 dynes/cm^2, E-selectin (CD62E) and ICAM-1 (CD54) were measured in the cocultures by flow cytometry. In further perfusion experiments at normalized flow (2 dynes/cm^2), these cocultures were again perfused with PMN to determine the effects of such pretreatment on secondary adhesion at restored shear stress. Student's paired t-test and analysis of covariance were used in the statistical analysis.

RESULTS. Shear stress reduction induced a 4-20fold increased adhesion of MO and PMN on non-activated HUVEC and reached values of the LPS-activated control ($p<0.01$). Bonds that were formed at 0.25 dynes/cm^2 could not be detached by subsequent increases up to 32 dynes/cm^2. As a consequence of MO-adhesion, the expression of CD54 and CD62E increased by 7-40fold on pretreated HUVEC ($p<0.01$). Upregulation of CD54 and CD62E was followed by a 100fold increased PMN- adhesion even under restored shear stress ($p<0.01$) which could be blocked by monoclonal antibodies against CD62E, L-selectin and CD18. Adhesion-induced endothelial inflammation at low shear forces was entirely dependent on activating signals generated by adherent MO since adhesion of PMN, lymphocytes and Brefeldin-treated MO had no effect.

CONCLUSION. Reduced shear stress irreversibly increases the adhesion of PMN and MO, resulting in a sustained endothelial activation. Regarding the largely increased adhesion even under restored flow, these early changes will have a profound effect on subsequent inflammatory reactions.

010

REGULATION OF CASPASE-3 IN APOPTOTIC LYMPHOCYTES DURING SEPSIS

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INTRODUCTION. Recently, apoptosis was shown to be increased in murine models of sepsis (1, 2) as well as in septic patients (1,3). The mechanisms of apoptosis in peripheral lymphocytes during sepsis are yet unclear. We hypothesized that the caspase pathway is activated in apoptosis of lymphocytes during sepsis.

METHODS. 10 Patients with severe sepsis were enrolled after informed consent. Blood samples were drawn on days one, three and five after enrolment. 9 healthy volunteers served as control. Enzyme activation and antigen expression were quantified by flow cytometry after immunophenotyping.

RESULTS. Caspase-3 was found to be activated in CD4+ T-cells, CD8+ T-cells and B-cells (all $p<0.05$). The activation of this central executioner caspase was reflected in an increased Phosphatidyl-serin externalisation ($p<0.05$). Caspase-3 may be activated via a receptor pathway. In septic patients the death-receptor Fas was found to be upregulated on all three cell types analyzed ($p<0.01$). Fas-Ligand, which is known to activate Fas, was upregulated on CD8+ cells ($p<0.05$), while TRAIL expression remained unchanged The expression of Bcl-2 in patients with sepsis decreased in all cell types but was downregulated most prominently in B-cells and CD8+ cells ($p<0.05$).

CONCLUSION. These results demonstrate that apoptosis in lymphocytes during sepsis is probably activated via the caspase-3 pathway. There is evidence for both the involvement of the Fas/FasL system and the mitochondrial pathway of apoptosis. It is likely that the decreased expression of Bcl-2 sensitises cytotoxic T-cells and B-cells to undergo apoptosis.

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Oral Presentations
Can we prevent errors in the ICU? – 011-015

011

THE INCIDENCE AND POTENTIAL SEVERITY OF PRESCRIBING ERRORS ON CRITICAL CARE

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INTRODUCTION. Multifactorial ICU medication error rates can be up to 33% (1). The Department of Health has targeted a reduction in the incidence of serious prescription errors of 40% by 2005. The aim of this study is to review and categorise errors in the prescription of drugs in critical care.

METHODS. ICU/HDU prescription charts were prospectively audited by Critical Care pharmacists over 4 weeks. Prescribing errors were entered onto a database using standardised definitions, categories and estimations of severity (2).

RESULTS. 1230 prescriptions were reviewed. 141 prescriptions contained 164 errors. ICU (11%) and HDU (12.5%) prescription error rates were similar. 45 errors resulted in no definite harm to patients. 28 errors were serious or life threatening – for example increasing the dose of aminophylline in a patient with already toxic levels and an emerging tachyarrhythmia. The most common errors by drug class were: iv fluids 22, nutrition 18, antibiotics 17 and anticoagulants 12.

Error rates, categories and severity: n

	Errors with no adverse consequence	Errors rectified by pharmacist before administration	Errors prescription inappropriate for patient	Errors failure to communicate essential information	Errors of transcription	Errors depending on clinical situation
Minor	23	14	10	31	0	2
Significant	12	11	14	2	2	9
Serious	7	6	11	3	1	2
Life threatening	3	3	6	0	1	3

CONCLUSION. There is a considerable rate of prescribing error within Critical Care. Clinical pharmacists can rectify a proportion of errors before drugs are administered. Identifying the most common drugs involved in prescribing errors may be helpful in targeting resources to prevent future errors.

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012

IDENTIFICATION AND CHARACTERIZATION OF ERRORS AND INCIDENTS IN A MEDICAL INTENSIVE CARE UNIT (ICU)

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INTRODUCTION. Errors and incidents occur frequently in medicine. Data about the frequency, type and consequences of errors and incidents in the ICU are scarce. However, few reports do suggest a significant contribution of avoidable adverse advents to morbidity and mortality in the critically ill. The objective of this study was to reveal the frequency, type and consequences of errors and incidents in a medical ICU of a University hospital.

METHODS. The study was conducted in a medical ICU predominantly admitting patients with cardiovascular and pulmonary diseases. All staff members (physicians, nurses and physiotherapists) of the ICU were asked to report any observed error and incident on a structured incident report form (IRF). All were repeatedly encouraged to make use of the IRF and detailed descriptions on how, why and when to use the IRF were provided.

RESULTS. During the observation period of 64 days a total of 216 patients were admitted to the ICU. Altogether 45 errors and incidents involving 31 patients (14%) were reported. 71% of all IRF were completed by physicians whereas 29% were reported by nursing staff. Patients subjected to errors were more severely ill (SAPS II on admission 42 ± 25 vs 32 ± 18, $p<.05$), had a higher predicted (SAPS II 34% vs 19%, $p<.05$) and observed hospital mortality (36% vs 9%), higher TISS-28 on day 1 (28 ± 9 vs 24 ± 7, $p<.05$), and a longer ICU stay (11 ± 18 vs 3 ± 5 days, $p<.05$). Gender, age and admission diagnosis were equally distributed. Four incidents were rated as harmful and 3 as potentially harmful. A high proportion of errors was related to drugs (17/45 and specific diagnostic procedures such as EKG (3/45) and echocardiography (7/45). Errors and incidents were mainly facilitated by inadequate communication (11), disregard of rules (8) and orders (5), lack of time (7) and insufficient experience with a procedure (6). The reporter rated 42 incidents and errors (93%) as „avoidable".

CONCLUSION. Most of the observed errors and incidents had negligible impact on the patients' outcome. The identification and characterization of errors and incidents combined with contextual information may provide sufficient background information for areas of quality improvement.

013

AGITATION RELATED INCIDENTS IN A SURGICAL ICU: FIRST STEPS OF A QUALITY IMPROVEMENT PROJECT

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INTRODUCTION. Agitation defined as an excessive, no purposeful motor activity associated with internal tension is common in the intensive care unit (ICU). Agitation induces multiple deleterious consequences which can range from disturbances of care, to effects on patients safety with a potential major impact on patient's morbidity and mortality.

METHODS. Agitation episodes (AE) and agitation related incidents (incidents) were prospectively retrieved from the electronic chart every day during 75 days, in our surgical ICU of 20 beds. Consecutive mentions of agitation were considered as one episode if they were not interrupted by a period of quietness, good collaboration or full orientation.

RESULTS. 387 patients were admitted for a total of 1115 patient-days during the 75 days. We observed a total of 192 AE (2.6 AE/day or 0.5 AE/patient). 22/192 (11%) AE were accompanied by severe incidents, potentially life threatening: 7 self-extubations, 9 ventilator disconnections, 2 patients discovered out of their beds, 2 attempts to central catheter removal, 1 effective removal of central catheter, 1 removal of thoracic drain. 13/192 (7 %) were moderate incidents without direct life threatening consequences: removal of 6 nasogastric tubes, 5 peripheral venous or 2 arterial catheters. 14/192 (7%) were mild incidents which consisted in 1 vesical catheter removal, 5 non-invasive monitoring devices removal or 8 aggressive behaviours towards the caregivers. The remaining AE 143/192 (74%) consisted mainly in contortion of the patients in his bed. The distribution of AE and incidents were significantly different through the 3 nurse working-shifts (43 AE and 10 incidents from 8 am to 4 pm vs 55 and 15 from 4 to 12 p.m. vs 94 and 24 from 0 am to 8 a.m.; $p < 0.0001$ for AE and $p < 0.01$ for incidents). No similar incident was observed during the same period in non agitated patients.

CONCLUSION. Agitation is noted as frequently as 2.6 times every day in a surgical ICU. Every third day one life threatening incident related to agitation occurs. Agitation as well as the related incidents are more frequently observed during the night working-shifts (from 0 a.m. to 8 a.m.). Continuous monitoring and active management of agitation may reduce the incidents and improve the safety of ICU patients. A quality assessment and improvement project has been started since March 2003 with the introduction of a continuous and systematic assessment of agitation. The planned interventional period with active management of agitation will start shortly.

014

CRITICAL INCIDENTS IN THE INTENSIVE CARE AND HIGH DEPENDENCY UNITS OF A DISTRICT GENERAL HOSPITAL

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INTRODUCTION. Critical incident (CI) reporting is well established in anaesthetic practice(1) and is widely used as a quality control measure. Studies have evaluated this technique in the intensive care unit (ICU)(2) but beyond these areas experience is lacking. We audited CIs occurring in adjacent high dependency (HDU) and ICUs of a district general hospital over a one year period.

METHODS. A critical incident was defined as an occurrence that could have led, or did lead to patient harm. Staff injury was included, as this detracts from patient care. CIs were recorded on anonymous questionnaires. Two designated doctors and nurses were responsible for increasing awareness of the audit and for 4-monthly review meetings.

RESULTS. 42 incidents involving 36 patients were reported; 20 in HDU and 22 in ICU. Considering HDU and ICU respectively, CIs related to airway management (1:6), ventilation (0:1), invasive lines (6:4), tubes and drains (3:1), drug delivery (2:5), equipment (2:4), staff injury (3:0) and others (3:1). Patient agitation (9), inadequate staffing levels (7) and poor attention to drug details (7) were the commonest factors contributing adversely. Additional problems arose from insufficient staff training (2), inadequate equipment checks (2) and poor techniques in communication (4), documentation (2) and patient handling (5). Whilst no adverse sequelae arose from most incidents, 2 deaths occurred, in one of which a CI was thought to have contributed. Further interventions were required in 9 patients. Five cases (2 patients, 3 staff) sustained minor morbidity.

CONCLUSION. The spectrum of incidents in our report is similar to those in previous ICU studies (2). Line and drain related problems predominated in the HDU where patients are more mobile yet often disorientated. Areas of weakness in our practice were highlighted, in particular the need for a sedation protocol. Finally, our study supports the greater involvement of anaesthetists in HDUs, as critical incidents arising in this setting are similar to those in ICUs.

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015

REDUCTION OF PRESCRIBING ERRORS WITH A RULES BASED PRESCRIBING AND INFORMATION MANAGEMENT SYSTEM

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INTRODUCTION. Drugs errors remain a significant source of concern. In 2000 the UK Audit Commission estimated 1100 hospital deaths occurred from drug errors adding an estimated € 500M / annum to NHS costs. Important factors in medicines mismanagement are failing to take into account declining organ function or a history of allergy; illegibility; drug interactions and incorrect dosages or route.

METHODS. In April 2002 a rules based electronic prescribing and information management system (CCIPS) was introduced to 26 of the Trust's critical care beds. The drugs database is user defined and is capable of linking together clinical and laboratory information to optimise prescribing decisions. Pre CCIPS we reviewed 31 consecutive case records; post CCIPS data is from its audit module. Clinical incident data relate to April - September 2001 vs. the same period 2002.

RESULTS. All pre CCIPS data except clinical incidents relate to 71 prescription charts with 1,166 prescription items; post CCIPS data relate to 19,062 prescriptions.

	Wrong dose	Allergy not recordet	Illegible	Undated alternation	Important interaction	Clinical incident
Pre CCIPS	68%	66%	62%	71%	19%	11
Post CCIPS	0%	0%	0%	0%	0%	4

Clinical incidents $p<0.05$ chi squared test.

CONCLUSION. It is not surprising that an electronic system will dramatically reduce the rate of simple errors, as shown above; undated changes are impossible; doses are constrained by the drug dictionary and illegible entries are eliminated. The rule base can also be used to combat the difficult problem of errors of omission as well as commission, for instance the requirement to record allergies is mandatory. The ability of CCIPS to integrate clinical, physiological and laboratory data allows it to support decision making. Critical Care pharmacological management is complex and rapid changes in patient's physiological status are common so in this environment the ability of the rules engine in CCIPS to deliver real time decision support is particularly exciting.

Oral Presentations
Bloodstream infections – 016-020

016

IMPACT OF BLOODSTREAM INFECTION ON THE OUTCOME OF PATIENTS WITH ACUTE RENAL FAILURE

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INTRODUCTION. Patients with acute renal failure (ARF) treated with renal replacement therapy (RRT) are prone to BSI, due to catheter manipulation and decreased immunity. Epidemiology of BSI in this population was evaluated.

METHODS. All ICU patients with ARF treated with RRT admitted during a 5 yr period were retrospectively analysed. Additionally, a matched cohort analysis was performed (1:2 matching ratio) in which ARF patients with BSI were compared with ARF patients without. Matching was on APACHE II score and admission diagnosis. Length of stay (LOS) of controls was at least as long as time between start of RRT and BSI of the case patient. This results in an equal predicted mortality of cases and controls. Attributable mortality of BSI was calculated as: mortality cases - mortality controls. Statistics used were the Mann-Whitney U test, chi^2 test, and Kaplan-Meier for univariate and Cox proportional hazard for multivariable analysis.

RESULTS. 704 patients were included, of which 62 patients (8.9 %) had BSI. BSI patients were younger compared to non-BSI patients (median 60 [interquartile range: 47-68] versus 64 [52-71], P=.041). APACHE II and gender were not different between both groups. BSI patients had more need for vasopressors (97 vs. 80%, P=.001), mechanical ventilation (89 vs. 77%, P=.039), and longer duration of RRT (25 [13-39] vs. 4 [2-12] d, P<.001). LOS after diagnosis of ARF was longer in BSI patients (33 [15-57] vs. 21 [8-47] d, P<.001), hospital mortality was equal in both groups (69 vs. 70%). Kaplan-Meier analysis illustrated that non-BSI patients had higher mortality early after start of RRT, the 2 curves merged later. Matched cohort analysis revealed that BSI was associated with an attributable mortality of 16.4 % (95%CI=1.3-31.5, P=.042). Multivariable analysis identified 2 factors independently associated with mortality: APACHE II score (HR=1.03, 95% CI=1.01-1.05, P=.010), and initiation of RRT with a continuous modality (HR=1.52, 95%CI=1.01-2.27, P=.043).

CONCLUSION. ICU Patients with ARF treated with RRT who had BSI, had equal mortality as non-BSI patients, despite having more co morbidity. Differences in baseline characteristics, e.g. younger age in BSI patients can be an explanation for this. Attributable mortality of BSI, as assessed with matched cohort analysis was 16.4 %.

017

FACTORS RELATED TO POSITIVE BLOOD CULTURES IN PATIENTS ADMITTED THE ICU

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INTRODUCTION. To identify factors associated with true positive blood cultures, as well as to determine those factors associated with contaminated haemocultures

METHODS. Prospective and observational study carried out in a polyvalent 18-bed ICU. All blood cultures carried out between February 1 and October 31, 2000, were included in the study and classified as true positive, contaminated positive, and negative according to microbiological findings and patient's clinical manifestations. To assess factors associated with true positivity, data of true positive and negative cases were compared, whereas to assess factors associated with contamination, contaminated haemocultures were compared with the remaining blood cultures. Data were analyzed by bivariate and multivariate methods.

RESULTS. In 141 (30.4%) of the 464 patients admitted to the ICU, a total of 560 blood samples were drawn for culture. In 111 cases (19.8%), blood cultures were positive and classified as true bacteraemia in 83 cases (14.8%) and blood culture contamination in 28 (5%). Independent variables significantly associated with true haemocultures were: chills (OR = 4.16, 95% IC 1.46 to 11.8); cyanosis (OR = 2.8, 95% CI 1.20 to 6.7); less than 60 s for the action of antiseptic solutions (OR = 2.70, 95% IC 1.59 to 4.61); haematomas (OR = 2.1, 95% CI 1.15 to 3.89); method used for cleaning the skin (longitudinal frictioning) (OR = 1.77, 95% CI 1.03 to 3.02); use of sterile gown (OR = 2.39, 95% CI 1.40 to 410); length of hospital stay until blood sampling (OR = 1.02, 95% CI 1.003 to 1.03), and older age (OR = 1.03, 95% CI 1.007 to 1.06). Independent risk factors associated with haemoculture contamination were: time of exposure to the antiseptic < 30 s (OR = 12.6, 95% CI 3.63 to 43.57) and reason for blood extraction especially when indicated by a study protocol (OR = 11.5, 95% CI 2.02 to 65.03).

CONCLUSION. Clinical signs that allow optimizing the practice of blood cultures as well as factors that should be corrected for decreasing the rate of blood culture contamination have been identified.

018

WIDE VARIATION IN PREVALENCE OF BACTERAEMIA: PRELIMINARY RESULTS OF A MULTINATIONAL SURVEY (BASIC-2)

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INTRODUCTION. The clinical presentation of bacteraemia can range from asymptomatic through to septic shock. ICU patients are at very high risk of developing bacteraemia (B) however the reported incidence varies widely, from 2.5-26% (1,2). As part of a stepwise international study of bacteraemia management, we sought to confirm whether this variation exists and, if so, to assess likely reasons.

METHODS. Between Jan 2002 - Jan 2003, prospective data were collected in each of 124 participating ICUs (97 European, 11 Australasian, 16 others, 77.5% general, mean (SD) of 11.0 (6.1) beds over a 4-8 month period. Clinically significant (B) were identified by daily prospective surveillance of all positive blood cultures. Information relevant to this abstract included total patient throughput, demographics, prevalence of (B), site of acquisition, infection control and antibiotic policies. SAS system software was used for statistical analyses including multivariate regression to identify factors responsible for practice variability. Only preliminary data are presented here.

RESULTS. A total of 1574 bacteraemic patients experienced 1897 (B) episodes. mostly (58.6%) were ICU-acquired. An infection control program was in place in 60% of ICUs, though only 25% had infection control nurses. Seventy-five percent have an agreed treatment strategy, predominantly (75%) antibiotic restriction. The recorded mean (SD) (B) prevalence was 10.9% (7.7), (median 9.5%, IQR 5-14.8, range 0.09-47.9), however a wide variation existed among centres, even those from the same country. Italy: mean (SD) 11.2% (7.5), (median 10.2%, IQR = 6.8-14.8, range 1.2-47.9%); Australia: mean (SD) 3.7% (3.5), (median 3.6%, IQR = 0.09-3.6, range 0.09-7.2); UK mean 7.4 (3.5) (median 7.4, IQR and range = 7.3-9.9).

CONCLUSION. Preliminary data from this large multinational survey confirm a wide variation in (B) prevalence in different ICUs from different countries, despite similar case-mix.

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019

ANALYSIS OF 122 EPISODES OF NOSOCOMIAL BACTEREMIA DUE TO ACINETOBACTER BAUMANNII

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INTRODUCTION. The objective of this trial is to analyze the risk factors for mortality (M) and other characteristics of *Acinetobacter baumannii* (AB) infection in the ICU.

METHODS. Over a 38 months period we studied 122, mechanically ventilated, ICU patients (pts), who developed bacteraemia and nosocomial infection due to AB (group A). As control cases (group B) we used 122 ICU pts of the same period who developed a nosocomial infection and bacteraemia due to other microorganisms (*Ps aeruginosa* 82, *St. aureus* 29, *St. epidemidis* 5, *Kl. pneumoniae* 4, *S. marcescens* 2). Pts met clinical and laboratory criteria for infection and had at least one positive blood culture (BC). Sex, age, length of stay (LOS), use of total parenteral nutrition (TPN), time of hospitalization before bacteraemia occurred (Hosp), number of positive BCs (nBCs), previous antibiotic treatment (PAT) and M rates were studied.

RESULTS. The results of the analyzed variables in the groups: All pts, Group A and Group B, respectively, were: male: 172 (70.5%), 82 (67.2%), 90 (73.8%); female: 72 (29.5%), 40 (32.8), 32 (26.2%); age (years): 43.4±18.5, 34.3±12.7, 52.5±26.1; LOS (days): 23.6±10.1, 24.4±9.2, 22.8±10.6; TPN: 34 (13.9%), 20 (16.4%), 14 (11.5%); Hosp,12.8±2.9, 14.5±2.7, 11.2±3.4; nBCs per pt: 2.3±0.6, 1.7±0.5,2.9±0.8; PAT: 232 (95.1%), 120 (98.4%), 112 (91.8%); M rate: 39/244 (16.0%), 21/122 (17.2%), 18/122 (14.8%). Sources of bacteraemia in group A and B were respectively: pneumonia 62 and 71, surgical infection 32 and 31, central venous catheter 12 and 12, CNS 3 and 2, unknown 13 and 6. Imipenem 68.1%, ampicillin / sulbactam 78.7% and piperacillin / tazobactan 63.9% were the most active agents against AB.

CONCLUSION. i) Pts of both groups had similar LOS, percentage of PAT and M rates. ii) AB bacteraemia was observed more frequently in pts receiving TPN and in pts with longer hospitalization before, but in not statistically significant degree (NS). iii) Pts of group B had increased number of positive BCs than AB-infected pts ($p<0.05$) iv) AB was isolated more frequently in younger pts ($p<0.01$) and rarely in pts >50 years (except 2 cases). v) Interestingly during AB outbreaks, *Kl. pneumoniae* is never isolated. vi) A more frequent and severe thrombocytopenia was observed in pts with sepsis due to AB.

020

HIDDEN INHOSPITAL MORTALITY IN ICU-BACTEREMIC PATIENTS

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INTRODUCTION. Clasically ICU bacteraemias have been associated with high global and related to infection ICU mortality rates. The aims of this study were to determine the prevalence of hidden in-hospital mortality in ICU bacteraemic patients after they have been discharged from ICU, to describe the main clinical, epidemiological and microbiological features of such patients and to know the factors which are directly related with hidden mortality of critically ill patients in order to prevent it.

METHODS. During a three year and a half period, from 1999 to 2002, 84 ICU-bacteraemic patients were prospectively evaluated after they were discharged from ICU. Patients who died in the ward were assigned to hidden in-hospital mortality group. Clinical and microbiological variables were studied. A multivariate analysis was performed to determine the factors associated with hidden mortality.

RESULTS. The prevalence of hidden in-hospital mortality was 15,47% (n = 13). No related mortality to bacteraemia was found in this group. The age of these patients was 63,2± 12.3 and its mean APACHE II and SOFA score were 17.9±9 and 7.8± 4 respectively. The most frequent source of bacteraemia in the hidden mortality group was the respiratory focus (46%) although there were no significant differences in these variables with the patients who survived. The principle aetiologies of cases with in-hospital mortality were: *Acinetobacter baumannii* (n = 4), and *Pseudomonas aeruginosa* (n = 3). The univariate analysis showed that factors as surgical procedure, length of hospital stay and *Pseudomonas aeruginosa* bacteraemia had an important relationship with hidden mortality. A multivariate analysis only demonstrated that *Pseudomonas aeruginosa* bacteraemia (OR 7.6, 95% CI 1.13-50.7) and the length of stay (OR 1.02, 95% CI 1 - 1.04) were factors associated with in-hospital hidden mortality of ICU-bacteraemias

CONCLUSION. The prevalence of hidden intra-hospital mortality is high after an episode of ICU bacteraemia. Hidden mortality was associated with the presence of *Pseudomonas aeruginosa* bacteraemia and length of stay. ICU prognostic factors as APACHE II or SOFA scores were not predictor factors of in-hospital mortality.

Oral Presentations
The circulation in sepsis – 021-025

021

SUBLINGUAL PCO_2 MONITORING IN PATIENTS WITH SEPTIC SHOCK

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INTRODUCTION. Experimental studies have documented dramatic increases in sublingual PCO_2 ($PslCO_2$) during circulatory shock. More recently, $PslCO_2$ measurements have been correlated with the degree of severity of shock in patients admitted in an emergency room. Hence, $PslCO_2$ monitoring may represent a simple, noninvasive, and rapidly responsive technique to quantify the severity of circulatory shock. The purpose of this study was to evaluate $PslCO_2$ monitoring during resuscitation of patients with septic shock.

METHODS. In 12 invasively monitored, sedated and mechanically ventilated patients in the early phase of septic shock, $PslCO_2$ was monitored continuously using a microelectrode CO_2 sensor (Capnoprobe SL Model 2000 Sensor, Optical Sensor Inc, MN, USA) and gastric mucosal PCO_2 ($PgCO_2$) using gas tonometry (Tonocap^R). In 6 of these patients, sublingual microcirculation was also assessed using the Orthogonal Polarization Spectral imaging technique (Cytoscan^R, Cytometrics, Philadelphia, PA, USA).

RESULTS. In each patient, resuscitation manoeuvres (volume expansion, followed by the infusion of dopamine, with or without dobutamine) increased mean arterial pressure and cardiac output. $PslCO_2$ progressively decreased from 87 ± 14 to 62 ± 11 mm Hg ($p < 0.05$).This was accompanied by a improvement in sublingual microcirculation with an increase in the vessels density from 3.6 ± 0.2 to 5.3 ± 0.8 vessels/mm and an increase in the percentage of perfused capillaries from 42 ± 5 to 59 ± 5%. The decrease in $PslCO_2$ was more significant than the decrease in $PgCO_2$ (- 27 ± 11 and - 15 ± 10%, respectively; $p < 0.05$). There was a significant correlation between the $PslCO_2$ and $PgCO_2$ values ($r^2 = 0.53$; $p < 0.05$).

CONCLUSION. $PslCO_2$ monitoring promises to serve as a technically simple and non-invasive method to assess haemodynamic resuscitation in critically ill patients with septic shock.

022

INCREASED BLOOD FLOW PREVENTS INTRAMUCOSAL ACIDOSIS IN SHEEP ENDOTOXEMIA

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INTRODUCTION. Increased intramucosal-arterial PCO_2 difference ($DeltaPCO_2$) is a common finding in experimental endotoxemia. However, its meaning remains controversial, as it has been ascribed either to hypoperfusion of intestinal villi or to cythopatic hypoxia. Our hypothesis was that increased blood flow could prevent the increase in $DeltaPCO_2$.

METHODS. In 12 anesthetized and mechanically ventilated sheep, we measured cardiac output, superior mesenteric artery blood flow (blood flow), lactate, gases, haemoglobin and oxygen saturations in arterial, mixed venous and mesenteric venous blood, and ileal intramucosal PCO_2 by saline tonometry. Intestinal oxygen transport and consumption (DO_2 and VO_2) were calculated. After basal measurements, *Escherichia coli* lipopolysaccharide (5 mug/kg) was injected. Then, sheep were assigned to normal blood flow (n = 6) or to increased blood flow group (n = 6) during 120 minutes. Saline solution was used to maintain blood flood at basal levels, or to increase it to about 50 % of basal. Data (mean ± SD) were analyzed with two-way ANOVA.

RESULTS. See Table.

		Blood flow (ml/min/kg)	DO_2 (ml/min/kg)	VO_2 (ml/min/kg)	$DeltaPCO_2$ (mm HG)	Lactate (mmol/l)
Normal	Basal	637 ± 192	71.5 ± 20.5	23.7 ± 4.1	7 ± 4	1.7 ± 0.8
Blood flow	Endotoxin	601 ± 163	64.3 ± 16.7	26.0 ± 9.8	19 ± 4*	2.3 ± 1.0
Increased	Basal	582 ± 154	64.2 ± 18.8	30.1 ± 9.6	5 ± 7	2.2 ± 1.6
Blood flow	Endotoxin	932 ± 224*§	87.1 ± 23.6	38.6 ± 10.8	9 ± 6§	1.7 ± 1.1

** p < 0.05 vs. BASAL. § p < 0.05 vs. normal blood flow*

CONCLUSION. Despite preserved global blood flow and oxygen transport, intramucosal acidosis developed in endotoxemic sheep. However, increased blood flow was able to prevent $DeltaPCO_2$ elevation. Our results suggest that intramucosal acidosis is mainly related to local hypoperfusion.

023

MICROVASCULAR ALTERATIONS ARE INDEPENDENT OF SYSTEMIC FACTORS IN PATIENTS WITH SEPTIC SHOCK

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INTRODUCTION. Microvascular alterations are common in patients with septic shock. We investigated whether systemic factors would influence these microcirculatory alterations.

METHODS. We used an Orthogonal Polarization Spectral (OPS) imaging device (Cytoscan A/RII; Cytometrics, Philadelphia) to explore the sublingual microcirculation in 96 patients with severe sepsis (n=8) or septic shock (n=88). All these patients were studied within 48h of the development of severe sepsis or shock. Most of the patients were treated with vasoactive agents: dobutamine (n=37, 6[5-20]mcg/kg.min), dopamine (n=82, 18[5-20] mcg/kg.min and norepinephrine (n=34, 0;22[0.07-1.65]mcg/kg.min). Epinephrine was also used in 3 patients. In each patient, 5 sublingual areas were investigated. Five sequences of 20 sec each were stored and analyzed off-line semi-quantitatively: vessel density was defined as the number of vessels crossing 3 horizontal and 3 vertical lines; flow was defined as continuous, intermittent, or absent. The vessels were then separated into venules and capillaries, using a 20 mm cut-off value. Data from the 5 areas were averaged. In addition, global haemodynamic parameters were obtained using an arterial line and a pulmonary artery catheter. Data are presented as median [range]. Relationship between microcirculatory perfusion (proportion of perfused small vessels) and systemic variables was assessed by linear regression.

RESULTS. Mean arterial pressure (MAP) was 70 [49-102] mmHg, cardiac index (CI) 3.48 [1.21-9.1] L/min.M², haemoglobin levels (Hb) 8.9 [5.9-14.6] g/dL, pH 7.36 [7.00-7.53], lactate 2.1 [3.9-11.0], APACHE II 18[4-31], SOFA 10[5-19]. The vessel density was 5.3 [2.8-7.9] n/mm, the proportion of perfused venules 99 [89-100] and proportion of perfused capillaries 54 [10-81]%. The relationship between the capillary perfusion and systemic factors is reported in the table.
None of these relationships were significant. In addition the severity of microcirculatory alterations were not related to the dose of vasoactive agents.

Relationship between capillary perfusion and systemic factors:

	MAP	CI	Hb	pH	Lactate	APACHE II	SOFA
R^2 values	0.09	0.04	0.02	0.13	0.04	0.06	0.06

CONCLUSION. Microvascular blood flow alterations are independent of systemic factors.

024

MICROCIRCULATORY BLOOD FLOW IN THE INTESTINE DURING ADMINISTRATION OF VASOPRESSIN IN SEPTIC SHOCK

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INTRODUCTION. Vasopressin has been proposed for treatment of catecholamine-resistant septic shock (1), however, very little is known about its effects on intestinal microcirculation. The aim of this study was to measure microcirculatory blood flow (MBF) in the gastrointestinal tract during administration of ornithin-8-vasopressin in septic shock.

METHODS. Pigs (20 - 25 kg, n = 16) were anaesthetised and ventilated. Cardiac index was measured with thermodilution. MBF was measured in the mucosa and muscularis of the jejunum and the colon using a multi-channel laser Doppler flowmetry. Peritonitis was induced by instillation of autologous feces in the peritoneal cavity. After 240 min, intravenous (i.v.) colloids were administered to transform hypodynamic shock into hyperdynamic septic shock. After 300 min, group V (n=8) received 0.06 IU/kg/h of ornithin-8-vasopressin continuously i.v. during 180 min while group S (n=8) received isotonic saline

RESULTS. Baseline measurements were taken at T = 300 min. Results are presented as percent of baseline. Mean arterial blood pressure increased by 25% ($p<0.05$) during infusion of vasopressin in the group V ($P<0.05$), while it remained unchanged in group S. Cardiac output decreased by 30% in group V ($p<0.05$) but remained unchanged in group S. MBF in the jejunal mucosa remained unchanged in both groups while MBF in the jejunal muscularis decreased by 20% (n.s.) in group S and by 25% ($p<0.01$) in group V. MBF in the colon mucosa decreased by 20% ($p<0.01$) in group S and by 10% ($p<0.05$) in group V. MBF in colon muscularis decreased by 17% in group S (n.s.) and by 40% in group V ($p<0.01$).

CONCLUSION. In this porcine model of fluid resuscitated septic shock, administration of vasopressin resulted in increased arterial blood pressure and decreased systemic and microcirculatory blood flow in the intestinal muscularis. In contrast, microcirculatory blood flow in the mucosa of the jejunum and colon was not affected by vasopressin.

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025

ARGININE VASOPRESSIN IN ADVANCED VASODILATORY SHOCK: A PROSPECTIVE, RANDOMIZED, CONTROLLED STUDY

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INTRODUCTION. Vasodilatory shock is a potentially lethal complication of severe disease in critically ill patients (1). Arginine vasopressin (AVP) has been shown to be a potent vasopressor agent to stabilize cardiocirculatory function even in patients with advanced vasodilatory shock (2).

METHODS. Forty-eight patients with catecholamine-resistant vasodilatory shock were prospectively randomised to receive a combined infusion of AVP and norepinephrine (NE) or NE infusion alone. In AVP patients, AVP was infused at a constant rate of 4 U/h. Haemodynamic, acid/base, single-organ, and gastric tonometrically derived variables were reported before, 1, 12, 24, and 48 hours after study entry.

RESULTS. AVP patients had significantly lower heart rate (p=0.003) and NE requirements (p<0.001) than NE patients during the 48 h study period. Mean arterial pressure (p<0.001), cardiac index (p=0.001), stroke volume index (p=0.005), and left ventricular stroke work index (p<0.001) were significantly higher in AVP patients. NE patients developed significantly more new-onset tachyarrhythmia's than AVP patients (54.3% vs. 8.3%; p<0.001). Gastrointestinal perfusion, assessed by gastric tonometry-derived variables, was better preserved in AVP-treated patients than in NE patients (PrCO2, p=0.03; Pr-aCO2, p=0.014). Total bilirubin concentrations were significantly higher in AVP patients (p=0.001).

CONCLUSION. In this study, the combined infusion of AVP and NE proved to be superior when compared with NE alone in the treatment of cardiocirculatory failure in catecholamine-resistant vasodilatory shock. Patients receiving AVP had a significantly higher blood pressure, improved cardiac performance, and needed less norepinephrine. A continuous infusion of AVP further reduced cardiotoxic effects of high catecholamine dosages such as new-onset tachyarrhythmia's. Gastrointestinal perfusion as assessed by gastric tonometry seemed to be better preserved in AVP-treated patients.

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027

STUDY OF COINCIDENCES BETWEEN TWO HEAD TRAUMA EVALUATION SYSTEMS

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INTRODUCTION. Evaluation of head trauma is usually performed by two methods, one clinical (Glasgow Coma Score -GCS-) and other structurally descriptive (Traumatic Coma Data Bank -TCDB-). Our aim is to estimate the concordances by using both methods and to ascertain their correspondence with the final clinical result (Glasgow Outcome Scale -GOS-).

METHODS. From 2000 to 2002, 2747 patients were admitted to our multidisciplinary ICU, 175 cases admitted because of head trauma (isolated or with other concomitant injuries), They were operated or not before ICU admission (118 non operated). All of them were assessed by GCS and TCDB. Severity and prognosis estimations were performed by SAPSII and ISS. Final clinical outcome was assessed by means of GOS.

RESULTS. Overall GCS at admission was 9.8 ± 3.9, and according to it, the head trauma was classified as mild (37 %), moderate (28%) and severe (35%). Forty five percent of cases were sedated when admitted (GCS was assessed in the previous out of ICU phase). TCDB classified patients in 18 % in category I, 52 % in II, 8 % in III, 4 % in IV, 14 % in V and 4 % in VI. Global ISS was 25.6 ± 19.3 and SAPS II was 33.5 ± 22.7, with a predicted mortality of 0.18. GOS showed values of 1 in 20 %, SMR was 1.11. Correlations GCS-TCDB showed no significant differences, but we found them when concordances GCS-GOS were analysed (p: 0.000) with higher mortalities associated to GCS values of 3-4. ANOVA test only gave values of p <0.05 when TCDB groups compared to ISS and GCS stratifications. Conversely, when comparing GOS either with ISS, SAPS II, GCS and age, p was always <0.05.

CONCLUSION. In our series, and in spite of greater objectivity associated to TCDB classification (and considering the possible inferences of previous sedation with GCS estimations), clinical assessment was better correlated with final clinical outcome (GOS) and its prediction by SAPSII than in terms of TCDB.

Oral Presentations
Traumatic brain injury: Clinical and experimental – 026-030

026

EXTRACRANIAL COMPLICATIONS IN ACUTE BRAIN INJURED PATIENTS: A LARGE EUROPEAN MULTICENTER STUDY

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INTRODUCTION. Sepsis and Acute Lung Injury/Respiratory Distress Syndrome (ALI/ARDS) have been reported to contribute to high incidence of morbidity and mortality. We performed a multicentric observational study to define incidence and management of sepsis and acute lung injury according to the actual standard in European intensive Care Units (ICUs).
METHODS. A cohort multicentric observational (SOAP) study included all adult patients admitted to the ICU between May 1 and May 15, 2002. Patients with Glasgow Coma Score (GCS) <=8 were identified as severe brain injured and followed up until death, hospital discharge or 60 days.
RESULTS. Among 3147 patients (198 centres from 24 countries) enrolled, 373 neurological patients were selected (189 with GCS <= 8) 62% male, mean age 54±19 years, SAPS II score 39±18. Out of 189 severe brain injured, 68 patients (36%) were admitted to ICU for trauma and 111 (59%) for cerebrovascular accident. Mean SOFA was 7±3. 39% of patients were transferred from another hospital or hospital floor, 45% from the ambulance and 16% from the operating room. Sepsis was present in 41% during the first week of the ICU stay and septic shock in 16% of patients. On admission severe sepsis was already present in 16% and septic shock in 4%. Respiratory tract was the most frequent site of infection (38%). ALI/ARDS occurred in 35 (18%). No difference were found in ventilatory parameters between patients with and without ALI/ARDS. The total fluid balance was more negative in patients with ALI/ARDS (p=0.03) and they were treated more often with vasoactive drugs (60% vs 27%, p<0.001).The median ICU length of stay was 5.6 (2-14) days. ICU mortality rate was 78 (41%) and the overall hospital mortality was 47%. In the most severe brain injured group (GCS <= 8), low GCS, medical admission and high SAPS II score were independent predictors of mortality (p<0.05).
CONCLUSION. Our study confirms that the occurrence of sepsis and ALI/ARDS is common in the early phase of the ICU stay in brain injured patients. Haemodynamic management but not ventilatory strategy is modified in brain injured patients who develop ALI/ARDS. However in brain injured patients the most powerful independent predictor of mortality remains the neurological dysfunction expressed by the GCS.
Grant acknowledgement: On behalf of the SOAP investigators

028

INACCURATE EARLY ASSESSMENT OF NEUROLOGICAL SEVERITY IN HEAD INJURY

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INTRODUCTION. Intubation, which requires sedation and myorelaxants, may lead to inaccurate neurological evaluation of severe head-injured patients. Aims of this study were: to describe the early clinical evolution of TBI patients admitted to intensive care unit (ICU); to identify cases of over-estimated neurological severity; to quantify the risk factors for this over-estimation.

METHODS. A total of 756 head-injured patients consecutively admitted to ICU of three academic neurosurgical hospitals (NSH) were assessed. Cases whose severity was potentially over-estimated are identified with the following four criteria and indicated as „mistakenly severe"(MS): no surgical intracranial masses; could not follow commands at neurological assessment; were dismissed from the ICU in ≤3 days to a regular ward; having regained the ability to obey commands. Associations of categorical independent variables with MS were assessed with chi-squared test: a p value less than 0.05 were considered significant. A multivariate analysis was done by logistic regression.

RESULTS. Hypoxia was clinically suspected or measured in 206 patients. A total of 678 patients were intubated and/or sedated-paralyzed at the post-stabilization evaluation. In all, 305 patients had surgical intracranial masses and were urgently operated. Among the 451 non-surgical cases 59 patients fulfilling the criteria for MS were identified. The main features distinguishing MS from really severe cases were a younger age, higher GCS score, less pupillary abnormalities and a reduced frequency of hypoxia, hypotension and extra-cranial injuries (chi^2 p<0.05). A logistic regression analysis indicated age <40 years, a CT Marshall classification of Diffuse Injury I and II, a GCS motor response ≥5 and a GCS verbal response (for the few cases assessable) ≥3 as independent predictors of MS.

CONCLUSION. In a certain proportion of non-surgical TBI patients, mostly intubated and sedated, neurological examination is difficult and severity can be over-estimated. Risk factors for this inaccurate evaluation can be identified and if it is the case, clinical decisions should be based on further examination.

029

IMPACT OF THE DURATION OF HYPERTHERMIA ON CEREBRAL HAEMODYNAMICS

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INTRODUCTION. Hyperthermia (HT) is associated with a poor outcome of critically ill patients with ischemic or cerebral injured and it can last for hours. A small variation of temperature (T) of 1°C can exacerbate the neuronal damage as shown in different experimental studies. We studied the effect and especially the duration of HT on the cerebral and global haemodynamics (HD) parameters in the above patients, in order to detect, and therefore prevent, their deterioration under a long episode of HT.

METHODS. Among 350 patients admitted in the neuro ICU, 95 needed a continuous intracranial pressure (ICP) monitoring for intracranial hypertension (ICH) in the first 24 hours after their admission. These patients' tympanic T was charted every two hours, with their values of ICP, cerebral perfusion pressure (CPP), heart rate (HR) and the mean arterial pressure (MAP) during 5 days. HT was considered if the T was above 38°C and Hypothermia (hT) if it was less than 36°C.The duration of time necessary for the patient's T to reach a peak of 38 °C or 39°C from their normal T was also considered. ANOVA tests were used for statistics.

RESULTS. 85% of these 95 patients developed at least one episode of HT and their mean age was 52 years old. The global mortality was 60% and it was significantly higher in patients who developed HT than those without HT or who developed hT ($p<0.005$). Neither the number of episode of HT nor the threshold at which fever occurred, influenced the mortality of patients with HT ($p>0.005$). ICP rose significantly and CPP was reduced, as well as HR and MAP, if HT lasted more than 5 hours ($p<0.005$). The same length of time was needed for all these parameters returned back to their values before HT occurred. 80% of microbiological cultures from these patients were negative when they developed HT during the first 5 days after their admission.

CONCLUSION. Critically ill patients that had ICH and developed HT were exposed to a high mortality rate. HT often significantly increased ICP and adversely affected the patients' HD parameters, if it lasted more than 5 hours. These evolutions of fever should be taken into account when treating HT in patients with brain injury.

030

IDENTIFICATION OF CERVICAL SPINE INJURIES IN UNCONSCIOUS TRAUMA PATIENTS: A CLINICIAN SURVEY

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INTRODUCTION. No universally accepted guidelines exist for the determination of cervical stability in unconscious trauma patients. We assessed current clinical practice and knowledge amongst intensivists and trauma surgeons at a tertiary level trauma centre.

METHODS. A questionnaire survey was distributed to all consultants involved in trauma care at the regional intensive care unit for Northern Ireland. These comprised 13 intensivists, 5 neurosurgeons and 16 orthopaedic surgeons.

RESULTS. All individuals completed the questionnaire. 10/13 (77%) intensivists, 2/5 (40%) neurosurgeons and 2/16 (13%)orthopaedic surgeons felt CT imaging, in addition to plain radiography, was necessary to exclude a cervical spine injury in an unconscious patient. All intensivists and neurosurgeons, but only 11/16 (69%) orthopaedic surgeons, recognised that prolonged cervical collar immobilisation could lead to skin pressure necrosis. 5/13 (38%) intensivists and 5/5 (100%) neurosurgeons were aware that cervical collars could adversely affect intracranial pressure. No orthopaedic surgeon was aware of this complication. All neurosurgeons, 11/13 (85%) intensivists and only 9/16 (56%) orthopaedic surgeons could be satisfied to „clear" the cervical spine after negative imaging.

CONCLUSION. Clinical practice and knowledge differed between the specialist groups. Orthopaedic surgeons were the least likely to discontinue cervical immobilisation in unconscious patients, even if radiological imaging was negative. This practice was associated with lower recognition of morbidity secondary to cervical immobilisation. A validated management protocol is urgently required in this contentious area.

Oral Presentations
Alveolar recruitment – 031-033

031

PRONE POSITION EFFECTS ON ALVEOLAR RECRUITMENT AND ARTERIAL OXYGENATION IN ACUTE LUNG INJURY

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INTRODUCTION. Evaluation of alveolar recruitment and arterial oxygenation during the 1st 48 hours in patients turned to PP as compared to SP.

METHODS. 16 patients with direct ALI randomised (H0) into SP (n=6) and PP (n=10; PP for 12 h/24) groups. Ventilation standardised using controlled volume mode with V_T 6-8 ml/kg, PEEP 2 cm H_2O above LIP determined by continuous flow inflation 5 l/min, frequency to get pH > 7.30. At H0, H24 and H48, measurements realised in SP: ABG, Cst with a 5-s end-inspiratory occlusion, respiratory system pressure-volume curve. Vrec at H24 and H48 calculated as volume difference at a pressure level of 20 and 30 cm H_2O relative to H0.

RESULTS. The 2 groups are comparable for SAPS2, LIS, ventilatory settings. 5 responders to PP during the 1st session and 2 for the 2nd. Vrec greater in the SP group at H48 vs H24 but no significant difference between the 2 groups concerning oxygenation and Vrec. No correlation between PaO_2 changes and Vrec.

Comparison between SP and PP groups

	H0	SP (n=6) H24	H48	H0	PP (n=10) H24	H48
PaO_2/FiO_2 ratio (mm Hg)	173 ± 98	182 ± 95	177 ± 95	150 ± 61	163 ± 39	183 ± 56
Cst (ml/cm H	63 ± 20	60 ± 22	63 ± 17	50 ± 19	51 ± 19	57 ± 26
Vrec/P=20 (ml)		-23 ± 246	126 ± 256*		-101 ± 171	-65 ± 183
Vrec/P=30 (ml)		-93 ± 390	171 ± 370*		-16 ± 196	-26 ± 123

**p<0.05 vs SP H24; Cst static compliance; Vrec recruited volume*

CONCLUSION. No significant difference could be found in oxygenation nor in alveolar recruitment between continuous SP and two 12-h daily PP sessions during a 48-hours observation period.
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032

BIPAP VERSUS PCV WITH EQUAL AIRWAY OR TRANSPULMONARY PRESSURE IN EXPERIMENTAL LUNG INJURY

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INTRODUCTION. Ventilation using biphasic positive airway pressure (BIPAP) with spontaneous breathing has lead to improvements in ventilation perfusion (V_A/Q) distribution in experimental lung injury. Due to a vertical gradient of superimposed pressure an increased regional transpulmonary pressure (P_{TP}) is needed in the dependent lung. We hypothesised that BIPAP effectively increases regional P_{TP} which can also be achieved by increasing inspiratory pressure (P_{INSP}) in controlled ventilation.

METHODS. We compared BIPAP (with PEEP=5 cmH2O, P_{INSP} to get a V_T of 8 ml/kg, and a portion of spontaneous breathing targeted at 20% of total V_E) to pressure controlled ventilation (PCV) in 8 anaesthetised pigs with saline lavage induced lung injury. Inspiratory pressure (P_{INSP}) during PCV was set to result in equal airway pressure (PCV_{AW}) or equal transpulmonary pressure (PCV_{TP}). Oesophageal pressure was measured and P_{TP} was calculated as $P_{TP} = P_{INSP} + DeltaP_{ESOPHAGUS}$. Haemodynamic changes and distribution assessed by the multiple inert gas elimination technique were analysed after a 60 minute equilibrium phase each. Data are presented as mean±SD and were tested for significant differences by ANOVA for repeated measurements.

RESULTS. Mean P_{TP} was 26.4±3.3cmH2O during BIPAP and 27.5±4.5cmH2O with PCV_{TP}, but 20.4±4cmH2O with PCV_{AW} ($p<0.005$). Peak pressure was higher in PCV_{TP} (31.6±4.6cmH2O) than in BIPAP and PCV_{AW} (24.7±3.7 and 24.5±4.1cmH2O), which led to an increase in tidal volume with PCV_{TP} to 11.7±2.1ml/kg, compared to 8.1±0.5ml/kg with BIPAP and 7.4±1.0ml/kg with PCV_{AW} ($p<0.0001$). Intrapulmonary shunt flow was 32±11% during BIPAP and increased with PCV_{AW} (39±10%), and less pronounced with PCV_{TP} (36±14%, n.s.). Cardiac output with PCV_{TP} decreased to 3.4±0.6 l/min (BIPAP 4.8±0.8 and PCV_{AW} 3.8±0.7, $p<0.024$). Oxygen delivery was 492±83 ml/min during BIPAP, 342±71 ml/min during PCV_{AW} and 305±70 ml/min during PCV_{TP}($p<0.002$).

CONCLUSION. Preserved spontaneous breathing activity leading to effectively increased regional transpulmonary pressure seems to be the main mechanism for oxygenation improvement during BIPAP. Ventilation with equal transpulmonary pressure during controlled ventilation results in similar distributions but causes decreased oxygen delivery and cardiac output.

REFERENCE(S).
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033

ALVEOLAR RECRUITMENT AFFECTS PEEP-INDUCED CHANGES IN CARDIAC FUNCTION IN ARDS

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INTRODUCTION. Aim of the study was to investigate the influence of alveolar recruitment on changes of cardiac function and intrathoracic blood volumes distribution induced by PEEP in ARDS patients.

METHODS. In 9 ARDS patients we randomly applied for at least 30 minutes three different levels of PEEP (5, 10 and 15 cmH_2O). All of them were monitored with a pulmonary artery thermodilution catheter and a 4 F thermistore-tipped, fiberoptic catheter inserted through a femoral artery, connected to an integrated monitoring system (COLD Z-021). At each PEEP level, we obtained: 1) main gas exchange, haemodynamic and respiratory parameters; 2) cardiac (CI), stroke volume (SVI=CI/heart rate), right heart end-diastolic volume (RHEDVI), and left heart end-diastolic volume (LHEDVI), all indexed for body surface area; 3) functional residual capacity at ZEEP (FRC_{ZEEP}) by helium dilution technique. For each variable we computed PEEP induced changes at PEEP 10 and 15 respect to 5. Alveolar recruitment was quantified by changes in FRC_{ZEEP} and VA/Q.

RESULTS. Increasing PEEP levels determined a significant increase in arterial oxygenation, and FRC_{ZEEP}, and a significant decrease in VA/Q, CI, SVI, RHEDVI, and right to left end diastolic volume ratio (RH/LH). LHEDVI was not consistently affected by PEEP. The RHEDVI, RH/LH and SVI changes were positively correlated with VA/Q and negatively correlated with FRC_{ZEEP} changes. LHEDVI changes were positively correlated with FRC_{ZEEP} changes. CI and HR changes were positively correlated with $PaCO_2$changes and negatively correlated with pH changes. Changes in SVI were strongly correlated to RHEDVI changes.

CONCLUSION. In ARDS patients, PEEP determined a decrease in CI, SVI, and RHEDVI, and a shift of blood from the right to the left cardiac compartment. The effect of PEEP on SVI was mainly related to changes in right heart function. The observed results are commonly explained by the negative mechanical effect of PEEP on venous return. However, the higher drop in SVI and RHEDVI in presence of higher alveolar recruitment and VA/Q improvement suggests that the effect of PEEP on cardiac function could be partially due to others pathophysiological mechanisms.
Grant acknowledgement: MIUR

035

THE EFFECTS OF HYPOMAGNESEMIA IN THE PHAGOCYTIC ACTIVITY OF NEUTROPHILS IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Mg disturbances are associated with metabolic, neurological and cardiovascular disorders. Hypomagnesemia is found in as many as 12% of hospitalized patients and in 50% to 60% of ICU patients. Several studies performed with experimental animals have suggested that phagocytosis is influenced by Mg concentration. Once phagocytosis by polymorphonuclear neutrophils and monocytes constitutes an essential arm of host defense against bacterial or fungal infections, we decided to investigate whether low plasma concentration of Mg results in reduced neutrophils and monocytes phagocitosis.

METHODS. 26 patients, 39 to 93 years old (mean age 66 years; SD=14.5 years), 50% of whom females admitted our ICU were studied. The quantification of phagocytic activity of monocytes and neutrophils was performed with fluorescein-labelled opsonized *E.Coli* (Phagotest – Orpegen Pharma – Germany). Serum Mg concentration and phagocytic activity of neutrophils and monocytes were determined in the first 24 hours of ICU admission. Immunocompromised patients were excluded from the study. The possible effect of hypomagnesemia on the percent fagocytic activity of the WBC was examined by linear simple and multiple regression analysis.

RESULTS. Hypomagnesemia (Mg<1.6 mg/dL) was associated with reduced phagocytic activity of monocytes. The mean difference in percent monocyte phagocytic activity in subjects with low Mg compared to those with normal or high Mg was 23.5% (95% CI=4.7 to 42.3; p =0.01).After controlling for the effect of gender, which acted as a negative confounder in the association, the mean difference was 29.5 (95% C.I. 9.0 to 50.0). Age, number and distribution of WBC were not associated with phagocytic activity. The association of hypomagnesemia and phagocitic activity of neutrophils nearly reached statistical significance. The mean difference in percent leukocytic phagocitosis was 23.0% (95% C.I. = 2.04 to 48.07; p=0.07).

CONCLUSION. Our results suggest a possible correlation between hypomagnesemia and reduced neutrophils and monocytes phagocytic activity.

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Oral Presentations
Metabolism: General aspects – 034-036

034

CYP2D6 GENOTYPE AND ADVERSE DRUG REACTION IN THE ICU

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INTRODUCTION. CYP2D6 genetic variability is supposed to be a major factor of adverse drug reaction, influencing hospital stay and total costs (1). Single nucleotide polymorphisms within the cytochrome P4502D6 have been associated with a poor metabolizer (PM) phenotype and display a frequency of about 10% in the Caucasian population (2,3). In contrast, gene duplications are associated with the ultrarapid metabolizer genotype. Several commonly used drugs like Beta-blockers, antiarrhythmics, neuroleptics, 5HT3-antagonists, tricyclic antidepressants and opioids are metabolised by this enzyme (2-4). Furthermore, inhibitors of CYP2D6 like amiodarone and cimetidine might block metabolization of CYP2D6 dependent drugs.

METHODS. DNA extracted from whole blood of 500 individuals was analysed. We developed a reliable and fast procedure to identify five PM associated mutations (*3,*4,*6,*7,*8) by real-time polymerase chain reaction (PCR) using subsequent fluorimetric melting point analysis of the PCR product. Additionally, the gene deletion *5 and duplication was investigated.

RESULTS. Genotyping results by real-time PCR proved to be 100% reliable, whereas conventional allele-specific multiplex PCR produced uncertain results in 12.1 % as confirmed by sequence analysis. Labour time was significantly reduced compared to former methods of genotyping like restriction assays or allele-specific PCR. The allele frequency of the population investigated was 0.2 for allele *4, 0.02 for allele *5, 0.01 for allele *3, 0.03 for allele *6 and 0.015 for the gene duplication. In addition, further mutations were detected, one of them displaying a PM genotype. In PMs treated with tramadol for postoperative pain analgesic efficacy was reduced by 33%.

CONCLUSION. Genotyping of CYP2D6 by real-time PCR with fluorimetric melting point analysis proved to be a quick and reliable method. In the future, intensivists should be aware of this possible mechanism of adverse drug response and should consider the individual metabolic capacity which is determined by genotype and co-medication.

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036

CARDIAC TROPONIN I RELEASE AND CYTOKINE RESPONSE DURING EXPERIMENTAL HUMAN ENDOTOXEMIA

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INTRODUCTION. Elevated cardiac troponin I (cTnI) levels are described in a high percentage of septic patients, including patients without other evidence of myocardial ischemia. Although being a highly specific and sensitive marker for angina and myocardial infarction, the value of cTnI as a marker of cardiac involvement in sepsis is still uncertain. It has been postulated that TNF, which is suggested to account for the myocardial depression that may accompany human septic shock, may induce leakage of cytoplasmic cTnI from cardiomyocytes. This could be a possible explanation of cTnI rise without damage to the contraction complex. We therefore used the human endotoxin model to study the relationship between proinflammatory cytokine levels and cTnI.

METHODS. Six healthy male subjects were admitted to the research unit of our ICU. The local medical ethics committee approved the study and written informed consent was obtained from all subjects before enrolment. A radial artery catheter was placed for blood sampling. A standard 12-lead electrocardiogram was recorded at baseline and 24 hours after dosing. During study vital signs were measured continuously. At time point zero, the volunteers received a one-minute infusion of endotoxin at a dose of 4ng/kg body weight. Blood for cTnI analysis and determination of cytokines was drawn at various time points.

RESULTS. TNF appeared in the circulation 30 minutes after injection (T=0.5h), reaching peak levels (5665±1910pg/ml) 2 hours after infusion. At T=24h TNF was still elevated in circulation compared to T=0. None of the 6 volunteers had a cTnI value > 0.1 ìg/L at T=0, 6h or 24h.

CONCLUSION. Our results show that a significant rise in TNF is not sufficient for cardiomyocyte injury as measured by cTnI levels. Further studies are needed to determine the mechanism behind increased cTnI levels and its role as a marker of cardiac injury in the setting of an inflammatory insult.
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Oral Presentations
Organisational issues – 037-039

037

END OF LIFE DECISIONS: WITHDRAWAL OF ACTIVE TREATMENT IN INTENSIVE CARE UNITS IN THE UNITED KINGDOM

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INTRODUCTION. The end of life experience frequently occurs in the intensive care unit (ICU). Withdrawal of active treatment has become accepted in many countries, but little is known regarding actual practice.

METHODS. Data came from the Case Mix Programme Database, covering 127 adult, general ICUs in England, Wales and Northern Ireland, from 1996 to 2001. The data were collected prospectively, by trained data collectors according to precise rules and definitions, and were extensively validated both locally and centrally. We examined admissions to determine the frequency of withdrawal of active treatment, the characteristics and outcome for those patients, and predictors of the decision.

RESULTS. In this cohort there were 118,199 admissions to intensive care and the decision to withdraw active treatment occurred during 11,694 (9.9%). The most commonly reported primary reason for admission to ICU for patients who had active treatment withdrawn was pneumonia, no organism isolated (n=794) followed by septic shock (n=693) and bacterial pneumonia (n=534).
There were 36,397 (30.8%) deaths before discharge from hospital and 11,586 (31.8%) of these occurred after treatment withdrawal. There was considerable variation between units in the percentage of hospital deaths that occurred after active treatment withdrawal (range 2.4% to 65.5%). For deaths that occurred in the ICU (n=11,083), the median time to death after the decision to withdraw active treatment was 2.2 hours (interquartile range 0.7 to 6.3 hours). After multivariate analysis, factors associated with the decision to withdraw treatment were: older age; higher Acute Physiology Score (APACHE II); increasing number of severe conditions in the medical history; longer length of hospital stay prior to admission to ICU; admission from the ward, or another ICU/HDU in the same hospital; CPR in the 24 hours prior to admission; ventilation or sedation/paralysis in the first 24 hours after admission; treatment in a non-university hospital; and having fewer ICU beds in the unit.

CONCLUSION. Overall 31.7% of hospital deaths following admission to ICUs in the United Kingdom occurred after the decision to withdraw active treatment. Although most deaths after treatment withdrawal occurred within a few hours, some took much longer. There was wide variation by unit regarding the practice of treatment withdrawal, suggesting improved guidelines may be needed to ensure appropriate decision-making.
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038

CULTURE, ORGANISATION AND MANAGEMENT IN INTENSIVE CARE (COMIC)

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INTRODUCTION. The aim of the study is to develop and validate a single questionnaire designed to assess culture, organization and management in intensive care units (COMIC).

METHODS. Multicentre, prospective study, including 26 ICUs located in the Paris area. All ICU personnel were asked to complete the questionnaire. The internal consistency of the items composing each scale was tested by using Cronbach's alpha coefficient; convergent and discriminant validity were assessed by factor analysis.

RESULTS. Construction of the questionnaire: The overall completion rate was 74%, with 1000 respondents (750 nurses, 26 head nurses, 168 physicians and 56 medical secretaries). The final version of the questionnaire comprises 106 items distributed in 9 dimensions and 22 scales: culture (n=3), coordination and adaptation to uncertainty (n=3), communication (n=3), problem-solving and conflict management (n=2), organizational learning and organizational change (n=2), skills developed in the patient-caregiver relationship (n=1), subjective unit performance (n=3), burn-out (n=3), job satisfaction and intention to quit (=2). The results supported the internal consistency of the scales (Cronbach's alpha > 0.7). Team satisfaction-oriented culture was positively correlated with good managerial practices, individual well-being, and perceived unit performance. Variability within ICUs was significantly smaller than variability among ICUs, for all the scales ($p<0.01$ by analysis of variance).
The COMIC questionnaire enables to identify outlier ICU that is confirmed by on-site visits. The ICU director and head nurses tend to favour a team-satisfaction culture while the other members of the team are more defensive. ICUs can be classified as High Reliability Organisations with results similar to nuclear industry and air control traffic. The multilevel logistic regression identified several factors explaining the quality of organisation: absence of burn-out, older staff, job satisfaction, high workload ($p<0.001$).

CONCLUSION. The COMIC questionnaire enables managers to assess the organizational performance of their ICU.
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039

THE OUTCOME OF A RADICAL MODERNISATION PROGRAMME OF CRITICAL CARE SERVICES IN ENGLAND

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INTRODUCTION. After 2yrs the NHS Modernisation Agency Critical Care Programme has delivered measurable outcomes in the implementation of recommendations in the report Comprehensive Critical Care-a review of adult services in England. The report described a new patient focused specialty based on the severity illness of each patient

METHODS. The programme used established collaborative methodology with the ultimate goal of improving access, experience and outcomes for all patients. There have been 3 strands of work: 1 Organisational development-facilitate the formation of a multiprofessional Critical Care Delivery Group in each hospital to develop intergrated critical care services. Critical Care Networks oversee the provision of services in affiliated hospitals. 2 Service redesign-a resourced service improvement team in each network plans, implements and analyses improvement projects. National and local educational events ensure training, experience and best practice are shared. 3 Influencing policy-relationships have been established with all stakeholders in the delivery of critical care services with working groups formed to address specific national issues

RESULTS. 1 228 hospitals with critical care are affiliated to one of 29 networks with the majority working to common standards, policies and protocols. All have communication stratergies-38% website/electronic. 170 hospitals have outreach services. There has been a 38% decrease in the number of transfers for non medical reasons. 2 552 improvements projects have been reported. Issues reviewed include-speed of diagnostic services, bed management, prevention of admission (MEWS),cancelled operations, role of the AHP(dieticians, physios), nurse led decisions (weaning, discharge),patient transfers, discovery interviews and care bundles. 3 € 145 million was invested into critical care. There has been an increase in the number of critical care beds from 2362 to 3097 (31%) in 3yrs. Links with all professional bodies are in place. Reports on Outreach, Weaning and Long term Ventilation, Role of AHP's, Commissioning, HRG's and a Minimum Critical Care Data Set have been produced

CONCLUSION. The NHS Modernisation Programme has resulted in measurable improvements in the organisational structure and the delivery of critical care services-they are now becoming more patient focused, cost effective, quality services delivered in the right place, at the right time by appropriately skilled staff

Oral Presentations
Highlights on nosocomial infections – 040-042

040

RELATIONSHIP OF NOSOCOMIAL INFECTION AND NURSE STAFFING : A PILOT STUDY WITH TIME SERIES ANALYSIS

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INTRODUCTION. The role of nurse understaffing and overcrowding to the occurrence of nosocomial infections has recently been suggested (1). The objective of the present study was to assess the relationship between nurse staffing level/patient crowding and nosocomial infection incidence rate in our 16-bed medical ICU.

METHODS. From April 1, 2001 to December 31, 2001 we collected on a day-by-day basis number of patients present in the ICU; number of pulmonary, venous catheter, arterial line, urinary tract, bacteraemia nosocomial infections; nurse and auxiliary nurse density. The density of nurse was computed as (number of nurse over 24 hours x 24) / number of hospitalized patients in the same 24 hours. Same computation was done for auxiliary nurse density. The data of nurse staffing density and nosocomial infection rate were analysed using exponential smoothing of time series and autocorrelations between series (2).

RESULTS. One-hundred and eighty-one patients were followed up their ICU discharge during the study period. Time series of all of nosocomial infections and nurse and auxiliary nurse hours per patient exhibited a marked variability. In particular, nosocomial infections peaked on August/September 2001 the days after a period of reduction in nursing staff. The coefficients of autocorrelation were significant ($p<0.05$) for a time lag between the two series of 2, 5, 6, 8, 9 and 10 days.

CONCLUSION. In this pilot study there was a significant link between nurse understaffing and nosocomial infection in our ICU. A prospective study on more patients and covering a greater period of time is ongoing in our ICU to confirm these results and to adjust with trend-cycle and seasonal components.

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041

DIFFERENCES BETWEEN KNOWLEDGE AND AWARENESS IN INFECTION PREVENTION

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INTRODUCTION. Everybody working in an ICU knows that hand-washing and semi-recumbent position of bed are very important in prevention septic-related complications, mainly ventilator-associated pneumonia. However the adherence of these measures is rare in the ICU setting, according many studies

METHODS. The period of the study was from June to September 2002. We made an audit about the position of the bed (three times a day, by the same physician) and we audited hand-washing opportunities (everyday, during one month, by chance for 2 hours and by a doctor with experience in hospital infection and hand-washing techniques). The audited staff, did not know the study, at any moment

RESULTS. We created 301 opportunities to audit the semi-recumbent position in 30 patients during 3 months and 100 opportunities to audit hand-washing.
In 80% of the opportunities, the beds were not in the correct position (= or > 45°) and 56% of opportunities, the staff did not wash their hands or washed it on a incorrect way

CONCLUSION. One very important point in controlling infectious acquired complications in ICU is the adherence to notorious measures. Two of these measures, audited in our study, are not put in practice in our ICU, although all staff was trained and has the knowledge of their importance. The unbalance between knowledge and awareness represents a challenge and was attacked, in our case, with more train, motivation campaigns and self-evaluation tests.
It is important that each ICU audits your practice, because, sometimes, the reality could be disagreeable

042

PREVENTION OF EYE DISEASE IN INTENSIVE CARE - A TELEPHONE SURVEY

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INTRODUCTION. Eye disorders such as corneal abrasion are common in intensive care(ITU)with a reported incidence of 40%(1) and can lead to bacterial infection (keratitis)with permanent loss of vision. Despite this awareness of preventative measures is poor with wide variation in standards of eye care(2).This study aimed to examine current practice of eye care and prevention of eye disease in ITU.

METHODS. A telephone survey was performed in which a single researcher spoke to a sister/senior staff nurse in 30 different intensive care units in England regarding eye care as performed in their ITU.

RESULTS. Estimated frequency of eye care varied from 2 hourly to daily. Only 23 out of 30 responders were aware of their ITU having an eye care policy. In 7 of 30 cases there was no policy or a senior staff nurse was unaware of the policy.12 out of 30 responders could recall serious recent eye problems with in at least 1 case permanent loss of vision. Despite this most responders felt eye disorders in ITU to be uncommon.

Perceived incidence of eye disorders in ITU

Perceived incidence	**Very common**	**Common**	**Uncommon**	**Rare**	**Don`t know**
Number	1	2	20	4	3

Eye disorders felt to be uncommon in ITU

CONCLUSION. Eye disorders remain common in ITU.40% of nurses could recall recent severe eye disease in their patients. Introduction of simple eye care algorithms has been shown to dramatically reduce incidence of eye disease(3).Despite this many units still have no eye care policy and awareness of eye disorders remains poor.While this continues preventable eye disorders will continue to occur frequently.

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Oral Presentations
Post-operative circulation – 043-045

043

LOW CENTRAL VENOUS SATURATION PREDICTS POST-OPERATIVE MORTALITY

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INTRODUCTION. Central venous oxygen saturation ($ScvO_2$) has proved a valuable resuscitation end-point in early sepsis. However there is little data regarding the use of $ScvO_2$ to guide resuscitation following high-risk surgery. We report the results of an observational study of post-operative variations in $ScvO_2$ and its relationship to outcome.

METHODS. Local research ethics approval was granted. $ScvO_2$ was recorded at baseline and hourly for eight hours. Data were not used to guide treatment. Various demographic and clinical data were recorded. Patients were followed up for 60 day in-hospital mortality.

RESULTS. Data was collected on 42 patients. The patients were divided into two groups: those in whom $ScvO_2$ fell below 65% for one hour and those in whom it did not. Outcome data are presented in table 1. Selected $ScvO_2$ data are presented in table 2. Data expressed as median (range) wherever appropriate.

	n	**Age**	**Morbidity**	**Mortality**
High $ScvO_2$	29	69 years (44-85)	0 (0-5)	2 (6.9%)
Low $ScvO_2$	13	67 years (55-80)	2 (0-6)	3 (23.1%)

Outcome data in high and low ScvO2 groups

	High $ScvO_2$	**Low $ScvO_2$**
Baseline	80% (65-91)	76% (47-84)
Hour one	79% (56-88)	63% (35-84)
Hour two	77% (63-90)	65% (54-88)
Hour three	76% (57-85)	64% (54-85)
Hour four	74% (61-89)	66% (56-85)
Hour six	78% (65-88)	69% (55-85)
Hour eight	75% (61-89)	70% (51-85)

ScvO2 variations in high and low ScvO2 groups

CONCLUSION. Morbidity and mortality in the low $ScvO_2$ group was much than the high $ScvO_2$ group. These data suggest post-operative $ScvO_2$ readings below 65% predict mortality in the high-risk surgical patient. Further work may demonstrate whether low $ScvO_2$ is a suitable goal for resuscitation in this group of patients.

044

THE USE OF THE NOVEL CALCIUM SENSITISER LEVOSIMENDAN IN POSTOPERATIVE ICU PATIENTS

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INTRODUCTION. Levosimendan (LS), a novel calcium sensitizer, improves cardiac performance and symptoms without increasing oxygen consumption, by stabilizing troponin C in a configuration that enhances the calcium sensitivity of cardiac myofilaments. We determined the haemodynamic effects of LS in postoperative ICU patients.

METHODS. Twelve postoperative patients (age 69± 9, mechanically ventilated and sedated n=10; diagnosis: cardiac surgery (n=9), lung transplantation (n=2), postoperative cardiopulmonary resuscitation (n=1). Patients were prospectively selected to receive LS, if haemodynamic data measured by a pulmonary artery catheter indicated a need for positive inotropic support. LS was administered either as an adjunctive inotropic therapy or as the only inotrope. One dose of LS (12,5mg) was infused at a rate of 0.1–0.2 mcg/kg/min. A pre-existing infusion with dobutamine or milrionon was remained constant or reduced if possible. A pre-existing infusion with epinephrine or norepinephrine was titrated to maintain a mean arterial pressure (MAP) of 65–85 mmHg. Cristalloids and colloids were administered to maintain a pulmonary capillary wedge pressure (PCWP) > 15 mmHg. Haemodynamic measurements were obtained at baseline, 3, 6, 12, and 24h after starting the LS infusion.

RESULTS. LS increased mean cardiac index (CI) from 2.3± 0.4 L×min-1×m-2 at baseline to 2.8±0.6 L×min-1×m-2 at 24 hours (p=0.015). The increase in CI was due to an increase in stroke volume from 47±15 ml to 57±25 ml (p=0.05), as heart rate remained stable during the study period. Systemic vascular resistance decreased from 1239±430 dyn×sec×cm-5 to 963±322 dyn×sec×cm-5 after 24h (p<0.001), which was paralleled by a fall in MAP, although this was not significant (p=0.09). The effect of LS on pulmonary vascular resistance (PVR) was less pronounced (PVR at baseline 281±112 dyn×sec×cm-5, after 24h 217±99 dyn×sec×cm-5, p=0.09.). Central venous pressure and PCWP remained within a narrow during the study. The total dose of epinephrine and norepinephrine (0.33±0.39 mcg×kg-1×min-1 to 0.30±0.37 mcg×kg-1×min-1) did not change significantly.

CONCLUSION. This study demonstrates that LS exerts favourable haemodynamic responses in postoperative critically ill patients. As LS exhibits its effects via a CAMP independent mechanism, its combination with inotropes acting via the cAMP pathway might be of special value.

045

NURSE-LED, HAEMODYNAMIC MANAGEMENT SHORTENS HOSPITAL STAY IN CARDIAC SURGERY PATIENTS

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INTRODUCTION. Polonen et al (1) demonstrated that 8 hours of post-cardiac surgical haemodynamic optimisation targeting SvO2>70% and lactate <2mmol/l reduced morbidity and shortened hospital stay. We sought to determine whether a nurse-led, protocolised approach to circulatory management using Doppler cardiac monitoring would produce similar results.

METHODS. 174 cardiac surgical patients were randomly assigned to receive either standard post-op management, or a protocolised (fluid+/-dilators+/-inotropes) approach targeting optimal filling (Starling curve) and a stroke index>35ml/M2 (2) for the first 4 hours utilising oesophageal Doppler monitoring (Cardio Q, Deltex, Chichester, UK) patient care thereafter was identical. Haemodynamic variables and outcomes (ICU and hospital stay) were recorded. Statistical analyses by intention to treat utilised 2 sample t- tests and Wilcoxon rank-sum tests, as appropriate (Stata 7.0)

RESULTS. The groups were well matched demographically, by risk and by type of operation. Four protocol and two control patients died. In the 4 hour period, protocol patients received more colloid than the control patients (mean[SD]), 1667[464] vs 1042[620]ml, p<0.001. changes in stroke volume and cardiac output were also significantly higher in the protocol group (p<0.001) Table shows length of stay (median days, IQR)

Length of stay

Outcome	Control (85)	Protocol (89)	p-value
ICU stay	2 (2-3)	2 (2-2)	0.21
Hospital stay	9 (7-12)	7(7-10)	0.02

CONCLUSION. Protocolised nurse-led haemodynamic management using minimally invasive cardiac output monitoring for the first four hours after cardiac surgery produced a non-significant reduction in ICU stay (28% saving in bed days) in addition to a significant reduction in hospital stay (16% saving in bed days). Our results support the concept of peri-operative circulatory optimisation.

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Grant acknowledgement: Deltex Medical, Chichester, provided an unrestricted educational grant

Oral Presentations
Paediatrics (I) – 046-048

046

CARDIAC TROPONIN T (CTNT) IN PAEDIATRIC INTENSIVE CARE UNIT (PICU) INFANTS

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INTRODUCTION. cTnT, a highly sensitive and specific marker of myocardial injury, is raised in sick neonates. cTnT is detectable even in healthy neonates shortly after birth. However, little is known about cTnT in infants, healthy or critically ill, outside of the neonatal period.
Objective: We investigated cTnT levels in infants (with a non-cardiac diagnosis) under 1 year old, in healthy control babies (referred for outpatient phlebotomy) and those admitted to PICU.

METHODS. A third generation cTnT assay was used (lower limit of detection of 10pg/mL). Statistical analysis used non-parametric tests.

RESULTS. Values are median (interquartile ranges). 35 PICU infants and 12 controls were recruited, ages were 1.5(0.1-5.5) and 3.8(2.4-6.3) months. PICU infants had higher cTnT levels compared with controls 18(10-56)pg/mL versus 10(10-12)pg/mL, p=0.024. There was no correlation between volume of resuscitation fluids (p = 0.244), nor requirement for inotropes (p=0.347), and cTnT levels in the PICU infants.
26 PICU patients had paired samples collected, on admission to PICU, 10(10-74)pg/mL, and 24 hours later, 10(10-44)pg/mL. cTnT levels were not different from each other, p=0.196.
Medical admissions were combinations of sepsis and/or respiratory tract infections. Surgical admissions were mainly correctable anomalies such as tracheo-oesophageal fistulae and diaphragmatic hernias. Surgical PICU admissions (n=15) were younger than medical (n=20) admissions, 2(1-4.5) days versus 4.8(1.5-6.5) months, p<0.001. cTnT was raised in more surgical infants (9/15) than medical cases (7/20), 39(10-92) versus 10(10-35)pg/mL, but not significantly so, p=0.158.

CONCLUSION. Controls had normal levels of cTnT. Many PICU admissions had elevated levels, predominantly surgical infants, who were much younger. Surgical infants are probably best matched to neonatal controls, in whom we have found elevated levels of cTnT, 26(10-62)pg/mL. It is possible these elevations in surgical infants were secondary to perinatal stress factors rather than their surgical diagnosis.
Grant acknowledgement: Royal Liverpool Children's Hospital Endowment Fund

047

THE PERIVENTRICULAR HAEMORRHAGE IN PRETERMS WITH RESPIRATORY FAILURE: ERYTHROCYTE MEMBRANES STATE

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INTRODUCTION. One of the neonatal principal problem is Periventricular/interventricular haemorrhage (PVH/IVH) in preterm newborns. It is proved that hypoxia may be the cause of structural-functional state of erythrocyte membrane disturbance. We studied the state of erythrocyte membrane lipid bylayer in 34 preterms with respiratory distress-syndrome required intensive care. 11 of them developed PVH/IVH.

METHODS. The structural-functional state of erythrocyte membranes lipid bylayer has been studied has been studied during early neonatal period. Erythrocyte membrane were isolated from blood by modified Dodge method. Membrane physic-chemical state was studied using fluorescent probe pyren and estimated by exymerization coefficient (Kex)of pyren.

RESULTS. PVH/IVH grade 3-4 were diagnosed by cranial ultrasonography, performed within the first 7 days of life. The investigation of lipofilic probe pyren fluorescence showed significant difference of Kex in cord blood of children with PVH/IVH and those without this pathology (0.895vs 0.660, respectively, p<0.01). Pyren Kex correlated with blood pH data in the neonates having developed PVH during the 1st postnatal week (r=0.675, p<0.01).

CONCLUSION. The increase of eximerization coefficient may be the early prognostic criterion of PVH grade 3-4 development. The hypothesis of changed erythrocyte membrane lipid bylayer state in the PVH pathogenesis is discussed.

048

CARDIAC TROPONIN T LEVELS IN CHILDREN WITH SEVERE RESPIRATORY SYNCYTIAL VIRUS LUNG DISEASE.

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INTRODUCTION. Previous case reports have documented arrhythmias and myocardial dysfunction in infants with respiratory syncytial virus (RSV) bronchiolitis (1). Cardiac specific Troponin T (cTnT)is a sensitive and specific marker of cardiac myocyte injury (2). In our study cTnT level measurements were used to determine the prevalence of myocardial involvement in infants with severe RSV disease. We compared patient characteristics and outcome in children with and without myocardial involvement.

METHODS. We conducted a prospective observational cohort study of infants with RSV infection admitted to the paediatric intensive care unit. Data collected comprised of age, gestational age at birth, Paediatric Index of Mortality (PIM) score, history of chronic lung disease, congenital heart disease, history of neonatal intensive care, duration of ventilation, inotrope use and its duration, death, cTnT levels, ECG- and echocardiographic findings. cTnT levels were measured with a third generation immunoassay (Roche Diagnostics Ltd). cTnT levels were considered to be elevated if >10pg/ml.

RESULTS. 34 children were included in our study. 12 (35%) had elevated cTnT levels. The levels measured after admission had a median (IQR) of 50 pg/ml (37.5 – 67.5). The initial increase in cTnT levels decreased to undetectable levels at a median of 4 days after admission. There was no significant difference (p>0.05) between patients with and without elevated cTnT levels with regards to the characteristics studied except for the following: Children with elevated cTnT levels [median (IQR) age: 1.4 months (0.8-2.0)] were significantly younger (p=0.04) than children without [median (IQR) age: 4.0 months (1.7-6.6)]. The PIM score was significantly higher (p=0.02) in children with elevated cTnT levels. This was due to the systolic blood pressure on admission being lower in infants with increased cTnT compared to those with undetectable cTnT.

CONCLUSION. Myocardial involvement is common in infants with severe RSV lung disease without congenital heart disease. cTnT level elevation was associated with hypotension without persistent reduction in myocardial function.

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Oral Presentations
Physiotherapy – 049-053

049

CARDIAC FUNCTION DURING INTRAPULMONARY PERCUSSIVE VENTILATION PHYSIOTHERAPY IN SEPTIC PATIENTS

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INTRODUCTION. Intrapulmonary percussive ventilation physiotherapy (IPV-P) has been shown to facilitate clearance of bronchial secretions in a wide variety of pulmonary diseases. The technique is also increasingly used for respiratory treatment in the ICU. Whereas IPV-P beneficially affects lung function in the critically ill, its cardiac effects remain largely uninvestigated. We therefore studied the evolution of different relevant echocardiographic parameters obtained during IPV-P sessions in a cohort of septic patients.

METHODS. Resuscitated haemodynamically stable mechanically ventilated patients eligible for pulmonary physiotherapy were subjected to a 30 min session of IPV-P delivered by the BIRD IPV-2 Percussionnair. Ventilator settings, including PEEP and FiO2 were kept constant during the procedure. Transoesophageal echocardiography was performed using a multiplane probe on the Philips SONOS 5500 at baseline (t0) and after 10 (t10) and 40 (t40) minutes (i.e. before, during and after IPV-P). Images and flows were obtained using a standardised procedure and stored for off line analysis. Arterial blood gas samples were taken at the same time points.

RESULTS. 20 patients were studied. At baseline, two groups could be distinguished: patients with normal left ventricular (LV) function [(average fractional area change of the LV (FACLV) = 0.36 + 0.16 ; group A (n=10)] and patients with a decreased LV function [(average FACLV = 0.15 + 0.06 ; group B (n=10)]. In group A, contractility decreased at t10 (average FACLV = 0.30 + 0.15; p = 0.05), returning to normal at t40. IPV-P did not influence FACLV in group B. End diastolic and end systolic LV area, right ventricular FAC, E and A wave amplitudes, E/A ratio and deceleration time at the level of the mitral valve, and amplitudes of S and D waves at the level of the left upper pulmonary vein did not change significantly during or after IPV-P in both groups. PaO increased ($p < 0.02$) during IPV-P in group A.

CONCLUSION. IPV-P has no clinically significant detrimental effects on cardiac function in haemodynamically stable septic patients regardless whether their heart function is normal or not. A slight and transient decrease in left ventricular function along with significantly enhanced oxygenation is observed only in those septic patients with preserved LV function. IPV-P causes no further deterioration of existing sepsis-induced compromised LV function.

050

THE COMPARATIVE EFFECT OF HELIUM-OXYGEN AND EXTERNAL PEEP IN MECHANICALLY VENTILATED COPD PATIENTS

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INTRODUCTION. The aim of the study is to compare the effect of helium-oxygen mixture inhalation and external PEEP on respiratory mechanics and gas exchange in mechanically ventilated COPD patients.

METHODS. Ten COPD patients were intubated, paralysed and mechanically ventilated. They were studied in the following conditions: T.1 : 30 min after air/O2 mixture inhalation with ZEEP ; T2 : 30 min after Helium-oxygen mixture inhalation with ZEEP ; T.3 = T1 ; T4 : 30 min after air/O2 inhalation mixture with PEEP 80% of PEEPi. Respiratory mechanics, haemodynamics and gas exchange were measured at the end of each ventilatory mode.

RESULTS. PEEPi and trapped gas volume were comparably reduced by helium-oxygen mixture (4.2 +/-4 vs 7.7+/-4 cm H2O and 98+/-82 vs 217+/-124 ml, respectively, $p<0.001$) and PEEPe (4.4+/-1.3 vs 7.8+/-3.6 cmH2O and 120+/-107 vs 216+/-115 ml, respectively, $p<0.001$). Helium-oxygen mixture reduced inspiratory and expiratory system resistance (15.5+/-4.4 vs 20.7+/-6.9 and 19+/-9 vs 28.8+/-15 cm H2O.l-1.s respectively, $p<0.01$) and peak airway pressure (23.5+/-8 vs 29.9+/-9 cmH2O, $p<0.03$). PaO2/FiO2 was slightly reduced by helium-oxygen mixture (T.1: 245+/-82 ; T.2 : 225+/-83 ; T.3 : 238+/-67 ; T.4 : 252+/-68).

CONCLUSION. Helium-oxygen mixture and PEEPe comparably reduced PEEPi and trapped gas volume. However, Helium-oxygen mixture decreased airway resistance and intrathoracic pressures. Helium-oxygen mixture represents an attractive option in COPD patients with severe PEEPi.

051

OPTIMAL EXPIRATORY TRIGGER SETTING DURING PRESSURE SUPPORT VENTILATION

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INTRODUCTION. During PS, transition from inspiration to expiration („cycling“) occurs when inspiratory flow (V'insp) decreases to a predetermined fraction of peak inspiratory flow (V'peak), the V'insp/V'peak ratio being termed „expiratory trigger“ (ETS). ETS, which is a fixed value (usually 0.25) in most mechanical ventilators, is now adjustable on some machines, within a range of 0.05 to 0.9. Theoretically, ETS depends mainly on respiratory system mechanics and the duration of inspiratory effort (ti). The goal of this study was to determine the ideal value of ETS in various conditions of respiratory system mechanics obtained in both normal volunteers rendered „obstructive“ with an external resistance on non-invasive ventilation and mechanically ventilated ICU patients.

METHODS. a) normal volunteers breathing through an external resistance, undergoing face mask pressure support (PS 10 and 25 cmH2O); b) intubated ICU patients ventilated with pressure support. Measurements: duration of inspiratory effort by external diaphragmatic electromyography, respiratory system time constant (RC), V'insp/V'peak at the end of ti.

RESULTS. V'insp/V'peak (Median and 25-75%)

	median	25%	75%
Normal volunteers with external resistance	0.650	0.525	0.730
Intubated ICU patients	0.840	0.765	0.940

$p < 0.0001$ Intubated ICU patients vs. volunteers

CONCLUSION. The ideal value of ETS during pressure support, in the conditions of this study, were higher than those available in current mechanical ventilators. Further evaluation of ideal ETS cut off values in larger series of patients, as well as in other conditions of respiratory mechanics and inspiratory effort, are warranted to help determine the optimal range of ETS setting possibilities.

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052

A REVIEW OF THE EXISTING ICU REHABILITATION WITHIN THE UK

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INTRODUCTION. Increasing numbers of patients are surviving their stay on Intensive Care (ICU). However, they are presenting with symptoms such as generalised muscle weakness and loss of balance following critical illness, and this is no longer thought to be due to bed rest alone. Physiological changes occur as a direct consequence of critical illness and ICU stay. This study explores the current service provision of rehabilitation within the ICU setting, throughout the UK. It reveals the outcome measures currently in use, and looks at physiotherapists experience and perception of follow up services for ICU patients.

METHODS. A questionnaire survey was carried out on Senior I physiotherapists working on ICU's in 36 teaching /large district general hospitals throughout the UK. It comprised of 13 questions that collected both qualitative and quantitative data. Analysis of the data was descriptive.

RESULTS. Only 38% of staff questioned work full time on ICU, however 100% of staff offer rehabilitation. 97% offer passive movements and 100% offer musculoskeletal assessment and an exercise regime. Only 21% of physiotherapists use outcome measures. 93% felt there was a role for physiotherapists in an ICU follow up service. 90% have experienced or foresee difficulties in running such a service, the main difficulty being staff shortages.

CONCLUSION. Rehabilitation is happening on ICU's throughout the UK. There is a need for the development of outcome measures for use in ICU, so that practice can be evaluated. More research into the effects of rehabilitation on this particular diverse patient group is needed. Physiotherapists need to be involved in the setting up and delivery of follow up services.

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BLOOD FLOW VELOCITY OF THE FEMORAL VEIN WITH FOOT EXCERCISE COMPARED TO PNEUMATIC FOOT COMPRESSION

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INTRODUCTION. Deep-vein thrombosis (DVT) is a major factor of pulmonary embolism. To increase blood flow in the deep veins is thought to be important to decrease the incidence of DVT1). In this study, we compared the effects of the pneumatic foot compression (A-V Impulse SystemTM, Novamedix, Andovor, England) and foot exercise on the blood flow velocity of the femoral vein.

METHODS. Twenty patients with bed rest in the ICU without any cardiac disease who had undergone gastrectomy, colectomy, pancreaticoduodenectomy and nephrectomy were divided into two groups; Group A, the pneumatic foot compression (A-V Impulse SystemTM) (n=10); and Group C, the foot exercise (n=10). The foot exercise was done once by a nurse for 5 min with the dorsoplantar flexion of the foot. The foot compression device worked continuously for two hours. We measured the peak blood flow velocity of the femoral vein using the ultrasound unit with 7.5 MHz linear array probe (ALOKA SSD-5500TM, ALOKA, Tokyo, Japan) at 0, 5, 15, 30, 60 and 120 min after starting the pneumatic foot compression using the A-V Impulse SystemTM or after the foot exercise.

RESULTS. Data were expressed as mean +/- SD. There was no significant difference in the peak blood flow velocity at 0 min (control value) between the two groups (Group A, 7.6+/-1.5; Group C, 7.3+/-2.0 cm/min). The peak blood flow velocities in both groups increased significantly than the control values. At 5 min, Group C showed significant increase in the peak blood flow velocity than the Group A.

% Change	**0 min**	**5 min**	**15 min**	**30 min**	**60 min**	**120 min**
Group A	100	113+/-11.4*	119+/-21.0*	111+/-18.8*	119+/-23.7*	120+/-29.6*
Group C	100	135+/-29.8*,*	119+/-22.0*	128+/-22.3*	131+/-15.4*	128+/-22.8*

**P<0.05 vs control value, *P<0.05 vs Group A*

CONCLUSION. Five min foot exercise by a nurse might be more effective than the pneumatic foot compression to increase peak blood flow velocity of the femoral vein for 2 hours.

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